Nurse-led detection of adverse events following cardiac admissions and procedures in a regional Australian health district

Mr Trent Daniel Williams BA Nursing. University of Newcastle 2001

Graduate Certificate in acute care/cardiology: NSW College of Nursing 2006

Certificate IV Risk Management: NSW TAFE 2005

A thesis submitted in fulfilment of the requirements for the degree of
Doctor of Philosophy (Nursing)
School of Nursing and Midwifery
Faculty of Health and Medicine
University of Newcastle, Australia

28th March 2019

This research was supported by an
Australian Government Research Training Program (RTP) Scholarship

Statement of Originality

I hereby certify that the work embodied in the thesis is my own work, conducted under normal supervision. The thesis contains no material which has been accepted, or is being examined, for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made. I give consent to the final version of my thesis being made available worldwide when deposited in the University's Digital Repository, subject to the provisions of the Copyright Act 1968 and any approved embargo.

Trent Williams

"TRADITONAL THESIS CONTAINING PUBLISHED WORK"

ACKNOWLEDGMENT OF AUTHORSHIP

I hereby certify that the work embodied in this thesis contains published paper/s/scholarly work of which I am a joint author. I have included as part of the thesis a written declaration endorsed in writing by my supervisor, attesting to my contribution to the joint publication/s/scholarly work.

By signing below I confirm that Trent Williams contributed: Design and conceiving of data collection tool*;* Designing and maintaining of research register*;* Collection of data*;* Carrying out data cleaning*;* Performance of data analysis*;* Devising the research concept*;* Preparing majority of the manuscript*;* Submitting the manuscript - *to the paper/ publication entitled "Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting"*. **Williams T**, Savage L, Whitehead N, Orvad H, Cummins C, Faddy S, Fletcher P, Boyle A, Inder K. International Journal of Cardiology: Heart & Vasculature. 22 (2019) 177-180. https://doi.org/10.1016/j.ijcha.2019.02.013 (Chapter 2: Appendix A)

And Trent Williams' contributed: Designing and maintain complications register; Collection of all data for both complications and control group; Carrying out data cleaning; Devising the research concept; Preparing all sections of the manuscript; Submitting the manuscript to "*Femoral vascular complications following cardiac catheterisation*. **Williams T**, Khan A, Savage L, Condon J, Boyle A, Collins N, Inder K." British Journal of Cardiac Nursing 2018 Vol 13, No 12. https://doi.org/10.12968/bjca.2018.13.12.593 (Chapter 3: Appendix B).

And Trent Williams contributed: Designing and maintain complications register; Collection of all data for both complications and control group; Clinical training and supervision, Carrying out data cleaning; Devising the research concept; Preparing all sections of the manuscript, submission of manuscript. **Williams T**, Davies A, Khan A, Ferreira D, Savage L, Inder K, Boyle A, Collins N. "*A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction"*. Under review. International Journal of Nursing Practice; Submitted March 2019 (Chapter 4)

And Trent Williams contributed: Successful recipient of grant to fund the research, devising the research question, clinical training and supervision, formulation of data collection tool, data cleaning analysing research, preparing all sections of the manuscript, submitting the manuscript. **Williams T**, Condon J, Davies A, Brown J, Matheson L, Warner T, Savage L, Boyle A, Collins N, Inder K. *Nursing led ultrasound to aid in trans-radial access in cardiac catheterisation; A feasibility study*. Journal of Research in Nursing; submitted 3rd June 2018, revised and resubmitted 4th February 2019, Accepted April 2019 (Chapter 5)

And Trent Williams contributed: Devised research question, co-ordination of project, clinical training and supervision, formulation of data collection tool, clinical liaison with statisticians, preparing large sections of the manuscript. Whitehead N, **Williams T**, Breinesse S, Ferreira D, Murray N, Inder K, Beautement S, Spratt N, Boyle A, Collins N. *Contemporary Trends in Stroke complicating Cardiac Catheterisation.* Accepted Internal Medicine Journal. Accepted April 2019 doi: 10.1111/imj.14405. [Epub ahead of print] (Chapter 6).

Associate Professor Kerry Inder
Signature of supervisor_____

Co-supervisor written declaration

By signing below we confirm that Trent Williams contributed to the study design, ethical approval, data collection and management, data analysis and interpretation, and writing of the publications / manuscripts entitled:

Publications

1) **Williams T**, Savage L, Whitehead N, Orvad H, Cummins C, Faddy S, Fletcher P, Boyle A, Inder K. *Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting*. International Journal of Cardiology: Heart & Vasculature. 22 (2019) 177-180. https://doi.org/10.1016/j.ijcha.2019.02.013 (Chapter 2: Appendix A)
2) **Williams T**, Khan A, Savage L, Condon J, Boyle A, Collins N, Inder K. *Femoral vascular complications following cardiac catheterisation*. British Journal of Cardiac Nursing 2018 Vol 13, No 12. https://doi.org/10.12968/bjca.2018.13.12.593 (Chapter 3: Appendix B)
3) **Williams T**, Condon J, Davies A, Brown J, Matheson L, Warner T, Savage L, Boyle A, Collins N, Inder K. *Nursing led ultrasound to aid in trans-radial access in cardiac catheterisation; A feasibility study*. Journal of Research in Nursing; submitted 3rd June 2018, revised and resubmitted 4th February 2019, Accepted April 2019 (Chapter 5)
4) Whitehead N, **Williams T**, Breinesse S, Ferreira D, Holder C, Murray N, Inder K, Beautement S, Spratt N, Boyle A, Collins N. *Contemporary Trends in Stroke complicating Cardiac Catheterisation*. Accepted Internal Medicine Journal. Accepted April 2019 doi: 10.1111/imj.14405. [Epub ahead of print] (Chapter 6).

Manuscripts under review

1) **Williams T**, Davies A, Khan A, Ferreira D, Savage L, Inder K, Boyle A, Collins N. *A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction*. Under review. International Journal of Nursing Practice; Submitted March 2019 (Chapter 4)

Trent Williams: Student no.: 9806725

Trent Williams collaborated with his fellow authors from Hunter New England Local Health District and the University of Newcastle to undertake this work.

Signature of Supervisors

Dr Kerry J Inder
Associate Professor of Nursing
School of Nursing and Midwifery

Date: March 2019

Mr Lindsay Savage
Cardiac Liaison Manager
Hunter New England Health district

Date: March 2019

Dr Nick Collins
Cardiologist,
Cardiovascular Medicine
John Hunter Hospital
New Lambton

Date: March 2019

Dr Andrew J Boyle
Professor of Cardiovascular Medicine
University of Newcastle

Date: March 2019

Professor Liz Sullivan
Assistant Dean Research Training
Faculty of Health and Medicine
University of Newcastle

Date

Invited conference presentations resulting from this thesis

1. **2018**- Invited Oral presentation: A review of adverse events after Cardiac Catheterisation: A nursing led approach. Australia and New Zealand Endovascular Therapies Meeting. Brisbane, August 2018.
2. **2018**- Invited Oral presentation: A nursing led examination of radial artery complications: A pilot study. Australia and New Zealand Endovascular Therapies meeting. Brisbane. August 2018.
3. **2017**- Invited Oral Presentation- Invited Speaker: Monitoring Door to Balloon times and adverse outcomes: A nursing perspective. Australia and New Zealand Endovascular Therapies Meeting. Perth, August 2018.

Grants and Awards associated with this thesis

2018: A Boyle, P Fletcher, J French, I Savage, J Attia, J Leitch, K Inder, **T Williams**, D McIvor, H Orvad, C Loten. **Management of Rural Acute Coronary Syndrome (MORACS).** Aim: To improve identification and management of patients with ACS in rural hospitals across 3 LHDs by implementing a hub and spoke ACS management system. TRIGS Grant NSW Health: $600,000.

2016: T Williams, K Inder, A Boyle. A prospective systematic examination of radial artery occlusion, injury and complication post cardiac catheterisation: A nursing led review of procedural complications. The 2016 Hunter Medical Research Institute (HMRI) BRICs (Building Research and Interprofessional Collaborations) Nursing Research and Innovation Grant: $5000.

Peer reviewed abstracts for oral and poster presentations at scientific meetings arising from this thesis

1. Savage L. Whitehead N. Stewart P. **Williams T**. 2017 Missed Acute Myocardial Infarction (MAMI) Heart, Lung and Circulation 26:S87.
2. Khan AA, **Williams T**, Ezad S, Ekmejian A, Boyle A, Collins N. 2017 Unchanged Femoral Complication Rate in the Radial Era: Ten-Year Experience. Heart, Lung and Circulation.
3. Khan AA, **Williams T**, Savage L. Boyle A. 2016 Pre-hospital thrombolysis in ST-segment elevation myocardial infarction: a regional Australian experience real world long term follow up. Journal of the American College of Cardiology.
4. **Williams T**, Inder K, Savage L, Collins N. 2016 Risk Factor Profile of Patients Sustaining Femoral Vascular Complications in a Tertiary Referral Cardiac Catheterisation Laboratory. Heart, Lung and Circulation 25(2):S301-S302.
5. **Williams T**. Fletcher P. Stewart, P. Faddy, S. Savage, L. 2014; PM211 Pre Hospital Thrombolysis. Mar 2014- An Examination of Clinical Outcomes. Heart, Lung and Circulation.
6. **Williams T.** Savage L. Inder K. Collins N. 2014 Impact of Change to Vascular Access Route on Patient Outcomes for PCI Following Thrombolysis for AMI. Global Heart, 9 (1), S e334.
7. **Williams T**, Savage L, Inder K, Collins N. 2014 PW368 Impact Of Change To Vascular Access Route On Patient Outcomes For PCI Following Thrombolysis For Ami. 2014. Vol 9.
8. Savage L, Stewart P, Whitehead N, Faddy S, Orvad H, **Williams T**. 2017. Missed Acute Myocardial Infarction (MAMI). Vol 26.

Associated publications during PhD candidature

1. Ezad, S, **Williams T**, Condon, J. Boyle A, Collins, A. Common Themes in Patients requiring Urgent Cardiothoracic Surgery after Percutaneous Coronary Interventions: Case Series and Review of the Literature. Cardiovascular Revascularization Medicine, 2018. March. https://doi.org/10.1016/j.carrev.2018.03.017
2. Khan AA, **Williams T**, Savage L, Stewart P, Faddy S, Ashraf A, Davies AJ, Attia J, Oldmeadow C, Bhagwandeen R, Fletcher P and Boyle AJ. Pre-hospital thrombolysis in ST-segment elevation myocardial infarction: a regional Australian experience Medical Journal of Australia. 2016;205:121-125. https://doi.org/10.5694/mja15.01336
3. Ezad S, Davies A, Cheema H, **Williams T**, Leitch J. Keys to achieving target first medical contact to balloon times; bypassing emergency department more important than distance. Cardiology Research and Practice 2018 1-5. https://doi.org/10.1155/2018/2951860

Abbreviations

ACS- Acute Coronary Syndrome

ACT- Activated Clotting Time

AF- Atrial Fibrillation

AIHW- Australian Institute of Health and Welfare

BARC- Bleeding Academic Research Consortium measure

BMI- Body Mass Index

BP- Blood Pressure

BSA- Body Surface Area

CABG- Coronary Artery Bypass Graft

CCL- Cardiac Catheterisation Laboratory

CHD- Coronary Heart Disease

CIN- Contrast Induced Nephropathy

CT- Computerised Tomography

CVD- Cardio Vascular Disease

D2B- Door to Balloon

D2N- Door to Needle time

ECG- Electrocardiogram

FA- Femoral Artery

FACEM- Fellow Australasian College of Emergency Medicine

FVC- Femoral Vascular Complication

HDL- High Density Lipoprotein

HNE- Hunter New England Health

HTN- Hypertension

IABP- Intra- Aortic Balloon Pump

IDDM- Insulin Dependant Diabetes Mellitus

JHH- John Hunter Hospital

LDL- Low Density Lipoprotein

LHD- Local Health District

LOS- Length of Stay

MAMI- Missed Acute Myocardial Infarction

MACE- Major Averse Cardiac Event

mRS- Modified Rankin Score

MI- Myocardial Infarction

NACE- Net Adverse Cardiac Event

NIDDM- Non Insulin Dependant Diabetes Mellitus

NSW- New South Wales

PCI- Percutaneous Coronary Intervention

PVD- Peripheral Vascular Disease

RA- Radial Artery

RAO- Radial Artery Occlusion

RCT- Randomised Control Trial

STEMI- ST Segment Myocardial Infarction

TAVI- Trans Aortic Valve Implantation

TIA- Trans Ischaemic Attack

TRA- Trans- Radial Access

VCD-Vascular Closure Device

WHO- World Health Organisation

YLL- Years Life Lost

Acknowledgements

I would like to sincerely thank the people who have helped, contributed, and supported me in completing this thesis. I sincerely could not have done it without you all.

Thank you to my supervisors, your passion for your work is inspiring. Associate Professor Kerry Inder, a trail blazer for local cardiac nursing academics. Kerry laid a path so that others who follow her have it easier. She guided me, supported, and challenged me to be the best I could be, no higher praise can be given. Kerry is the first to congratulate and the last to criticise. Thank you so very much Kerry. To Lindsay Savage, an amazing cardiac systems pioneer within our district and state. He has mentored me for a long period of time over copious amounts of coffee and has had a great vision for nurses. Lindsay's love of cardiology, friendship and nursing development has left a lasting impression on me. Thank you dearly hatchett, enjoy retirement! Professor Andrew Boyle, who has provided no end of support, passion and guidance. His vision and knowledge of cardiology is amazing and has shown what mastery of a profession looks like, how to support all of your colleagues, and provide leadership. He has truly transformed research in our area and has been a constant champion for getting nurses to lead research, thank you so very much Andrew. Associate Professor Nick Collins, his support of those who can never do anything for him is the true mark of this fine person. His skill as a cardiologist, researcher, and human being make him the ultimate leader. He has shown me that hard work, raising others up, and loving your job is true success. I owe most of my

professional accomplishments to him and have never met a finer role model. Nick, you make others around you better.

Thankyou most sincerely to the nursing staff of John Hunter Hospital Cardiac Catheterisation Lab. I truly am very proud to work in such a great area. The staff are a wonderful, kind, caring group of professionals who inspire me each day to pursue excellence, utilising the CORE values. Your support of your most nerdy of colleagues is appreciated. In particular, to Deb Bick for your unwavering and constant support, thankyou dearly Deb your support has been truly incredible. To Jen Brown, Lucinda Matheson, Tom Warner, Brooke Ikinofo, Brooke Keeble, Kath Dodd and to my great mate Jeremy Condon. Thank you for your friendship, guidance, support, humour, and for being amazing nurses. I would also like to thank and acknowledge the support of Marie o Donnell and Amanda Turrell, this work does not happen without the foresight, vision, and acceptance from senior management of nurses who undertake this work to improve nursing outcomes, thankyou to you both for your wonderful, genuine support.

Thank you to Professor Peter Fletcher, Dr Bruce Bastian, Dr Greg Bellamy and Dr Jim Leitch, who have shown nursing staff a great deal of support and guidance to foster a great department. I am in awe of your careers and how you have managed to build such a fine department. Thanks to Rohan Bhagwandeen, your support has been incredible, I cannot begin to thankyou enough for the faith you have shown me. I would also like to say thankyou to Associate Professor Aaron Sverdlov and Associate Professor Doan Ngo, your kindness, professionalism and your desire to

improve the health of people in Newcastle is nothing short of inspiring, thankyou for taking this interventional nurse “under your wing” Thank you to Dr Allan Davies, Dr Michael McGee, Dr Mohammed Al- Omary, Dr Arshad Khan and Dr Nick Whitehead, I can’t wait to see you become leaders in Cardiology long into the future.

To my family, Mum who has sacrificed her whole life for us and continues to be an amazing support in every way to my family. Mum instilled in us to never give up and to work hard always. You are just amazing mum. To my wonderful mother and father in law- Leigh and Karen whose support for our family has made this so much easier, we could not have done this without you. Thanks to my brother Mark and his wife Jenny- two ultimate achievers who have shown what being nice and humble is all about. Thanks to my sister Megan for continuing to be a great sister. And a big thankyou to my wife’s 98 year old grandfather Lionel- whose life motto of “he who thinks he can… can” has enabled me to persevere with this. His encouragement has been invaluable.

To my amazing wife Vanessa, thank you for making me laugh, your belief in me, and most importantly thank you for being my best friend, soulmate and wife. I love ya clarky! Thanks for your unwavering support and love, and most importantly introducing me to #JFDI. I could not have done this without you by my side. I can’t wait to be a “normal” married couple soon. To my two little mates, my beautiful boys Hamish and Ben, your smiles light up my life each day. You are my pride and joy, and easily my greatest achievement. I become prouder of you each day…. Dad’s weekends are now yours and he can’t wait.

Lastly and most importantly I want to dedicate this work to two people;

Ms Nicole Condon who passed away during this thesis. Nicole was a kind, dedicated nurse whose grace and lovely smile light up a room. She was the personification of beauty, bravery, kindness, a deep love of her family and friends, and fun!! The perfect combination for a nurse.

My father, who passed away during its production. The most honest, hardworking, kind gentleman that I have known. He was, and always will be the greatest influence on my life. He was simply the best man I have known…This one is for you dad!

Trent Williams

Abstract

Background: Heart disease is the number one cause of death in the world. Heart disease results in a significant number of hospitalisations, diagnostic testing, and requires ongoing access to health services to manage this complex disease process. Adverse events associated with treatment for heart disease have significant immediate and long term effects on patients, caregivers, service providers, and result in increased burden on the health system.

Aim: This thesis aimed to investigate adverse events during hospitalisation for heart disease in a large, diverse, regional health district, in particular in the major tertiary referral centre.

Methods: This thesis explores the relevance of individual factors, treatment factors, and organisational factors to the occurrence of adverse events in people hospitalised predominantly for acute coronary syndromes. Routine clinical data collection and data linkage systems were developed by the Candidate to facilitate this research.

Results: The thesis comprises five individual, interlinking studies: *Study 1* “Missed acute myocardial infarction (MAMI) in a rural and regional setting” describes factors associated with missed diagnosis of acute myocardial infarction in a regional setting. *Study 2* “Femoral vascular complications following cardiac catheterisation” aimed to determine the predictors of femoral access vascular complications in patients

following cardiac catheterisation or percutaneous coronary interventions. *Study 3 "*A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction" describes the change in practice from femoral artery access to trans-radial artery access in primary percutaneous coronary intervention. *Study 4* "Nursing led ultrasound to aid in trans-radial access in cardiac catheterisation" examined the feasibility of setting up a nurse led approach to identify radial artery complications. *Study 5 "*Contemporary trends in stroke complicating cardiac catheterisation" determines the causes and outcomes of a post cardiac procedural stroke.

Conclusion: This program of research emphasises the role specialised nurses have in monitoring adverse events, improving care and promoting patient safety. This research provides valuable information to inform clinicians for translation to other hospital systems to improve health outcomes for people hospitalised with heart disease.

Table of Contents

List of Tables

List of Figures

Chapter 1

Introduction

This chapter will outline the health service examined and the studies performed as part of this thesis to identify adverse events following cardiac admissions and procedures in a regional Australian health district. To set the scene, an overview of the incidence and prevalence of coronary heart disease (CHD) in Australia and worldwide, the risk factors for the development of CHD and the clinical manifestations of heart disease, including the diagnosis of myocardial infarction will be provided. This background information is important due to the role of invasive assessment in the diagnosis and treatment of CHD and the potential impact on patient outcomes. This review will explore adverse events associated with a cardiology admission to hospital, including the missed diagnosis of myocardial infarction, femoral vascular complications, radial occlusion post cardiac catheterisation, post procedural stroke and common complications that a cardiac patient may experience during an admission to hospital. While the incidence of complications and adverse health outcomes are relatively infrequent, these events carry significant morbidity and risk of mortality.

1.1 Thesis outline

1.1.1 Study Setting

The centre where the studies were undertaken as part of this thesis is a large regional health district located in New South Wales, Australia. The Hunter New England Local Health District services a population of 950,000 people and covers a geographical area of 131,785 square kilometres, see Figure 1.1. This area covers major cities, inner regional, outer regional and remote populations. Each year the district records approximately 15,000 chest pain presentations across 37 hospitals. These hospitals range from small nurse led hospitals, general practitioner hospitals, general physician led hospitals, through to the tertiary referral centre and teaching hospital, the John Hunter Hospital, which consists of 700 beds and is staffed by senior cardiology staff (Marsden et al., 2010, Williams et al., 2016)

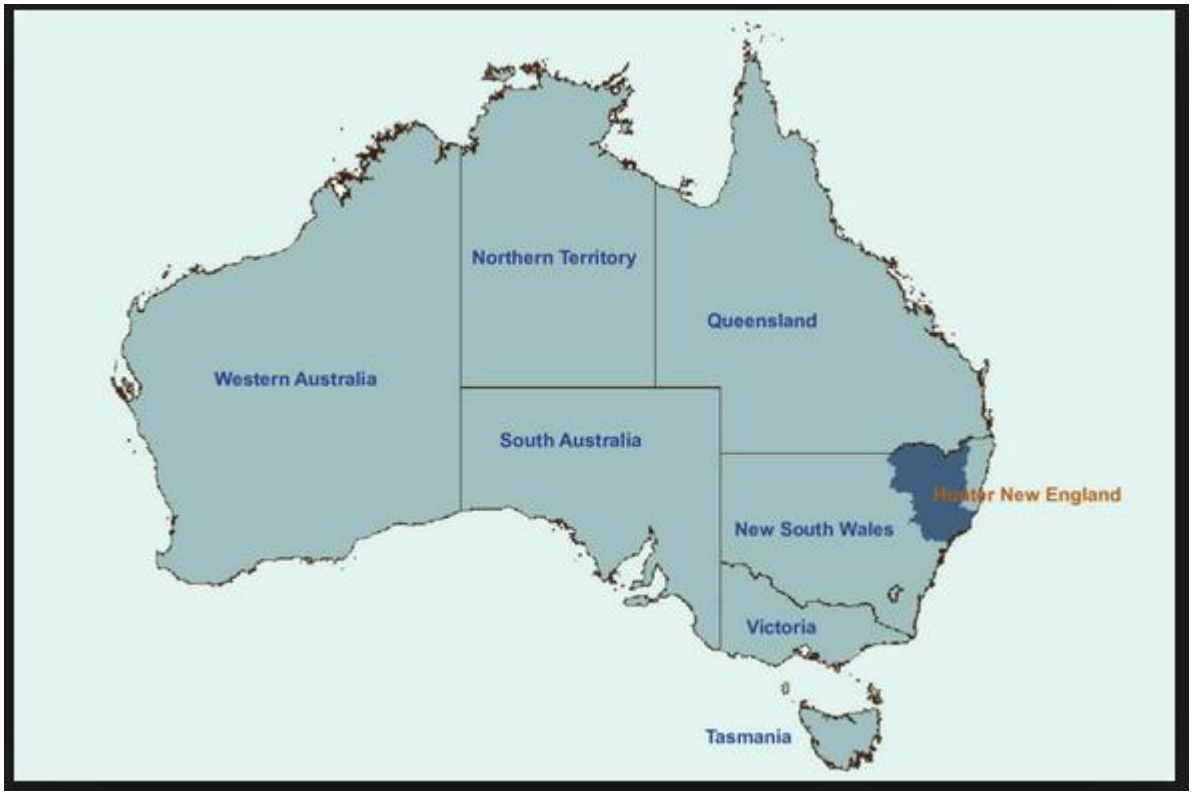


Figure 1.1: Hunter New England Health District: A large health service on the east coast of Australia

The John Hunter Hospital (JHH) cardiac catheterisation laboratory performs approximately 2,000 coronary angiograms and percutaneous coronary interventions each year. The laboratory is staffed by senior interventional cardiologists, fellow interventionalists and cardiology advanced trainees. The JHH cardiac catheterisation service has a large referral base extending to the major part of the east coast of NSW. The JHH catheterisation laboratory performs all major interventional procedures, including diagnostic cardiac catheterisation, percutaneous coronary intervention (PCI), primary PCI, and has an emerging structural disease programme. In line with global trends, the predominant arterial access method for cardiac catheterisation and PCI is via trans-radial access. The health service examined has

implemented and pioneered many of the state's reperfusion programmes and has a long standing record of system development and refinement (Mears et al., 2010, Khan et al., 2016).

The health service has its own independent clinical governance unit, which ensures adherence to the current policies and procedures of its governing body New South Wales (NSW) Health. Under this risk management structure all facilities are required to notify and manage all clinical adverse events within the service (Clinical Excellence CommissionAustralian, 2014). This policy requires a consistent and co-ordinated approach to the identification, notification, investigation, and analysis of incidents resulting in clinically appropriate intervention (Clincial Excellence CommissionAustralian, 2014). In addition, relevant current clinical guidelines outline the importance of systematic review and detection of adverse events (Levine et al., 2016, Neumann et al., 2018, Naidu et al., 2016). This thesis allows the incorporation of these polices and guidelines into clinical practice to provide meaningful research that aims to improve and inform patient care.

Given the complex nature of hospital care, and the high risk factor burden in people with CHD, adverse events may occur (Rafter et al., 2014). While the incidence of adverse events is small, the effect of adverse events for cardiology is significant, particularly in terms of the physical and psychological impact on patients and the cost to the health system. Determining the causative factors of these potentially catastrophic adverse events and establishing a method to monitor and predict

adverse events is crucial to inform policy development and improve clinical practice (Rafter et al., 2014). Greater awareness of risk factors for adverse events will lead to better management of patients at increased risk of adverse event after an admission to hospital with a cardiac diagnosis. Data generated from this thesis relies on innovative methods of clinical data collection across a diversely equipped health district. These methods of research are new to this health service. This will lead to better management of patients at increased risk of adverse events after an admission to hospital with a cardiac diagnosis.

1.1.2 Introduction to studies

This thesis is composed of an introduction, five individual manuscripts, and a final concluding chapter that discusses the conclusions of this body of research, the positive contributions this thesis has already generated, and potential future directions for research.

The overall aims of this thesis are to examine complications and health outcomes associated with a cardiology admission to a large regional health district, and to develop a nurse-led system of monitoring to identify and manage adverse events over a large geographical area. A synopsis of this thesis is as follows:

The introduction (Chapter 1) describes the burden of heart disease and places it in a local and international context. It summarises the risk factors for cardiac disease, investigations for diagnosis, current treatment methods, and differing clinical presentations. The introduction progresses to detail the occurrence of adverse events associated with an admission to hospital for treatment and investigation of heart disease from a clinical, procedural and organisational standpoint.

Study one (Chapter 2), “Missed acute myocardial infarction (MAMI) in a rural and regional setting” describes factors associated with missed diagnosis of acute myocardial infarction in a regional setting. The aim was to identify any differences in clinical characteristics between patients who had a myocardial infarction successfully treated, and those that had a missed diagnosis of myocardial infarction. Outcomes including length of hospital stay, 30-day readmission rates and mortality were assessed. This first study was implemented to provide a research framework with a focus on data linkage to identify adverse outcomes, in particular the missed diagnosis of myocardial infarction. Major findings from this work were that patients who had a missed diagnosis of myocardial infarction had a three-fold higher mortality rate than the treated infarct mortality rate, a 20% increased length of stay, and eight times the readmission rate compared to the treated myocardial infarction group. Anterior infarction was the most represented infarction type of those that were missed. This study identified an increased burden of missed myocardial infarction in rural and regional areas with a heightened mortality rate compared to metropolitan patients.

Study 2 (Chapter 3), “Femoral vascular complications following cardiac catheterisation” aimed to determine the predictors of femoral access vascular complications in patients following cardiac catheterisation or percutaneous coronary interventions. For this research a femoral vascular complication (FVC) is defined as a pseudoaneurysm or retroperitoneal haemorrhage. Factors that increased the odds of FVC were female gender, smoking, diabetes mellitus, hypertension, anticoagulant medication, elevated body mass index, and use of vascular closure devices. The described burden and impacts of femoral complications around the world facilitated further study into the impact that an alternative method of arterial access (trans-radial access) could have on improved patient outcomes and the reduction of adverse events. This led to Study 3.

Study 3 (Chapter 4), “A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction” describes the change in practice from femoral artery access to trans-radial artery access in primary PCI for the treatment of ST-segment elevation myocardial infarction (STEMI), on patient outcomes. Primary endpoints were death, stroke and myocardial infarction and secondary endpoints were length of hospital stay, 28 day readmission, 28 day survival and long term mortality. This study describes the outcomes of this transition period from femoral arterial access to trans-radial access in this high risk STEMI cohort, which may be particularly important for other institutions contemplating this change. This study showed benefits in time parameters, transfusions, and vascular complications in the trans-radial group.

Study 4 (Chapter 5), “Nursing led ultrasound to aid in trans-radial access in cardiac catheterisation: A feasibility study” builds on the previous study given the positive benefits of trans-radial access. This study sought to determine what complications occur in the trans-radial access group. This study focused on identification of radial artery occlusion, in a consecutive patient cohort after cardiac catheterisation. It aimed to examine a nursing led model of predicting radial artery occlusion using ultrasound guided radial artery diameter measurements. This study, the first of its kind within the literature utilising nursing led ultrasound showed a 4% rate of occlusion observed immediately following compression band removal. This work showed that an increased time of haemostasis device application was associated with radial artery occlusion. Male gender and height were predictors for a larger radial artery diameter. This study showed that trained specialist cardiac nurses can safely lead the assessment of radial arteries within a cardiac catheterisation laboratory to enhance planning and care. With the emergence of radial access throughout the world, this study can be replicated in any cardiac catheterisation centre to aid in nursing led research and improve patient outcomes.

Study 5 (Chapter 6), “Contemporary trends in stroke complicating cardiac catheterisation”. This thesis concluded by determining the causes and outcomes of a post procedural stroke, a devastating disease process with significant adverse long term health outcomes for patients. This study built on the research framework to examine the rate of stroke and trans ischaemic attack (TIA) for patients undergoing cardiac catheterisation, and determine if a post procedural stroke increases the risk of future stroke and death compared to a non-procedural related stroke. The study

evaluated the contemporary incidence of stroke following cardiac catheterisation over a ten-year period and assesses the long-term influence of stroke on outcome. Using a case control design, patients were identified by correlating cardiac catheterisation with neuroimaging to identify cases of suspected stroke. In a large patient group of 21,510 patients undergoing cardiac catheterisation during the study period, 60 patients (0.28%) experienced cerebral ischemia. Stroke incidence remained stable over the study period despite changes in procedural practice. Stroke complicating cardiac catheterisation was associated with an increased risk of readmission and a significant risk of early and cumulative mortality.

The discussion chapter (Chapter 7) synthesises this body of work. The immediate translation of this research into clinical practice is outlined, describing the improvements in clinical practice that have occurred. Chapter 7 outlines the contribution this thesis makes to cardiovascular nursing care and outlines potential areas for further research.

In summary, this approach enabled the research aims and objectives for the thesis, and each individual study to be met. This thesis has generated significant new knowledge and innovative methods of informing research and practice. This nurse led investigation into health outcomes in cardiology patients enables significant enhancement of the nursing role through investigation of clinical outcomes.

1.2 Background of the Researcher

My nursing journey commenced with graduating with a Bachelor of Nursing from the University of Newcastle in 2001. I completed my new graduate year at Gosford Hospital in 2002, then completed a transitional programme at Maitland Hospital. I am now a Clinical Nurse Consultant in Cardiology at John Hunter Hospital. This programme of research was undertaken while working full time in a senior role, with significant on call commitments.

Early in my professional life I moved to John Hunter Hospital, to the Coronary Care unit and the cardiac catheterisation laboratory in 2003. During this time I undertook studies in risk management and a graduate certificate in Cardiology. Fortunately I was offered the newly formed position of clinical risk manager in cardiology. This position enabled me to co-ordinate cardiology adverse events for the district under the guidance of an incredible leader Professor of Cardiology, Peter Fletcher. This role enabled me to establish the Hunter New England Health STEMI database and play an active role in system development and monitoring of the STEMI systems within the district. During this time I developed a keen interest in the causative factors of adverse events, and the design and implementation of registers to guide practice and system monitoring. All the data systems that are the basis of each of the manuscripts were designed, instigated, and implemented by me. I have been an invited speaker on cardiology risk management, cardiology system monitoring, and STEMI management. The basis of this thesis was to combine my three passions of

nursing and nursing development, system review, and cardiology to enhance care delivery to improve health outcomes.

1.3 Coronary Heart Disease

Coronary heart disease (CHD) is a disease of the blood vessels supplying the heart musculature (WHO, 2011). The clinical manifestations of CHD include stable angina, acute coronary syndromes (including unstable angina and myocardial infarction), heart failure, and sudden cardiac death (WHO, 2011). Coronary heart disease is typically caused by the process of atherosclerosis, reflecting the accumulation of cholesterol laden plaque in the coronary artery (Marshall, 2011).

1.3.1 Incidence, Prevalence, and Cost of Coronary Heart Disease

The World Health Organisation estimates that cardiovascular diseases account for 17.9 million deaths each year around the world (WHO, 2011). In Australia, there were 1.1 million hospitalisations for heart disease in 2015-16, which represents 11% of all hospitalisations nationally (AIHW, 2018). Heart disease accounts for 1 in 3 deaths in Australia each year, and is the leading cause of death in Australia (NSWHF, 2011). In addition, each year the cost of CHD within Australia is $5.9 billion. Nationally, rural populations are 20% more likely to have CHD compared to metropolitan populations (Brieger and Redfern, 2013). In the United States of America 735,000 citizens have a myocardial infarction, and 610,000 people die each year due to heart disease (Mozaffarian et al., 2015). Heart disease is the leading cause of death in the United States of America and accounts for 43.8% of total deaths each year (Benjamin et al., 2018). By 2035 total cost burden of heart disease in America is expected to be $1.1 trillion (Hibbert et al., 2012).

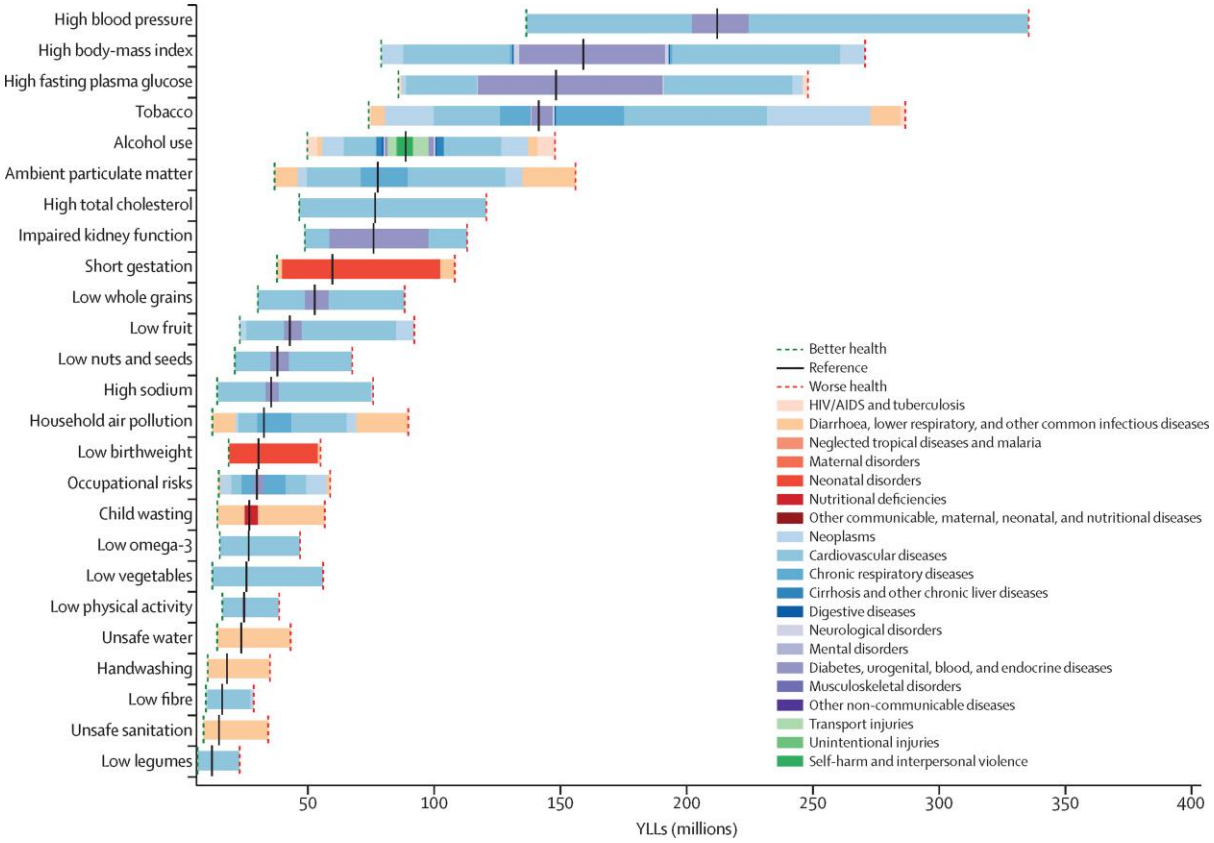
1.3.2 Risk Factors in the Development of Coronary Artery Disease

Globally the major risk factors for the development of CHD include modifiable and non-modifiable risk factors (WHO, 2011). Non modifiable risk factors include age, gender, and family history (WHO, 2011). Modifiable risk factors, include abnormal blood cholesterol levels, hypertension, and diabetes, plus behavioural risk factors including, smoking, obesity, and inactivity (WHO, 2011). Cardiac risk factors are forecast to be a challenge and cause of reduced life expectancy for the foreseeable future. In a large scale epidemiological study, 250 disease pathologies were modelled and subsequent cause groups of all major worldwide diseases demonstrating the interplay between risk factors and health outcomes (Foreman et al., 2018). This study is timely from a cardiac perspective as it quantified the leading 20 risk factors contributing to the projected worldwide difference in years of life lost (YLL) (Figure 1). This well constructed study across diverse patient group, shows the leading causes of CHD, will continue to be the leading international causes of reduced mortality till the year 2040 (Foreman et al., 2018).

Given the burden of heart disease, the literature on risk factors is significant. This discussion seeks to provide an overview of the examination into risk factors in the development of CHD, based on historical and contemporary reviews.

Increased age is an independent risk for CHD and a major contributor to mortality within this group (Avezum et al., 2005). This is reflected in the elderly comprising an

increased admission rate of hospitalisations for CHD. In a large registry study (n=24,165) of patients with CHD which aimed to document the prevalence of co-morbidity in elderly patients statistical analysis showed that older patients (age > 75 years) had a higher prevalence of previous myocardial infarction, diabetes mellitus, cardiac failure, previous coronary artery bypass surgery, history of chronic angina, hypertension and atrial fibrillation (Avezum et al., 2005).



Legend: *The differences between reference and better and worse health scenarios are grouped by Global Burden of Disease Study (GBD) Level 2 causes attributable to risks, colour coded to correspond with the causes contributing to the change in YLLs between scenarios for each risk factor. Black solid vertical lines represent all-cause attributable YLLs in the 2040 reference forecast, red dashed vertical lines represent all-cause attributable YLLs in the 2040 worse health scenario, and green dashed vertical lines all-cause attributable YLLs in the 2040 better health scenario. Traditional cardiac risk factors of smoking, obesity, diabetes and smoking are the major contributors to years of life lost*

Figure 1.2: The leading 20 risk factors contributing to years of life lost (YLL) between the 2040 forecast, 2040 better health scenario, and 2040 worse health scenario *(Foreman et al., 2018)*.

Gender has been described in the literature as an independent risk, with the male gender a risk factor for the development of CHD (Lloyd-Jones et al., 2018). In a major registry study which examined 7,733 patients as a part of the Framingham data group, 1,157 (15%) developed CHD. The authors further examined the lifetime risk of developing CHD at predefined ages of 40 and 70 years of age. The reported data is the chance over a lifetime of participants developing CHD which showed that at age 40 years there was 48.6% likelihood of males developing heart disease (95% CI 45.8–51.3), while for females there was a 31.7% likelihood (95% CI 29.2–34.2). At age 70 years, lifetime risk was 34.9% (95% CI 31.2–38.7) for men and 24.2% (95% CI 21.4–27.0) for women (Lloyd-Jones et al., 1999, Lloyd-Jones et al., 2018). The Framingham studied predominantly Anglo-Saxon populations in one country, the adaptability of findings to ethnic diverse populations should be guarded. It has long been the source of reliable data in particular long term risk of cardiac events and has contributed enormously to our knowledge of risk of heart disease related events (Albarqouni et al., 2019).

In America, the age-adjusted CVD death rate in men was 300 per 100,000 compared with 212 per 100,000 women. While the burden of heart disease is predominantly in males, in women aged 35 to 44 years of age, heart disease mortality rates have increased by 1.7% in the last decade (Mosca et al., 2011). While this data is registry data, this large dataset includes reliable mortality data which may guide future policy development.

Family history as a risk factor in the development of CHD was examined as part of the landmark Framingham study where a significant proportion of historical risk factor data is drawn (Myers et al., 1990). This large cohort study of 5,209 patients followed patients in the context of the cause of death of their parents. The primary hypothesis was to assess the effect of established risk factors in the setting of a family history of CHD. Data showed that a person who had a parent die from CHD was significantly more likely to develop CHD when compared to other previously defined risk factors (Odds Ratio (OR) 1.29, 95% CI 1.13-1.47), using logistic regression modelling. Participants who reported a positive family history were shown to have a 29% greater relative risk of developing CHD than participants without a family history of CHD. This study further demonstrated that of males considered low risk for developing CHD based on modifiable risk factors, having a strong family history was noted in those who subsequently developed CHD.

The genetic risk of developing heart disease and the extent to which it can be modified was examined in a prospective cohort study 51,425 patients (Khera et al., 2016). The relative risk of CHD events was 91% greater in those in a high genetic risk group compared to those whose family was unaffected by CHD (hazard ratio, 1.91; 95% CI, 1.75 to 2.09). This study further expanded on the potential for life style modification to reduce CHD events. Of patients with a higher genetic likelihood of developing CHD, a favourable lifestyle (defined by non-smoking, nil obesity, regular physical exercise and a healthy diet), was associated with a 46% lower risk of coronary events than an unhealthy lifestyle (hazard ratio, 0.54; 95% CI, 0.47 to 0.63) (Khera et al., 2016).

The role of cholesterol is an important discussion point in the development of CHD. Atherosclerosis development may occur as an inflammatory response that has resulted from injury to the walls of the artery caused by cholesterol and lipids deposits in arteries (Moser, 2008), in particular, the presence of low density lipoprotein (LDL) and high density lipoprotein (HDL). The Framingham study, illustrated that raised levels of LDL cholesterol has a significant role in the development of atherosclerosis and subsequent heart disease (Lloyd-Jones et al., 1999). In addition, higher levels of HDL have a clear inverse relationship. The treatment of choice for high cholesterol, has been statin therapy which has been demonstrated to reduce major adverse cardiovascular events for patients at risk of developing atherosclerotic cardiovascular disease (Tousoulis et al., 2016). In a large meta-analysis of 27 RCTs of 174,000 subjects, it was shown that for every 40mg/dl LDL reduction with statin therapy, the likelihood of cardiovascular events in patients with known high LDL was reduced by 25%. Additionally, the rate of major vascular events (heart disease, MI, strokes, and repeat coronary procedures) was also reduced during each year after the first dosage. Consequently, the reduction of LDL cholesterol of approximately 2mmol/L reduces the risk of developing vascular events by about 45%. Importantly, it should be noted that the risk benefit ratio may depend on the risk of the patient and the amount of LDL reduction that occurs (Collins et al., 2016).

The need for a wide ranging approach to the management of cholesterol and identification of at-risk cohorts was the subject of updated guidelines on cholesterol management. The 2018 guidelines enhanced the 2013 guidelines (Stone et al.,

2014) with a particular focus on the need for health professionals to address the cholesterol health burden with a more intensive approach (Grundy et al., 2018). The basis of the guidelines is analysis of large randomised controlled trial (RCT) data and consensus statements. (Eisen et al., 2016, Sabatine et al., 2017, Moriarty et al., 2016, Lloyd-Jones et al., 2018). These guidelines emphasise the importance of a multidisciplinary and a more personalised approach to lipid management across the life span and providing guidance on the emergence of non HMG-CoA reductase inhibitors (i.e. statins). These guidelines do not place a target range for LDL in the unaffected population, rather an emphasis on achieving the lowest possible LDL level (Grundy et al., 2018).

Hypertension is the single largest modifiable cause of cardiovascular disease, in addition to being the biggest cause of death around the world (Williams et al., 2018). Elevated blood pressure is an independent risk factor in the development of myocardial infarction, chronic kidney disease, stroke, and premature death (Gabb et al., 2016). Hypertension is defined as: stage 1 hypertension 130-139/ 80-89 mmHg and stage 2 hypertension >140 / >90 mmHg; based on more than 2 readings on two separate occasions (Whelton et al., 2018). Internationally, it is predicted that hypertension will be diagnosed in 1.5 billion people across the world (Williams et al., 2018). An important sub type of hypertension has historically been isolated systolic hypertension, which may affect up to 15% of the population over 60 years of age and is the major cardiovascular risk factor which can be modified (Staessen et al., 1998). Isolated systolic hypertension may indicate underlying significant organ damage or may be considered a secondary form of hypertension characterized by remodelled

and stiffened arterial walls (Scholze, 2010). The long term effects of hypertension on the vascular bed leads to remodelling of the inner lining of the artery producing an increase in medial thickness. This change results from hyperplasia of the connective tissue fibres in the inner aspects of the artery. It is believed that this functional change accounts for the association between hypertension and CHD (Camm et al., 2006).

Diabetes mellitus plays a large role in the development of CHD through the long-term effects that uncontrolled hyperglycaemia has on the microvasculature of the coronary arteries (Rawshani et al., 2017). The direct effect of poorly controlled diabetes and the establishment of adverse outcomes is now well established with several large landmark trials defining this link (Colhoun et al., 2004, Orchard et al., 2015, Gaede et al., 2003). CHD is the predominant cause of a reduced life expectancy in patients who have diabetes mellitus (Schnell 2005). Alarmingly fewer than 50% of adults diagnosed with diabetes currently meet the recommended treatment regime, which demonstrates the current immediate challenges and potential long term ramifications (Fox et al., 2015). The impact of diabetes on all-cause mortality in patients who present with an acute coronary syndrome was examined in the landmark “Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries” GUSTO-1 trial (Mak et al., 1997). Diabetes was shown to be an independent risk factor for higher mortality, when compared to non-diabetic patients. Mortality outcomes at 30 days were higher in Type 1 diabetics (12.5%) compared with non-insulin-treated diabetic (9.7%) and nondiabetic (6.2%) patients ($p< 0.001$). Interestingly, these poor outcomes were

reflected in one year mortality with diabetes being an independent predictor for mortality, (14.5% vs. 8.9%, p< 0.001) (Mak et al., 1997). Importantly this group predominantly received thrombolysis, and is a landmark historic trial that provided reliable clinical data for this period. These results have remained largely unchanged in the contemporary population illustrated in a large multicentre trial of patients presenting with STEMI, who underwent primary PCI and had long term follow up investigated (De Luca et al., 2013). The diabetic group had higher rates of death (19.1% vs. 7.4%; p< 0.0001), re-infarction (10.4% vs. 7.5%; p< 0.001), and stent thrombosis (7.6% vs. 4.8%; p= 0.002).

Smoking has long been considered a significant risk factor. The main cardiovascular effects of smoking includes an increase in heart rate, increase in blood pressure, activation of platelets resulting in an increasing tendency to thrombosis and an increase in the volume of vascular plaque. Smoking contributes significantly to increasing the inflammatory processes in the coronary artery wall and predisposes to the development of coronary thrombosis (Burke et al., 2017, Burke et al., 1997).

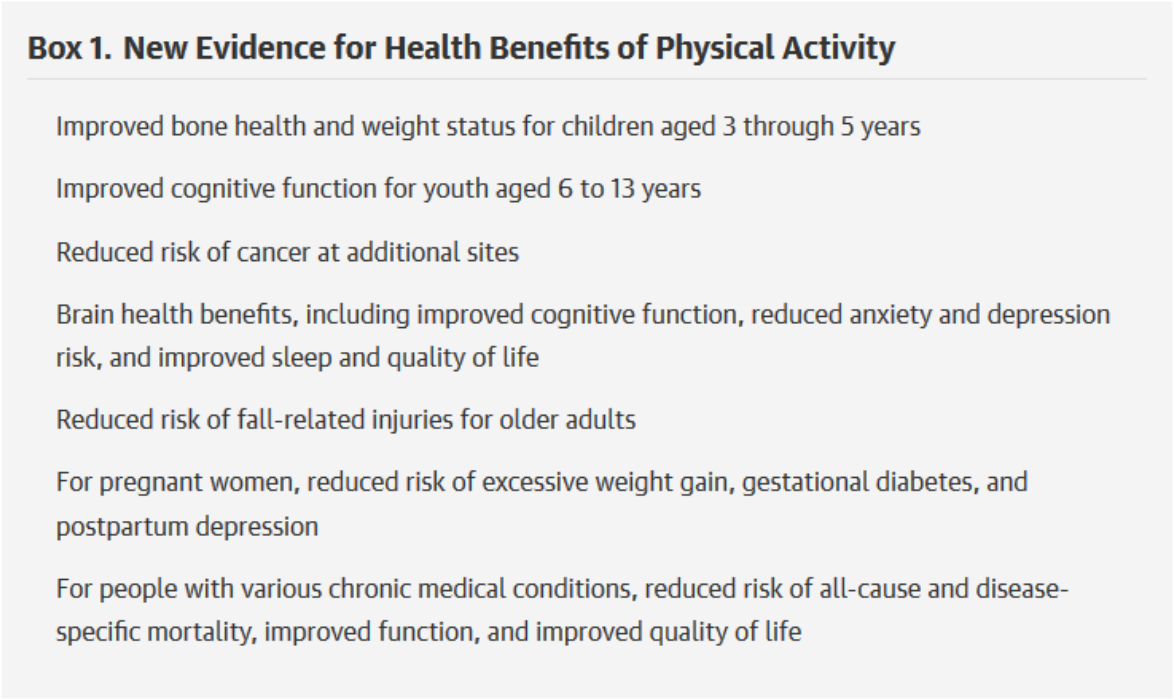
The success of public initiatives to quit smoking have led to reduced smoking prevalence internationally (Burke et al., 2017). In a large longitudinal study of 5401 patients taken from the Framingham heart offspring cohort, with a mean age of 36.1 years and 52% women there was a doubling of CHD risk in men who were smokers compared with non-smokers over 30 years of follow-up. Women who smoked had a 1.5 times greater likelihood of developing CHD than those participants who did not

smoke (Burke et al., 2017). Reinforcing the importance of health promotion, those patients who stop smoking showed a reduced incidence of CHD and subsequent reduction in morbidity and mortality outcomes (Reiner, 2018).

Obesity and inactivity, or sedentary lifestyle are independent risk factors in the development of CHD (Aronne et al., 2007). While previously thought to work in conjunction with other risk factors such as hypertension and diabetes, it is clear that central obesity is now considered an independent risk factor. Data from the Framingham study, which followed up 5,000 people over a 44 year period showed obesity to be an independent risk factor for CHD with a hazard ratio of 1.58 (95% CI 1.24- 2.03, $p<0.001$).

One of the landmark studies into the effect of exercise on the development of heart disease was the nurses' health study. This observational study examined the frequency, duration and intensity of exercise, and how exercise impacted on the diagnosis of CHD in 93,676 nurses. Those who walked for greater than 180 minutes per week had a multivariate reduced risk of CHD of 0.65 compared with those who did not exercise at all (Manson et al., 2003). This data provided significant information to public health providers, however comes with the important limitation of observational studies that the study group could not control for the development of these lifestyle factors (Nelson, 2000).

The positive effects of exercise above the recommend guidelines was also studied in a male only study of 35,402 healthy recreational joggers, for a period of 7.7 years. The recommended minimal exercise activity is 30 minutes per day. This noteworthy article demonstrated that for each kilometre (km) per day increment in running distance demonstrated a 5% risk reduction for nonfatal heart disease, a 7% risk reduction for nonfatal myocardial infarction, a 5% risk reduction for revascularization procedures, and a 10% risk reduction in angina. Compared to the 3km per day group, the 9km group showed a 65% reduction in reported angina ($p=0.008$), 29% lower risk of non-fatal CHD ($p=0.04$) and 26% lower risk for fatal and non-fatal CHD (Williams, 2009). Physical inactivity is shown to be responsible for a 9% increase in premature mortality (Lee et al., 2012). The burden of inactivity and its immediate long term adverse health outcomes, has resulted in revised activity guidelines by the American Heart Association (Piercy and Troiano, 2018) based on consensus statements and RCTs recommending 150 to 300 minutes per week of moderate exercise activity, in addition to muscle building activities, see Figure 2. The guidelines reported a 14% reduced risk of developing a CHD.



Box 1. New Evidence for Health Benefits of Physical Activity

Improved bone health and weight status for children aged 3 through 5 years

Improved cognitive function for youth aged 6 to 13 years

Reduced risk of cancer at additional sites

Brain health benefits, including improved cognitive function, reduced anxiety and depression risk, and improved sleep and quality of life

Reduced risk of fall-related injuries for older adults

For pregnant women, reduced risk of excessive weight gain, gestational diabetes, and postpartum depression

For people with various chronic medical conditions, reduced risk of all-cause and disease-specific mortality, improved function, and improved quality of life

Figure 1.3: The Physical Activity Guidelines for Americans (2018) shows new benefits of increased physical activity (Piercy and Troiano, 2018).

1.4 CHD Presentations

Angina occurs when there is a reduction of the lumen of the epicardial coronary arteries (Braunwald and Morrow, 2013). The most common type of angina which is considered a common manifestation of ischaemic heart disease, is stable angina. This occurs when there is an increased myocardial oxygen demand on the heart, typically during exertion, resulting in typical chest pain of variable duration (Braunwald and Morrow, 2013). Unstable angina is usually characterised by a change in the frequency, nature and intensity of chest pain resulting from progressive coronary insufficiency. Angina can occur at rest, and may be unrelieved by medical therapy (Peate, 2011).

Acute Coronary Syndrome is the result of unstable atheromatous plaques or endothelial disruption with associated transient or permanent thrombotic occlusion of the coronary vascular tree leading to myocardial ischaemia and infarction (Chew et al., 2016b). Each year in the United States of America there are approximately 780,000 presentations for acute coronary syndromes (ACS), while in Australia there are 68,000 ACS presentations each year. The correct clinical care and application of treatment pathways of patients presenting with ACS, including acute myocardial infarction is the subject of comprehensive and well described clinical guidelines nationally, and internationally (Roffi et al., 2016, Levine et al., 2016, Amsterdam et al., 2014). Timely access to evidence-based management of ST segment elevation myocardial infarction (STEMI) is imperative for optimal clinical outcomes.

The “4th Expert Consensus Document, on the Fourth Universal Definition of Myocardial Infarction (MI)” was recently updated, and the ongoing definition may be reflective of the evolving diagnosis and treatment modalities in particular high sensitivity Troponin (Thygesen et al., 2018, Chew et al., 2016b).

This definition for a myocardial infarction includes detection of a rise and/or fall of the biomarker Troponin, with at least one value above the 99th percentile in combination with one of the following:

- Symptoms of acute myocardial ischemia;
- New ischemic electrocardiographic (ECG) changes;
- Development of pathological Q waves;
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic aetiology;
- Identification of a coronary thrombus by angiography including intracoronary imaging or by autopsy (Thygesen et al., 2018).

The above conditions involve impaired blood flow to the heart and in order to determine the exact extent and severity of impaired blood flow, further investigation is undertaken to optimise therapy. Investigations to determine the presence of CHD include electrocardiography (ECG), exercise stress testing, including the adjunctive use of echocardiography or nuclear perfusion (for example sestamibi or thallium scanning) and cardiac catheterisation (Qaseem et al., 2012).

1.5 Diagnosis of CHD

A variety of diagnostic methods, both invasive and non-invasive can be utilised to diagnose CHD. Non-invasive methods of assessment of CHD remain of the utmost importance in the managements of patients with stable CAD including physical examination, electrocardiography and exercise stress testing, radioisotope perfusion imaging and echocardiography (Neumann et al., 2018).

Electrocardiography maybe the first diagnostic tool that is used to diagnose those patients with suspected heart disease by members of the interdisciplinary team (Sampson and McGrath, 2015). An ECG can provide clinical staff with a range of clinical data in addition to the quantification of the rate and rhythm of the heart. These include cardiac ischaemia, myocardial infarction, the size of heart chambers, congenital heart problems, the detection of electrical abnormalities, and heart failure (Sampson and McGrath, 2015). In addition, an ECG provides vital information to define non-cardiac diagnoses including respiratory illness, electrolyte imbalances and traumatic injuries (Van Mieghem et al., 2004).

The importance of the diagnostic utility of ECGs in the diagnosis of ischaemia is supported by the requirement by most guidelines that performance of ECGs should occur within 10 minutes of arrival to hospital (Levine et al., 2016, Steg et al., 2012, Chew et al., 2016b). The time sensitive approach that is often required for the management of chest pain and instigation of timely evidenced based treatment has

been shown to be a vital step in the management of the acute patient (Yiadom et al., 2017).

In addition to the ECG, more sophisticated, non-invasive diagnostic tests have emerged, such as coronary computerised tomography. The major invasive diagnostic tool to guide the management of CHD is the coronary angiogram/cardiac catheterisation and one of the subsequent available treatment modalities is percutaneous coronary intervention (PCI).

1.5.1 Cardiac Catheterisation

A cardiac catheterisation is defined as a “radiographic diagnostic study of the heart in which valves and vessels are examined via x–ray and fluoroscopy following the introduction of contrast media” (Lange and Hillis, 2003). Cardiac catheterisations are performed by accessing predominantly the radial and femoral artery; less common routes are the brachial and axillary arteries (Kern, 2011). Heart disease management guided by cardiac catheterisation is an accepted means to manage heart disease and its varied clinical presentations (Chew et al., 2016a).

In the United states of America it is estimated that one million cardiac catheterisations are performed each year (Slicker et al., 2016). The majority of these are performed on males with 48% performed in those over 63 years of age (Slicker et al., 2016). While in Australia during the period 2015/2016, 127,000 cardiac catheterisations were performed, and 41, 200 percutaneous coronary interventions (PCI) were performed with 66% performed on males (AIHW, 2018).

Indications for cardiac catheterisation are varied and reflect the diverse range of complex cardiac presentations. These include settings in which CHD is suspected or known such as new onset angina, unstable angina, evaluation of coronary anatomy before surgery, silent ischemia, positive exercise stress test, or atypical chest pain. Following myocardial infarction cardiac catheterisation is indicated for unstable angina post myocardial infarction, failed thrombolysis, shock, and mechanical

complications of infarction. Cardiac catheterisation is also indicated for survivors of sudden cardiac death, patients with valvular heart disease, heart disease, congenital heart disease, aortic dissection, pericardial tamponade, cardiomyopathy, and the initial and subsequent assessment of a heart transplant (Levine et al., 2016, Gibbons et al., 2003, Stout et al., Yancy et al., 2017).

1.5.2 Diagnosis of STEMI

The diagnosis and treatment of STEMI requires a time senstive approach and immediate reperfusion where indicated using one of two methods of reperfusion therapy - primary PCI and thrombolyis (Steg et al., 2012, O'Gara et al., 2013). Primary PCI has been the prefered method of reperfusion for the past decade, if delivered in a clinically appropriate time frame (Thomas and Bates, 2017). Given the tyranny of distance and the lack of availability of cardiac catheterisation laboratories, particularly in rural and regional areas, thrombolysis offers a safe and effective reperfusion strategy with similar outcomes to primary PCI (Khan et al., 2016) (Armstrong et al., 2013). The benefits of early instigation of reperfusion therapy were demonstrated by landmark work which is the basis for much of the reperfusion strategies developed (Gersh et al., 2005). This work developed a widely used graph which articulates, based on a hyopthetical curve, that during the first 120 to 180 minutes after symptom onset, a notable benefit of reperfusion therapy on mortality is demonstrated (Figure 1.3). Within this period, time to the instigation of evidence based treatment is critical. In addtion, a mortality benefit is still present but noticeablely decreases over time.

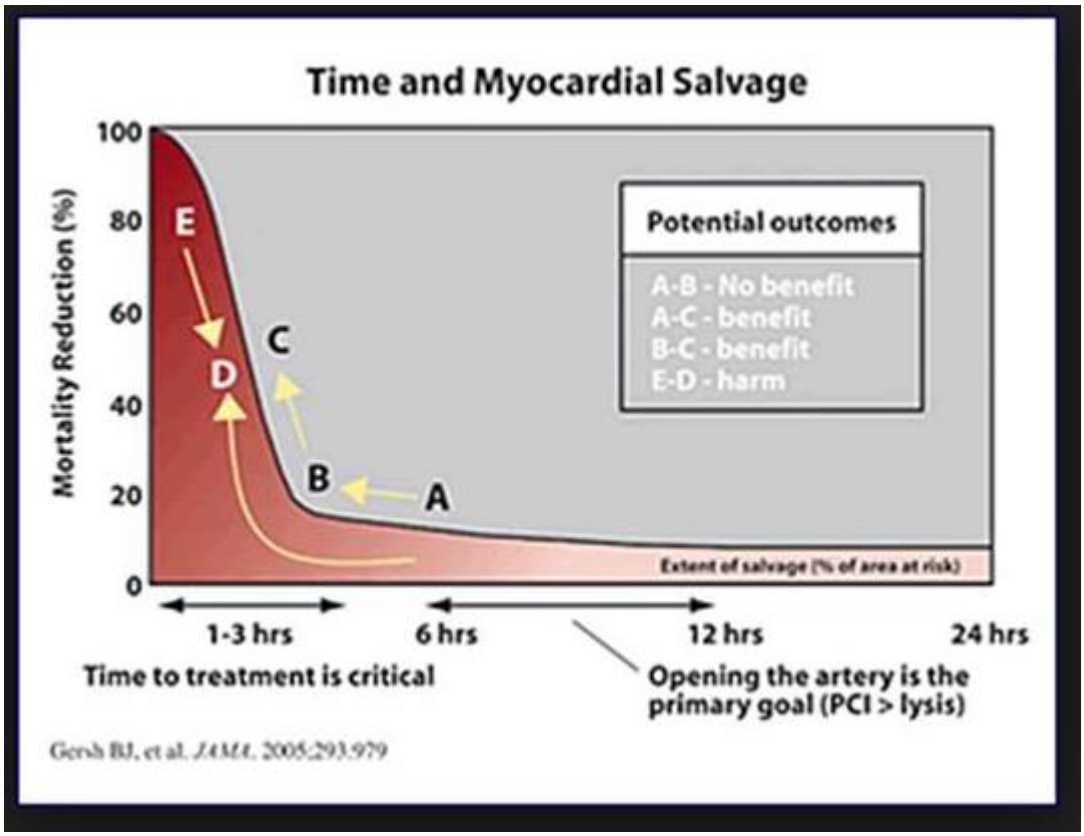


Figure 1.4 A hyopthetical curve which demonstrated the maximum mortality benefit of reperfusion occurs within the first 180 minutes of symptom onset time (Gersh et al., 2005).

Both methods of reperfusion have been shown to be effective. In a landmark study, the widely cited “Strategic Reperfusion Early after Myocardial Infarction (STREAM) study” 1,892 patients were enrolled prospectively and randomised to undergo Primary PCI or thrombolysis prior to tranpsort to a PCI centre (Armstrong et al., 2013). Importantly this study had an enrollment criteria of patients who presented within three hours of first symptom time and, who were not within one hour of a primary PCI cabable centre. The end point for this trial was a composite of death,

shock, congestive heart failure, or reinfarction at 30 days. The primary end point occurred in 116 of 939 patients (12.4%) in the fibrinolysis group and in 135 of 943 patients (14.3%) in the primary PCI group (relative risk in the fibrinolysis group, 0.86; 95% confidence interval, 0.68 to 1.09; p=0.21) (Armstrong et al., 2013). Important limitations of this trial, which come into consideration in large geographical areas, is that this trial did not take a “all comers approach”, late onset symptom patients were not included in the analysis. Therefore, defintive conclusions around treatment for delayed myocardial infarction presentations cannot be made from this study. In Australia, with a large geography those patients who live a large distance from a PCI capable hospital receive thrombolysis (Khan et al., 2016). However, standard practice has now further evolved to include a pharamco invasive strategy where thrombolysis is given and cardiac catheterisation performed within 24 hours, with reliance on pre-hospital interpretation of the ECG (Khan et al., 2016). This strategy is an effective strategy and has shown efficacy in immediate and long term patient outcomes (Sinnaeve et al., 2014) (Gershlick et al., 2005, Fernandez-Aviles et al., 2004, Danchin et al., 2014, Armstrong et al., 2013).

1.5.3 Systems of care in the diagnosis of ACS

The importance of system-based care in the recognition and management of ACS and STEMI, is well understood, this becomes of the upmost importance in regional centres where there is more generalised care (Steg et al., 2012). Internationally, clear guidelines exist to support and direct care for patients with ACS including

STEMI (Amsterdam et al., 2014, Ibanez et al., 2018, Chew et al., 2016b). The diagnosis of STEMI, according to the above guidelines includes;

- Clinical history of chest pain of more than 20 minutes
- ECG with persistent (20 minutes) of ST segment elevation in more than 2 contiguous leads (1.5mm in inferior leads) or the development of new onset left bundle branch pattern.
- Important additional factors include a history of CHD, and radiation of pain to the neck, lower jaw and arm, noting that women may frequently present with nausea/vomiting and fatigue (Ibanez et al., 2018).

Due to the challenges faced with regional cardiac care, electronic algorithms are now embedded in ECG machines within paramedic vehicles and hospital emergency departments (Tideman et al., 2014). These algorithms, supported by clinician oversight, have shown an accurate ability to instigate clinical care, via the first, crucial step of interpretation of STEMI among patients (Savage et al., 2014). The use of this software is now included in most ACS guidelines to guide systems of care, in addition to establishing clinical networks to govern care, and increasing the availability of specialised resources at point of care, particularly in non-metropolitan centres (Tideman et al., 2014). The use of these algorithms must be supported by a clinician interface, particularly in the setting of arrhythmia, bundle branch block, and ECG interference (Faour et al., 2017). Clinician interface between the paramedic and the physician has been demonstrated to be the most effective system of care which

will ultimately reduce false positive ECGs which can negatively impact the institution from a financial perspective (Khan et al., 2016).

1.5.4 Identification of High Risk patients

In a review paper predicting death after presentation of MI, the authors reviewed risk factors that place an individual at higher risk of mortality after presentation with STEMI (Castro-Dominguez et al., 2018).

Patient factors- include advancing age, female gender, diabetics, renal failure, heart failure on arrival and cardiogenic shock. Those with arrhythmia including ventricular tachycardia, ventricular fibrillation, and atrial fibrillation had a higher 30 day mortality than those with sinus rhythm (13% vs 2.2%, AOR 6.73, 95% CI 2.68-16.9) (Castro-Dominguez et al., 2018).

System factors- Various clinical system factors have been shown to have an effect on clinical outcomes. These include the number of cardiac patients a clinician sees, availability of cardiac facilities, rural hospitals and socioeconomic profile; all influence the outcome of a patient presenting with myocardial infarction (Castro-Dominguez et al., 2018). The importance of guideline-based care in myocardial infarction is now established. In a registry study of 147,429 patients five evidenced based AMI admission therapies which form the basis of all treatment guidelines embedded

within hospitals (aspirin, beta-blockers, acute reperfusion therapy, door-to-balloon [D2B] time ≤90 min, and time to fibrinolysis ≤30 min) were examined for their effect on mortality (Bucholz et al., 2016). Patients who received aspirin, beta-blockers, and acute reperfusion therapy on admission (either primary PCI or thrombolysis) had a higher life expectancy of 0.78 years (standard error [SE]: 0.05), 0.55 years (SE: 0.06), and 1.03 years (SE: 0.12), respectively, compared to those who did not. Timely reperfusion therapy for both primary PCI and thrombolysis were examined. Patients who received a primary PCI in less than 90 minutes lived 1.08 (SE: 0.49) years longer than patients with door to balloon (D2B; from arrival to hospital to inflation of catheter balloon) times greater than 90 minutes. Door-to-needle (D2N; from arrival to hospital to thrombolysis administration dose) times less than or equal to 30 minutes were associated with 0.55 (SE: 0.12) increased years of life expectancy compared to those with a D2N time of greater than 30 minutes (Bucholz et al., 2016).

Despite guidelines on the diagnosis and management of ACS and STEMI, the missed diagnosis of this disease process has been documented within Australia and around the world. The occurrence of STEMI patients not receiving standardised therapy is widely described in the literature and has been examined over a long period of time, with as much as 30% non-treatment (Farshid et al., 2016, Welsh et al., 2016). The reasons for this remain varied and multi factorial, however common themes included a higher preponderance of rural hospitals, diverse presentation symptomatology, clinical experience and organisational factors (Chew et al., 2013, Masoudi et al., 2006, Welsh et al., 2016, Tricomi et al., 2008, Farshid et al., 2016).

The impact of delay in treatment, particularly in STEMI and failure to provide evidenced based reperfusion therapy has been shown to double mortality, and may impact on morbidity outcomes (Farshid et al., 2016). Given the burden of CHD, in particular ACS, understanding this broad issue is timely and important.

1.6 Treatment of CHD

Controversy exists within the literature concerning the best treatment options available to a patient with a confirmed diagnosis of CHD. Medical therapy alone in addition to coronary artery bypass grafting (CABG) will be briefly discussed with a broader discussion on PCI due to the relevance to vascular access.

1.6.1 Medical therapy

Medical therapy or medical management includes the utilisation of antiplatelet agents, antianginal therapy, antihypertensive medication and dyslipidaemia management. This is in combination with cigarette smoking cessation, dietary improvements, diabetes control and exercise if applicable (Blumenthal et al., 2000). The acute management of CHD relies on the commencement, maintenance or dosage adjustments of those medications shown to be effective reducing in-hospital and out of hospital adverse cardiac events by 20 to 40% (Ganz and Hsue, 2009). These drug groups are 3-hydroxyl-3-methylglutaryl-coenzyme A reductase inhibitors

(statins), beta-blockers, angiotensin converting enzyme inhibitors, and antiplatelet agents.

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial was reviewed by Brown and Bittner (2007). The COURAGE trial was the first to examine if revascularisation of the coronary arteries performed in combination with medical therapy would reduce endpoints of death or myocardial infarction in patients with stable CHD. This large multicentre randomised controlled trial with 2,287 patients showed that after a mean follow up period of 4.6 years revascularisation performed in combination with intensive medical therapy had no impact in the reduction of mortality or myocardial infarction compared with standard medical therapy alone. While the COURAGE trial produced important data, the trial remains controversial due to stable CHD patients being included in the trial, in addition to unstable patients. However, this trial strongly suggests that patients who have stable CHD can be managed effectively in the initial stages of treatment with appropriate medical therapy.

Seven major studies were examined in this review to determine the overall benefit of PCI versus medical management (Brown and Bittner 2007). This literature review showed that medical therapy and PCI should be considered complimentary treatment options rather than being mutually exclusive treatment options. Currently not all patients receive optimal medical management to alter the atherosclerotic process however patients who have PCI would benefit from aggressive management

of their cardiovascular risk factors (Brown and Bittner 2007). In a large multicentre RCT of the treatment outcomes comparing optimal medical management to PCI, 1,149 patients were allocated to PCI *with* medical management and 1138 patients were allocated to medical management alone. The patient's long term outcomes were followed. Importantly, there were no noted differences between the PCI group and the medical-therapy group in the composite of death, myocardial infarction, and stroke (20.0% vs. 19.5%; hazard ratio, 1.05; 95% CI, 0.87 to 1.27; p=0.62). In this important study the results demonstrated optimal medical management was safe and effective treatment strategy in the treatment of stable CHD (Boden et al., 2007). This data was further supported in a meta-analysis of 7182 patients which demonstrated no significant improvement in mortality outcomes (risk ratio, 0.85; 95% CI, 0.71–1.01) and non-fatal myocardial infarction (risk ratio, 0.93; 95% CI, 0.70–1.24) at five year follow up. This review demonstrated, however, that angina symptoms showed a significant improvement in the PCI group compared to the optimal medical management group (RR, 1.20; 95% CI, 1.06–1.37) (Pursnani et al., 2012).

1.6.2 Coronary Artery Bypass Surgery

Coronary artery bypass surgery (CABG) as a means of revascularisation remains an available and frequently used treatment option. In Australia, CABG is the second most used method of revascularisation for CHD (Yan et al., 2011). In a review of historical revascularisation strategies for patients with stable multi-vessel coronary artery disease as well as patients with unprotected left main disease (Hahalis et al.,

2010). The results suggest that older patients, those with diabetes, those with extensive multi-vessel CHD, and those with significant ischemia and with poor left ventricular function may benefit most from CABG for revascularisation (Hahalis et al., 2010).

The SYNTAX trial is one of the landmark trial which compares CABG to PCI in those patients with three vessel disease, in addition to left main coronary stenosis. This multicentre trial, importantly reported on 5 year outcomes for 1800 patients randomly allocated to PCI or CABG (Mohr et al., 2013). The study's endpoints were major adverse cardiac and cerebrovascular events (MACCE) (defined as a composite of cardiovascular and cerebrovascular outcomes). Kaplan-Meier estimates of MACCE were 26.9% in the CABG group and 37.3% in the PCI group ($p<0.0001$). In patients that were deemed high risk defined by a syntax score (a scoring system that defines lesion complexity and predicts clinical health outcomes), MACCE was statistically significantly increased in the PCI group (26·8%vs 44·0%; $p<0·0001$). This trial provided robust evidence for first generation drug eluting stents which have undergone significant change since this trial (Mohr et al., 2013).

Contemporary data for patients with diabetes and significant CHD and the preferred method of revascularisation was reported in the FREEDOM follow on study (Farkouh et al., 2018). Participants were 1900 patients from 140 hospitals, 953 randomised to PCI vs 947 to CABG, with a follow up period of 8 years. In patients with diabetes and severe CHD, CABG was more favourable compared to PCI (18.7% vs 23.7%, HR

1.32, 95% CI 0.97-1.78, p=0.07) in the reduction of all-cause mortality. This data supports the continuation of the current recommendations for patients with diabetes and significant CHD to be offered CABG as the preferred method of revascularisation (Farkouh et al., 2018).

An examination of stroke rates, in CABG vs PCI was undertaken and followed up over a 10 year period (Moreyra et al., 2017). This study compared patients who had drug eluting stents (n=115,942), bare metal stents (n=46,641), on pump CABG (n=47,254) and off pump CABG (n=19,118). Cox proportional hazard models were used to compare the risk of stroke. Post PCI stroke was lowest in the drug eluting stents participants (0.5%), followed by bare metal stents (0.6%), off-pump CABG (1.3%), and on-pump CABG (1.8%). On examination of the CABG patient alone, on-pump CABG had the greatest risk of stroke compared with off-pump (OR 1.36, 95% CI 1.18 to 1.56, p<0.0001). Drug eluting stents had reduced risk of stroke compared with off-pump CABG (OR 0.64, 95% CI 0.55 to 0.74, p<0.0001) (Moreyra et al., 2017).

1.6.3 Percutaneous Coronary Intervention

One of the most widely used treatment modalities for CHD is percutaneous coronary intervention (PCI) which is currently the primary choice for invasive management of CHD internationally (Banning et al., 2015). PCI involves advancing a balloon tipped catheter to an area of coronary narrowing, inflating the balloon, and then removing the catheter following deflation (Torpy et al., 2004). The first PCI was performed by

Andreas Grüntzig, in 1977, he subsequently reported findings of the first patients to undergo this procedure (Grüntzig, 1978). The advent of PCI revolutionised the treatment of CHD, with a significantly less invasive approach to the management of CHD compared to CABG (Bates, 2016). The equipment, knowledge and medication management associated with PCI have undergone significant refinement and enhancement, which has resulted in improved patient outcomes (Yan et al., 2011). A "successful PCI produces a significant enlargement of the lumen at the target site" (Anderson et al., 2007). The performance of PCI is a very safe and effective procedure, with the small adverse event rate declining over the past 20 years (Hilliard et al., 2010). In a retrospective analysis over a 25 year period results of PCI were examined. The procedural success rates have improved each five year period (81%, 92%, 96%, and 97%, respectively, $p< 0.001$), and the overall in-hospital mortality has declined (1.0%, 0.8%, 0.1%, and 0.1%, $p< 0.001$) respectively during the study period. In a large cohort study of 18,885 patients, gender differences and procedural outcomes were reviewed (Hilliard et al., 2010). In this study design patients who had their PCI performed between 1979 and 1995, were compared to patients who had their procedure performed between 1996 and 2004, In the most contemporary group, 30-day mortality was reduced compared with that in the early group in women (2.9% vs. 4.4%, $p=0.002$) and men (2.2% vs. 2.8%, $p=0.04$). Reassuringly, long-term survival was similar between the early and recent groups among both men and women. There was no difference between men and women from 1994 onward for either 30-day or long-term outcomes.

The use of drug eluting stents, characterised by the local delivery of anti-proliferative agents to reduce intimal hyperplasia following stent implantation, is the preferred stent type rather than bare metal stents (Lakovou et al., 2005). Despite the initial experience of reported adverse events, the long term safety and efficacy of drug eluting stents has been confirmed in multiple large trials (Caixeta et al., 2009, Galloe et al., 2017, Iqbal et al., 2016, Philip et al., 2016). Invasive management is now supported and in many respects guided by the addition of invasive haemodynamic monitoring. This allows health professionals to be more reliably informed based on quantified data in regard to the decision to perform a PCI. These methods include fractional flow reserve, intra vascular ultrasound, and optical coherence tomography which are now standard practice in most cardiac catheterisation laboratories, supported by evidence based guidelines (Neumann et al., 2018).

1.7 Complications associated with Cardiac catheterisation and Percutaneous Coronary Intervention.

The need for institutions that perform interventional cardiology to monitor actual and potential adverse events has been articulated in guidelines by leading governing bodies (Naidu et al., 2016). The need for major complications to be examined, in particular post procedure stroke, radial artery occlusion, vascular access complications, issues related to radiation dosage, renal impairment and mortality are clearly defined for all cardiology centres in these guidelines (Naidu et al., 2016).

Importantly, potential causes and the reported incidence of post procedural complications are discussed at length in all guidelines. The basis of these guidelines is the analysis of data from large RCTs, meta-analyses, and leading observational studies in these areas. One of the cornerstones of all the major guidelines is the imperative for each institution to analyse the complication rate. The requirement for nurses employed in these settings to be actively involved in the performance of research around patient safety issues is well described and is now considered a requirement for cardiovascular nurses (White et al., 2018).

Percutaneous coronary intervention procedures, including cardiac catheterisation, are invasive and rely on arterial access. The complications of this procedure have historically been grouped into five broad categories; death, myocardial infarction, stroke, renal impairment related to contrast agents and vascular access site

complications (Anderson et al., 2007). These complications carry significant morbidity and mortality as outlined below.

1.7.1 Death

The reported risk of death post diagnostic cardiac catheterisation is less than 0.2%, with the risk following PCI reportedly less than one percent. These levels have remained historically largely unchanged. Historically produced data from a 9-year period that showed mortality of 0.16% for cardiac catheterisation and PCI; in the last 3 years of the study the mortality rate was 0.07% (Jansson and Fransson, 1996). Currently a diagnostic cardiac catheterisation carries a 0.6% chance of inpatient mortality, while a PCI in the setting of acute STEMI carries a 5.38% of death (Naidu et al., 2016). For PCI without STEMI there is a 0.65% likelihood of death (Naidu et al., 2016). Importantly any discussion of mortality does require some risk adjustment, particularly in the setting of acute patients, and for those with extensive co-morbidities and disease complexity (Naidu et al., 2016). Higher risk PCI may be defined by patient risk factors, such as diabetes, respiratory impairment, chronic kidney disease, and advanced age. Disease complexity includes multi vessel disease, left main disease, bifurcation lesions, and haemodynamic instability, including ventricular dysfunction, valvular disease or instability (De Marzo et al., 2018).

1.7.2 Acute myocardial infarction

Counter intuitively the diagnosis of post procedure myocardial infarction is not straight forward. There has been various definitions placed as part of guidelines and consensus statements, however these have been enhanced, revised and reworded (Thygesen et al., 2007, Thygesen et al., 2018, Paiva et al., 2015, Thygesen et al., 2012). Previous guidelines have recommended a rise in cardiac biomarkers only to define post procedure myocardial infarction. New advice embraces the inclusion of clinical factors in addition to an increase in biomarkers, noted angiographic complications, ECG changes, and symptoms of ischaemia (Thygesen et al., 2018).

1.7.3 Stroke

One of the most serious complications of cardiac catheterisation, in terms of the debilitating effect and adverse effects on patient well-being and outcomes is post procedure stroke. (Lin et al., 2010, Fuchs et al., 2002). Any review of the incidence of post procedural stroke must come with an important caveat that these events are rare, so establishing causation is problematic.

Severe strokes have been reported by patients as having a similar viewed consequence as death (Solomon et al., 1994, Pandit et al., 2014). The risk of developing a stroke post cardiac catheterisation is 0.2%, and for post PCI is 0.44% (Hamon et al., 2008). These strokes were either embolic or cerebral haemorrhage

events complicating adjunctive antithrombotic therapies. The reported rate of post procedure stroke was 0.21% for data over a 9-year period in a real world examination (Wijesinghe et al., 2008).

Patient characteristics and predictors of post procedure stroke have been reported, and have remained largely unchanged. Those characteristics included being over 80 years of age compared with patients under 50 (OR 5.1, 95% CI 3.6-7.0 p=0.001), a background of chronic renal impairment (OR 3.4, 95% CI 2.7- 4.2 p<0.001), non-insulin dependent diabetes mellitus (OR 1.9, 95% CI 1.5-2.3 p<0.001) and female gender (OR 1.3, 95% CI 1.1-1.5 p=0.003) (Fuchs et al., 2002). The documented predictors of stroke may be grouped by procedural related factors and patient characteristics. Procedural factors include multiple catheter changes (median 3, p< 0.001), greater contrast volume use (250ml vs 218ml, p=0.006), and usage of large calibre guiding catheters (median 7 French (Q1, Q3: 6 8) versus 6 French (Q1, Q3: 6, 8), p< 0.001), while no difference was detected between radial and femoral access (0.4% vs 0.4%, p=0.78) (Hoffman et al., 2012).

In a further study examining the predictors of stroke after cardiac catheterisation patients who developed a stroke after cardiac catheterisation or PCI were more likely to have received Glycoprotein IIb/IIIa antagonists compared to those who did not sustain a stroke (54% vs 45% p<0.001). The use of an intra-aortic balloon pump more than doubled the likelihood of stroke (OR 2.59, 95% CI- 2.10-3.19 p<0.001) (Aggarwal et al., 2009).

The “Thrombus Aspiration during Primary Percutaneous Coronary Intervention” (TAPAS) trial was the first trial to show survival benefit of thrombectomy catheters in primary PCI (Svilaas et al., 2008). This resulted in thrombectomy devices becoming standard practice for primary PCI (Svilaas et al., 2008). Of note, this single centre experience was not replicated in previous, nor subsequent trials of these aspiration devices. However, in a multi-centre RCT of primary PCI, with or without routine upfront manual thrombectomy, for 10,732 patients presenting with STEMI there was a higher 30-day stroke event in the thrombectomy group compared to the PCI alone group (0.7% vs 0.3%, hazard ratio 2.06; 95% CI, 1.13 to 3.75; p=0.02). This showed that thrombectomy conferred a stroke risk without any further clinical benefit; reasons for this were not reported (Jolly et al., 2015a).

The reported rate of post procedure stroke is low, which makes analysing this clinical scenario difficult (Fuchs et al., 2002). The complex health history of patients undergoing cardiac catheterisation and PCI, the equipment used, and the potentially complex anticoagulation regime, highlight the higher risk of stroke compared to the general population. Absolute predictors of stroke remain challenging to conclude definitively; increased age is an independent risk for CHD and a major contributor to mortality within this group (Avezum et al., 2005). This is reflected in the elderly comprising an increased admission rate of hospitalisations for CHD. In a large registry study (n=24,165) of patients with CHD which aimed to document the prevalence of co-morbidity in elderly patients statistical analysis showed that older patients (age > 75 years) had a higher prevalence of previous myocardial infarction,

diabetes mellitus, cardiac failure, previous coronary artery bypass surgery, history of chronic angina, hypertension, and atrial fibrillation (Avezum et al., 2005).

The benefits of trans-radial access for PCI have demonstrated improvement in clinical outcomes, particularly in bleeding complications, mortality and vascular complications (Cantor et al., 2015). While observational studies reported an increase in stroke after trans-radial access (Jurga et al., 2011), this was not supported in larger trials (Sirker et al., 2016b). Given the emergence of trans-radial access as the default method of arterial access for many institutions (Roffi et al., 2015, Santos et al., 2012) and the impact of stroke post procedure, further examination of the effect of arterial access should be a priority for institutions contemplating a change in arterial access method.

1.7.4 Renal impairment related to contrast agents

There remains no single clear definition of renal impairment post cardiac catheterisation, which is reflected in various reported rates of contrast-induced nephropathy (CIN). One accepted definition is a rise in serum creatinine by greater than 25% within 48 hours of the contrast agent being administered (Balghith et al., 2011). Reported incidence of renal impairment varies ranging from one to 15% for both coronary angiography and PCI. Major risk factors for the development of CIN, in cardiac patients are known chronic kidney disease, older age, ejection fraction of less than 40%, diabetes, perhipheral vascular disease, cardiogenic shock and sepsis. (Deek et al., 2014). Class I indications are to assess all patients for potential risk prior to procedures, in addition to minimising contrast administration with the well described impacts of the adverse effcts on renal function (Deek et al., 2014) In a large study (n=58,957 patients) the risk of CIN requiring diaysis was directly associated with increasing contrast volume. Results reached statisical significance when increasing amounts of contrast were given (dose exceeded the ratio of 3): adjusted OR for CIN: 1.46, 95% CI: 1.27 to 1.66 and adjusted OR for renal impairment requiring diaysis: 1.89, 95% CI: 1.21 to 2.94. Continued vigilence in examination of pre and post procedural renal function remains an important aspect of nursing care for the cardiology patient (Deek et al., 2014).

1.7.5 The impact of bleeding in vascular access site complications.

Post procedural anticoagulation strategies remain complex, and despite guidelines, the anticoagulation of choice remains unclear and ongoing vigilance in balancing bleeding risk and preventing a thrombosis event is required (Lancet, 2017). Globally, radial access for cardiac catheterisation and PCI accounts for approximately 6 to 12% of cases (Kern, 2011). The European Society of Cardiology‘s “Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation” (Roffi et al., 2016) has made trans-radial access the default access route for cardiac catheterisation and PCI.

In a meta-analysis of RCTs major bleeding episodes following PCI was shown to be an independent risk factor for death and post procedure ischaemic events (Jolly et al., 2009). The increase in ischaemic events may be due to the activation of coagulation cascade, cessation of anti-platelet and antithrombotic therapies or adverse effects of the resulting blood transfusions (Jolly et al., 2009). This meta-analysis showed that radial access reduces the odds of major bleeding by 73% compared with femoral access (OR 0.27 (95% CI 0.16, 0.45 $p<0.001$). There was a trend towards a reduction in the composite endpoints of death, myocardial infarction and stroke, however due to the low number of events with radial access, the analysis lacked power to make more definitive statements (Jolly et al., 2009).

One of the major trials within interventional cardiology was the RIVAL trial, which resulted from the previous meta-analysis (Jolly et al., 2011b). This study of 7,021 patients presenting with ACS including STEMI randomly assigned to radial access or femoral access evaluated the safety and efficacy of radial versus femoral access with the primary outcome of a composite of death, myocardial infarction, stroke, or non-coronary artery bypass graft at 30 days. Results showed that 3.7% of patients from the radial access group versus 4.0% in the femoral group experienced the primary outcome; hazard ratio (HR) 0.92%, CI 0.72- 1.17, p=0.50, a non-significant result. However the reported incidence of vascular complications (secondary endpoint) at 30 days post procedure was significantly different between the radial and femoral group, with 42 out of 3,507 radial access patients (1.2%) sustaining a large haematoma compared with 106 out of 3514 femoral access patients (3.0%) (HR 0.40, 95%CI 0.28 – 0.57 p<0.0001). Seven out of 3507 radial access patients (0.20%) experienced a pseudoaneurysm requiring closure compared with 23 out of 3514 femoral access patients (0.65%); p=0.006. For high risk patients such as those with STEMI or non STEMI there was a significant reduction in death in the radial group compared with the femoral group (p=0.001). The authors noted the reduction in radial site vascular events in centres that used radial arterial access as standard of care, 0.7% (HR 0.18 CI 0.08-0.37 p<0.001) compared with the femoral access group. While both radial and femoral access sites are relatively safe, there are positive outcomes and clinical benefits of using radial access for coronary interventions. The contribution this study made to the literature is significant and importantly drove practice change and further research.

The benefits of trans-radial access when compared with femoral access, including improved outcomes in terms of mortality, myocardial infarction, bleeding complications and vascular injury were supported in further trials (Cantor et al., 2015, Brener et al., 2017). Benefits of trans-radial access for all patient groups, not just ACS patient presentations, was the focus of a meta-analysis of 24 studies with 22843 participants. A subgroup analysis based on clinical presentation of STEMI, non-STEMI, or stable CHD confirmed the benefits of radial access for all patients, without any described penalty, and enforced the use of the radial approach to enhance patient safety outcomes. Cardiac catheterisation performed via trans-radial access when compared to femoral access was associated with reduced risk for all-cause mortality (OR 0.71; 95% CI 0.59 to 0.87; p=0.001), major cardiovascular events (OR 0.84; 95% CI 0.75 to 0.94; p=0.002); major bleeding (OR 0.53; 95% CI 0.42 to 0.65; p< 0.001), and significant vascular complications (OR 0.23; 95% CI: 0.16 to 0.35; p< 0.001).

With the adoption of trans-radial access there has been a need to determine the impact of adoption of trans-radial access on vascular complications, which as previously described has a significant impact on morbidity and mortality outcomes (Azzalini et al., 2015). The study aimed to determine if the positive benefits conferred by radial access at an individual level, are offset by a greater incidence of vascular access site complications at a population level when the traditional femoral access was employed (Azzalini et al., 2015). In this large cohort of 17,059, the vascular complication rate was higher in the contemporary trans-radial cohort compared with the historical cohort (adjusted rates: 2.91% vs. 1.98%; OR 1.48, 95% CI 1.17 to 1.89; p= 0.001). There was a higher rate of complication in the femoral access patients in

the contemporary cohort compared with the historical cohort (adjusted rates 4.19% vs. 1.98%; OR 2.16, 95% CI: 1.67 to 2.81; p< 0.001). Both rates were consistent for diagnostic cardiac catheterisation and PCI (Azzalini et al., 2015)

1.7.6 Femoral access complications

The two major femoral artery access complications are psuedoaneurysm and retroperitoneal haemorrhage. A pseudoaneurysm is defined as the occurrence of an decilitre dilatation of the artery at the site of catheter entry demonstrated by arteriography or ultrasound (King III et al., 2008). The more serious vascular complication, retroperitoneal haemorrhage, occurs when there is a blood loss into the retroperitoneal space; features of a retroperitoneal bleed are abdominal pain, groin pain, back pain, diaphoresis, bradycardia, and hypotension (Cox, 2008).

In the era of trans-radial access an important area of research was conducted with a focus on whether the uptake of radial access, results in higher rates of femoral complications due to patient selection and reduced experience of the operator in femoral access. A total of 17,059 participants were examined for femoral complications (Azzalini et al., 2015). Patients were retrospectively examined based on the era the performance of their cardiac catheterisation of PCI was performed in. They were assigned the labels of contemporary cohort (predominately trans-radial access era) and historical cohort (predominantly femoral access era). The contemporary cohort trans-radial participants experienced fewer femoral

complications than the historical cohort (adjusted rates: 1.44% vs. 4.19%; OR: 0.33, 95% CI: 0.23 to 0.48; p< 0.001). There were a higher rate of femoral complications in the contemporary femoral access patients compared with the historical cohort (adjusted rates: 4.19% vs. 1.98%; OR: 2.16, 95% CI: 1.67 to 2.81; p< 0.001). This data concluded that in the trans-radial access era, there was a higher rate of femoral artery complications. Despite the benefits of radial access, in cases that require femoral access, continued vigilance is required due to the reduced exposure of the health care team to managing the femoral artery (Azzalini et al., 2015).

Risk factors for femoral access complications

There is a significant body of literature detailing risk factors for the development of femoral access complications following cardiac catheterisation. The literature includes reviews of factors relevant to both coronary angiogram and PCI.

Gender – One accepted risk factor is female gender, particularly in relation to retroperitoneal haemorrhage (Bogabathina et al., 2018, Piper et al., 2003, Tiroch et al., 2008). Female gender has been historically reported in the development of retroperitoneal haematoma with female gender an independent risk factor for developing femoral access complications following cardiac catheterisation when compared to control groups who did not sustain a complication (OR 7.75, 95% CI 2.65-22.73 p<0.0001) (Farouque et al., 2005). The authors hypothesise that differences in arterial structure, vascular effects of oestrogen post menopause, the

presence of smaller diameter and smaller length femoral arteries when compared to males may contribute.

Renal insufficiency- has been independently shown to have an adverse impact on all facets of angiography in addition to its impact on vascular complications. In a study comparing patients with severely impaired renal function to patients with normal or mildly impaired renal function, patients with impaired renal function had a poorer angiographic outcome: success rate (89.6% vs. 95.5% $p<0.0001$), higher mortality (4.2 % vs 0.2% $p<0.0001$), increased adverse events (18.2% vs 4.6% $p<0.0001$) and increased length of stay (2.8 days vs 1.7 days $p<0.0001$) (Osten et al., 2008).

In a prospective cohort study (n=3,062), predictors of retroperitoneal bleed were examined in patients who had a history of renal insufficiency. Complications were observed more frequently in the retroperitoneal bleed group compared to overall the patient cohort. When comparing patients who sustained a retroperitoneal bleed, 29% (n=5, out of 17) also suffered from renal insufficiency, in contrast only 6% of patients had renal insufficiency that did not suffer a retroperitoneal bleed (n=196 out of 3,465). The overall mortality rate of patients with chronic renal insufficiency in this group was 3% compared with 1.4% for those without renal insufficiency ($p=0.17$) (Tiroch et al., 2008). While not clearly defined the potential mechanisms that place patients with renal insufficiency at an increased risk of vascular complications include more complex anatomy resulting in longer procedural times and greater

contrast usage, higher co-morbid conditions, and higher acuity presentations - which may translate to higher procedural acuity and complexity (Osten et al., 2008).

Body Mass Index and Body Surface Area- Various studies have suggested the importance of body surface area (BSA) in the development of femoral access complications, noting some uncertainty in the literature. This has been both historically and contemporarily documented. A BSA <1.73m (OR 7.1 p<0.002 univariate analysis) was an independent risk factor in the development of a retroperitoneal haematoma in their dataset (Farouque et al., 2005).

The challenges of high BMI remain in contemporary practice. BMI was examined as a risk factor in a study of 3500 participants who underwent cardiac catheterisation over a two year period. When compared to the control group of normal BMI, in a multivariate logistic regression analysis, the odds of developing a femoral complication were higher in the high BMI group compared to the control group of a normal BMI (OR 1.74- 95% CI 1.08-3.15 p=0.04) (Kassem et al., 2013). After reviewing the data further detail regarding each individual hospital's experience would be useful particularly as there appears to be varying degrees of evidence regarding the importance of BSA/BMI in the risk of developing vascular complications post cardiac intervention.

Patient acuity- The issue of the patient's medical history and current medical condition is an important factor in the development of femoral access complications.

Emergency PCI was strongly associated with the development of vascular complications post PCI compared with elective and urgent procedures (OR 2.26 95% CI 1.50-3.41) (Piper et al., 2003). Patient acuity was further addressed in a study of 112340 consecutive patients who underwent cardiac catheterisation or PCI. The overall complication rate was low in this large sample, 0.4% (n=482). However this analysis showed that emergent PCI (50% versus 29.7%, p<0.0001), cardiogenic shock (7.5% versus 2.0%, p<0.0001), MI within 7 days prior to cardiac catheterisation (32.6% versus 16.9% p<0.0001), MI within 24 hrs (32.6% versus 16.9% p<0.0001) and the use of thrombolysis treatment for acute MI (3.9% versus 2.2% p=0.01) were all independently associated with the development of retroperitoneal bleed when compared to those who did not suffer a vascular complication (Trimarchi et al., 2010). With the evidence for acute STEMI management to be treated with Primary PCI, early treatment strategies and interventions aimed at improving patient acuity will have advantages for the reduction in vascular complications.

Anticoagulation- One of the more complex issues that faces cardiology is anticoagulation, particularly in the area of interventional cardiology. Effective anticoagulation strategies have been consistently shown to reduce immediate, short term and long term outcomes (Zeymer et al., 2016). The most effective antithrombotic regime is not known (Valgimigli et al., 2015). A brief overview of anticoagulation in terms of the historical and contemporary issues, both in terms of all bleeding outcomes and vascular complications is provided below. Of note, low

molecular weight heparin is the only anticoagulant evaluated in a randomized control trial with guidelines relying on consensus statements (Zeymer et al., 2016).

Anticoagulation regimes prior to and during cardiac catheterisation and PCI are an increasingly complex issue, however critical to the discussion of vascular complications in cardiac catheterisation and PCI. Unfractionated heparin has been the predominant anticoagulant for the last fifty years (Kokolis et al., 2004). The relationship between heparin anticoagulation and clinical outcomes after coronary stent interventions have been investigated. In a RCT designed study to determine the appropriate dosage of Heparin as measured by Activated Clotting Times (ACT) compared to Heparin and Bivalirudin (Tolleson et al., 2003), 48 hour, and 30 day end points comprising death, myocardial infarction and urgent revascularisation were assessed to document the relationship between ACT and bleeding, and ACT and ischaemic events. All patients underwent femoral vascular access using a 6 French system, with all patients receiving stents, and were maintained on dual anti platelet therapy and weight adjusted Heparin dose. Interestingly in this study the actual incidence of ischaemic events did not increase as ACT decreased. In contrast, the EPILOG investigators (Lincoff et al., 2000) report that lower, more appropriate and targeted heparin doses, substantially reduced vascular complications maintaining that when angioplasty was in its infancy there was a tendency to over anti coagulate which led to a range of largely preventable bleeding complications. Weight adjusted Heparin remains frequently used in interventional procedures however additional options are now available.

The types of anticoagulation now commonly used in cardiac catheterisation and PCI are more complex, and include glycoprotein IIb/IIIa inhibitors, and bivalirudin in addition to the use of low molecular weight heparin. Heparin's action is indirect inhibition of thrombin (factor IIa) and factor Xa mediated through binding activation of antithrombin III (Camm et al., 2006). Platelet IIB/IIIa receptor blockers (Abciximab, Tirofiban and Eptifibitide) work by inhibiting the bridging of activated platelets by blocking the interaction between IIb/IIIa receptors with fibrinogen (Camm et al., 2006). Bivalirudin is a synthetic polypeptide that directly inhibits thrombin by binding simultaneously to its active catalytic site and its substrate recognition site. The peak concentration is two minutes after administration with a prompt offset of action after discontinuation (Gladwell, 2002).

Bivalirudin has been shown to decrease bleeding complication after PCI in stable, unstable and acute patients with a related mortality benefit when compared to Heparin and GP IIb/IIIa inhibitors (Ndrepepa et al., 2012). In a pooled analysis of randomised controlled trials of 3,798 patients, 1,928 patients were allocated treatment bivalirudin and 1,870 patients were allocated heparin and GP IIb/IIIa inhibitors. The major end points were a composite of death, recurrent myocardial infarction or urgent target vessel revascularization (defined as the efficacy end point), major bleeding (safety end point), and the composite of death, recurrent myocardial infarction, urgent target vessel revascularization, or major bleeding (net adverse clinical events [NACE]) at 30 days The efficacy endpoint was reached for 10.6% (n=205) in the bivalirudin group and 10.2% (n=191) in the heparin and GP IIb/IIIa inhibitor group (OR, 1.04; 95% CI, 0.85–1.27; p=0.69). The safety end point

was 3.4% (n=66) in the bivalirudin group vs 6.3% (n=117) in the heparin plus a GP IIb/IIIa inhibitor group (OR, 0.54 95% CI 0.40–0.72; p<0.001). NACE (Net Adverse Cardiac Events) occurred in 13.4% (n=258) of participants in the bivalirudin group vs 14.7%, (n=275) in the heparin group plus a GPI group (OR, 0.90 95% CI 0.76–1.06; p=0.21) (Ndrepepa et al., 2012). The positive effects of bivalirudin on reducing major bleeding events was further supported in a double blind randomised controlled trial of 4,570 participants with stable or unstable angina who underwent PCI after pre dosing of clopidogrel, in line with standard practice. Participants were allocated to either bivalirudin (n=2,289) or Heparin (n=2,281) with no major differences in endpoint data shown. However, the incidence of major bleeding was 3.1% (n=70) in the bivalirudin group and 4.6% (n=104) in the unfractionated-heparin group (relative risk, 0.66; 95% CI, 0.49 to 0.90; p=0.008) (Kastrati et al., 2008). Major bleeding was defined as intracranial bleed, or retroperitoneal bleed, haemoglobin fall of more than 3g per decilitre; any decrease in decilitre of more than 4 g per decilitre; or transfusion of 2 or more units of packed red cells. Important design characteristics of this trial need consideration as potentially patients were included with normal levels of Troponin and normal renal function, which make translation of these results to high risk populations more guarded.

Literature regarding bivalirudin focuses on the issue of vascular complications and the broader issue of bleeding following intervention. Bivalirudin was examined, to assess whether bivalirudin which had been previously used in conjunction with other anticoagulants could be used effectively in the clinical setting as monotherapy. Patients were randomised by open label using a central telephone system. The

cohort of 1,056 patients undergoing PCI were divided in two, those receiving bivalirudin alone compared to those who received heparin alone. In this trial the adjunct use of GP IIb/IIIa inhibitors was at the discretionary use of the physician. The data showed lower levels of bleeding complications, without reaching statistical significance (2.1% compared to 2.7%, p=0.52) in the bivalirudin group (Lincoff et al., 2004).

The experience of anticoagulation in female populations was taken from the dataset for the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE) 2 trial. This trial compared bivalirudin with heparin and GP IIb/IIIa inhibitors showing that in terms of bleeding complications, bivalirudin had reduced rates of major bleeding episodes (5.9% heparin and GP IIb/IIIa inhibitor versus 16% bivalirudin), access site complications (4.1% heparin and GP IIb/IIIa versus 1.6% bivalirudin) and need for blood transfusion (4.6% heparin and GP IIb/IIIa inhibitors versus 3% bivalirudin). While this is a retrospective analysis it provides useful observational data in regards to women and bleeding complications. However, importantly one of the limitations is that women in this data set were more likely to be older, have a diagnosis of hypertension, heart failure and diabetes than the comparison group of males. In this light of this the data should be with these limitations in mind (Chacko et al., 2006).

One of the most important issues for cardiology is vascular complications and the effect bleeding has, particularly on major endpoint data (Jolly et al., 2011a, Jolly et

al., 2011b). In a prospective cohort study which reviewed risk factors for the development of retroperitoneal bleeds the issue of GP IIb/IIIa inhibitors were examined. Data drawn from 3,482 procedures over a two-year period. In those that sustained retroperitoneal haemorrhage, GP IIb/IIIa inhibitors were used significantly more often (p=0.005). Using logistical regression techniques GP IIb/IIIa inhibitors were the major factor in developing a retroperitoneal haemorrhage (p=0.002). This study clearly identified the use of GP IIb/IIIa inhibitors as an independent and modifiable risk factor in developing retroperitoneal haemorrhage (Klaus et al., 2008).

In a large retrospective cohort analysis (n=18,821) of data obtained from the Society for Cardiac Angiography and Interventions Registry (United States of America), 215 bleeding events, 42 haemorrhages, 180 haematomas with seven combined events occurred (Horwitz et al., 2003). Overall bleeding risk was 1.9% with the GP IIb/IIIa inhibitors compared with 1.0% of patients who did not receive GP IIb/IIIa inhibitors. Significant differences emerged also in the haemorrhage and haematoma group. In the GP IIb/IIIa group 0.4% of patients had a haemorrhage compared with 0.2% of patients who did not receive a GP IIb/IIIa inhibitor (Horwitz et al., 2003). In the GP IIb/IIIa inhibitors group 1.5% of patients suffered haematoma formation compared with 0.9% of patients who did not receive a GP IIb/IIIa inhibitor. Multivariate analysis adjusted for multiple potential confounding variables showed while there was a risk of bleeding, this was not statistically significant suggesting a modest increase in the rate of bleeding (Horwitz et al., 2003).

Puncture of the artery and fluoroscopy- When a review of vascular complications occurs it is important to discuss the issue of arterial puncture, which may reliably predict the nature and severity of haemorrhagic complications. Optimal femoral artery access occurs above the femoral bifurcation and below the inferior portion of the inferior epigastric artery. A puncture that is not considered ideal predisposes patients to an increased risk of developing retroperitoneal haematoma and additional vascular complications (Pitta et al., 2011). In a retrospective study on 300 patients who underwent PCI, the authors sought to determine the correlation between femoral puncture site and the development of vascular complications. Vascular complications occurred in 5.7% of the total study group. In those with optimal femoral access the event rate was 4% vs 18% in those with sub optimal femoral access ($p<0.001$). While being a retrospective examination of data this study suggests that location of appropriate vascular landmarks is a crucial part of the femoral access process (Pitta et al., 2011).

Arterial puncture at the site of the infra-inguinal portion of the common femoral artery is considered ideal as it allows effective digital pressure against the femoral head post sheath removal. A puncture that is above this point has long been thought to be causative in the development of complications and an independent risk factor. In a large, widely cited trial, on vascular complications, data on a high puncture was reported and its impact of femoral access complications. A retrospective analysis comparing a group of patients who suffered a retroperitoneal bleed with a control group of patients who did not suffer any complications, estimated that 16% of the

control group had a high puncture compared with 55% of patients in the retroperitoneal haemorrhage group ($p<0.003$) (Farouque et al., 2005).

As various authors have identified the risk of high punctures in the development of femoral access complications, the impact of imaging the access site (either by fluoroscopy or ultrasound) has been assessed. In a large single centre, randomised controlled trial the use of fluoroscopy versus traditional landmarks for obtaining vascular access was investigated. While the primary reason for doing this study was to compare which method better enabled the use of vascular closure devices to be used, it provided data determining the appropriateness of imaging a patient's femoral artery prior to arterial puncture (Abu-Fadel et al., 2009). This study randomised 972 patients into vascular access using fluoroscopy compared to traditional surface anatomy landmarks. While they found no meaningful difference in primary outcome in these categories important data emerged in reference to the use of fluoroscopy in the femoral artery. This study demonstrated a significant decrease in the incidence of pseudoaneurysm in the fluoroscopy group (0.2% compared to 0.8% $p<0.001$) as well as reduced incidence of dissection (0.2% compared to 0.4% $p<0.001$), and haematoma of greater than 10cm in radius (0.63% compared to 1.2% $p<0.001$). Importantly fluoroscopic imaging of the femoral head was also found to significantly reduce the number of punctures below the femoral head in comparison to the traditional land mark technique (3.3% compared to 6.4% $p<0.001$). The authors noted the benefits of fluoroscopy in female patients and obese patients both considered important risk factors in the development of vascular complications (Abu-Fadel et al., 2009).

Vascular Closure Devices (VCD) - The traditional method of achieving haemostasis post arterial puncture has focused on manual compression of the femoral artery or the application of a compression device. However during the early 1990s devices were developed to achieve haemostasis post arterial puncture (Hon et al., 2010). VCDs have well defined benefits as a means of providing arterial closure, including early patient ambulation post procedure, enhanced patient satisfaction resulting from reduced sheath insertion time and digital compression times (Vidi et al., 2012, Al-Lamee and Nowbar Alexandra, 2018). Efficiency benefits include increased staff availability, resulting from staff no longer needing to undertake the time consuming task of manual compression of femoral arteries.(Vidi et al., 2012, Al-Lamee and Nowbar Alexandra, 2018).

Various methods of obtaining vascular closure include compressing the common femoral artery by hand usually for a period of 10 minutes, or using one of three manufactured devices. The Angio-seal™ device (Terumo Medical Corporation, Somerset New Jersey), is a collagen plug with a suture anchor mechanism to allow compression of the vessel wall between the anchor mechanism and the collagen plug. The StarClose device (Abbott, USA), involves the use of clip in the extravascular surface of the vessel. The Perclose device (Abbott, USA) works by deploying suture material on both sides of the artery, the suture material is tied, compressed down and then cut close to the arterial wall (Cox, 2008).

The early experience of VCDs was the subject of a systemic review and meta-analysis to investigate the safety of vascular closure devices comparing VCDs with manual compression. Authors examined 30 trials of 4,000 patients and concluded that VCDs may increase the risk of haematoma and pseudoanerurysm, noting the inclusion of trials early in the experience of vascular closure devices with early generation devices. The relative risk of developing groin haematoma was 1.14 (95% CI, 0.86-1.5, not significant), and the relative risk of pseudoaneurysm formation was 1.19 (95% CI, 0.75- 1.88, not significant). This review did show that while VCDs were implicated in the development of haematoma and pseudoaneurysm, the safety of VCDs is uncertain due to the variable quality of studies included. The authors note that when they reviewed articles considered to be of higher methodological quality vascular complications occurred more often in the VCD group (Koreny et al., 2004).

Later data which provided a comprehensive overview on complications from the use of VCDs concluded that adequate randomised control data is yet to be provided for patients at higher risk of complications (Dauerman et al., 2007). The authors report a vascular complication rate of between two and five percent in patients who receive VCDs and highlight that in the first decade of use there were significant complications, with improvements in devices and experience of users resulting in improved outcomes (Dauerman et al., 2011). They conclude their broad discussion of VCDs with a summation of the evidence gathered over a nine year period from registry data. For patients undergoing diagnostic coronary angiography there was a reported risk of vascular complications ranging from 0.5% to 1.7% and in patients undergoing PCI the rate of vascular complication ranged from 0.8% to 5.5%. The

author's note that these figures are similar to published data reported on manual compression and conclude that there appears to be benefit in using VCDs in diagnostic cardiac angiography with negligible benefit in the setting of PCI. However the authors conclude that most data relevant to this topic is from smaller datasets (n= 500) and is retrospective in nature. To allow definitive conclusions to be drawn more robust data must be obtained from large randomised controlled trials, particularly around high risk sub-groups (Dauerman et al., 2007).

More contemporary data show great advances in the use of VCDs, perhaps driven by the emergence of structural disease programmes. In a recent large systematic review of 34 VCD trials, VCDs have excellent clinical outcomes with minimal complication rates; however with a higher complication rate compared to manual compression (MC). Overall complications were similar with (12% for VCDs vs 13% for manual compression), infection rate 0.6% with VCDs vs 0.2% with MC, p=0.02), and importantly, the risk of thrombotic events (0.3% with VCDs vs 0 with MC, p=0.07). The authors conclude that a key limitation of this work, is that most studies involving VCDs are under powered, and that continued vigilance is important in the training and updating of skills of all member of the cardiology team (Noori and Eldrup-Jørgensen, 2018). The emergence of structural disease programmes will drive the imperative for adequately powered trials to address the significant issues of vascular complications in contemporary practice.

Management of Vascular access Complications

Treatment of pseudoaneurysm has had several options, including conservative management of bed rest and historically direct pressure (which may be guided by ultrasonography) or surgical repair, and ultra-sound guided pressure (Chua et al., 1998). Ultra-sound guided pressure involves applying an ultrasound probe directly at the point of the channel which communicates between the pseudo aneurysm and the femoral artery to prevent arterial flow into the pseudoaneurysm. This avenue of treatment is generally perceived as a conservative treatment modality (Chua, et al., 1998). The author's note that usually the compression requires multiple attempts and patients are required to be on bed rest while the psueudoaneurysm repairs.

Surgical repair of psuedoaneursym is indicated for an ongoing, painful or expanding psueodoaneurysm, rapid expansion of the pseudoaneurysm, concomitant distal ischemia or neurological deficit. While being a highly effective method of treatment, surgical management carries the usual risk of anaesthetic risks, pain during the postoperative period, and infection (Bhatty, 2011).

Retroperitoneal haemorrhage is usually treated conservatively, however in a progressively deteriorating patient surgical intervention is indicated. Retroperitoneal haemorrhage should be considered following interventional procedures such as angiography, noting anticoagulation alone may be causative in the development of a spontaneous retroperitoneal bleed (Higgs and Smith, 2005). Initially treatment

centres on conservative measures such as bed rest, discontinuation of any anticoagulation, blood transfusion if clinically indicated, and analgesia. Surgical management is indicated if shock symptoms persist, and centres around surgical repair of the affected site, embolisation of the site, or ligation of the blood supply (Higgs and Smith, 2005).

Percutaneous Thrombin Injection

A further method of management of vascular complications is thrombin injection. A systematic review of two randomised controlled trials and 11 observational studies compared the results of ultrasound based compression techniques (ultrasound guided compression (UGC) versus ultrasound guided thrombin injection (UGTI)) to treat post procedural cardiac catheterisation/PCI femoral pseudoaneurysms. This analysis, including 786 and 318 subjects who underwent UGC and UGTI respectively, demonstrated a number of clinically significant findings. Importantly, UGTI demonstrated a significantly higher success rate compared to UGC (97.4% vs. 69.3%, OR 0.06, 95% CI 0.03–0.11) while the overall complication rate for both methods of closure was small (0.69% versus 0.78%, OR 1.77, 95% CI 0.40–7.88). While not definitive due to absence of high quality data, UGTI may have benefits in terms of length of stay, without reaching statistical significance (MD 1.99 days, −0.33–4.29) (Kontopodis et al., 2016).

Thrombin injection was reviewed in a Cochrane review, which aimed to assess treatment for pseudoaneurysm. Treatments examined included manual or

mechanical compression, ultrasound-guided compression, and/or percutaneous thrombin injection. Four studies were included in the analysis adjudicated by two authors. Compression defined by digital pressure or the use of the Femostop device was demonstrated to be effective in achieving pseudoaneurysm closure although ultrasound-guided application failed to confer any benefit (risk ratio 0.96; 95% CI 0.88 to 1.04). Thrombin injection was more effective than a single episode (time varied) of ultrasound-guided compression in achieving primary pseudoaneurysm closure within the available RCTs. However, when merged the data did not reach statistical significance (RR 2.81; 95% CI 0.44 to 18.13). While this conclusion was based on limited data it suggests the use of thrombin injection is effective and safe, with clinical utility in the closure of pseudoaneurysm after cardiac catheterisation (Tisi and Callam, 2013).

Methods of Improving Vascular Access

Vascular complications can be reduced by the adoption of ultrasound of the femoral artery and fluoroscopy. The two main methods to ensure optimal femoral artery access location is by fluoroscopy to visualise the femoral head and the use of hand held ultrasound to identify the femoral artery, the femoral artery bifurcation and the presence of calcification. Handheld ultrasound is used to guide arterial puncture to avoid the bifurcation allowing more accurate and successful access of the common femoral artery, reducing the risk of vascular access, improving the first-time access rate and reducing the time taken for arterial access (Seto et al., 2010). In a randomised control trial of 280 participants, comparing ultra-sound guided access to

manual palpation to guide femoral puncture, success of puncture was defined through, total number of attempts required for access, time to sheath insertion, pain during puncture, and access-related complications. Technical success and the overall adverse rates were lower in the ultrasound group (p= 0.052 and p= 0.052 respectively) (Gedikoglu et al., 2013).

The use of fluoroscopy has been shown to enhance arterial access in cardiac catheterisation. In a randomised controlled trial of 972 participants allocated to either fluoroscopy guided ultra-sounded arterial access (n=474) or the traditional method of palpation only (n= 498), the fluoroscopy group had significantly less arterial sheath placement below the inferior border of the head of the femur (p= 0.03). This is important as it is perhaps one of the most significant drivers in the development of FVC. Additional data showed the total time for sheath insertion (105.7 ± 130.7 vs. 106.5 ± 152.6 sec) and number of times femoral artery access was attempted 1.1 ± 0.4 vs. 1.1 ± 0.5) did not differ between groups (fluoroscopy vs palpation) (Abu-Fadel et al., 2009). In more contemporary data, fluoroscopy was compared to no fluoroscopy usage to assist in femoral artery puncture in 4,534 patients, comprising 1,890 who had no fluoroscopy (palpation alone) versus 2,644 with fluoroscopy guidance. Primary endpoint was any access site complication compared using an interrupted time-series analysis. Data demonstrated a reduction in femoral complication rates after the introduction of fluoroscopy guided puncture (40% decrease RR 0.58; 95% CI 0.25–0.87; $p < 0.01$). Overall there was a significantly lower incidence of access site complications after the introduction of fluoroscopy guided puncture (0.9% vs. 2.0%, $p < 0.001$) (Castle et al., 2019).

1.7.7 Radial access complications

The European Society of Cardiology consider radial artery occlusion, injury, and vascular complications following cardiac catheterisation and PCI to be an infrequent occurrence (Roffi et al., 2015). Radial access complications are described within the literature as occurring between 5% and 30% of patients, however the majority of reported data is between 5 and 10% (Beyer et al., 2013). Radial access complications can have a significant impact on patients undergoing this procedure (Uhlemann et al., 2012).

Radial artery occlusion (RAO) is considered a complication of trans-radial access and the mechanism is thought to be due to the formation of thrombus (Kanei et al., 2011). Risk factors for RAO have been described in a study by one of the pioneers of trans-radial access to include, female gender compared with male gender (6.5% vs 3.0% p=0.006), diabetes (2.0% in the non-diabetic cohort vs 7.5% in diabetics p=0.001), patients who were not given Heparin (6% in those that did not receive Heparin vs 3.9% in the cohort that received Heparin, p=0.0001), and importantly a failure to maintain appropriate radial patency while the haemostasis device is in place (9% in those without patency vs 0.5% in those with patency, p=0.002) (Pancholy et al., 2012). The main impact of RAO is that it does not allow the radial artery to be utilised for further procedures which may be problematic as this patient cohort may require more interventions in the future (Kiemeneij and Boink, 2016).

The role of ultrasound measurements has been to shown to assist in the reduction of RAO, due to an increased ability to undertake radial artery measurements to guide equipment selection (Chugh et al., 2015). The role of all members of the interventional team in facility radial ultrasounds may offer a valuable adjunct to clinical care.

Trans-radial access complications were reviewed for patients undergoing radial cardiac catheterisation. The documented complication rate for radial access site vascular complications is 0.59%, compared with femoral access site complications of 3.71% (Kanei et al., 2011). Additional radial access site complications can be categorised as the following (Kanei et al., 2011):

Radial artery occlusion with ischaemia- This should not occur when appropriate circulation is evident prior to puncture. Traditional methods of assessing palmar dual blood supply such as the Allen's test and modified Allen's test are non-evidence based methods of predicting vascular injuries. The reported incidence of this occlusion has only occurred in the longer term monitoring of critically ill patients and remains a non-significant problem in the cardiac catheterisation laboratory as sheaths are removed immediately post procedure (Kanei et al., 2011).

Radial artery spasm- While not regarded as a serious adverse event radial artery spasm has the potential to cause both access and procedural failure. The occurrence of spasm drives difficult to manage clinical situations including pain, loss of pulse, and transient entrapment of the arterial sheath (Ho et al., 2012). This complication occurs in approximately five to 10% of cases (Boyer et al., 2013). Risk factors for the development of radial artery spasm include smaller diameter radial arteries, female gender, multiple catheter exchanges, and level of experience of operator (Boyer et al., 2013) The use of procedural sedation and usage of glyceryl trinitrate are thought to be protective against the occurrence of radial spasm (Boyer et al., 2013, Deftereos et al., 2013).

Arterial perforation – Perforation of the radial artery may lead to large haematomas in the forearm and compartment syndrome. Perforation usually occurs due to incorrect guide-wire manipulation and over anticoagulation and is reported to occur in less than 1% of cases (Jolly et al 2009).

Radial artery pseudoaneurysm- Reported in less than 0.1% of cases occurs after multiple puncture attempts, over anticoagulation and the use of larger sheath sizes (Kern, 2011, Romagnoli et al., 2011).

1.8 Conclusion

This literature review has provided an overview of CHD and the burden it places on health care, in addition to describing common adverse events, and negative health

outcomes of patients presenting with heart disease. The review has combined both historic and contemporary literature to provide an overview of the disease process. The review has provided detail on various factors that contribute, or may contribute to the development of cardiac associated adverse events which carry potential morbidity and mortality consequences.

The research in this thesis has been undertaken using local health district data to provide an evidence based approach to improving patient safety for people undergoing diagnosis or treatment of CHD. This research will enable improved health outcomes for people being hospitalised for treatment and management of heart disease. This thesis seeks to instigate a method of monitoring or addressing issues that enhance positive outcomes for patients requiring cardiac interventions, using a nursing model. An analysis of adverse events, as well as developing a predictor model would be beneficial at a local and international level. This analysis provides an avenue for routine, nursing led reviews of health outcomes, identifying potential management solutions, implementing evidence-based treatment paradigms, and potential avenues for further research and collaborations.

Historically in nursing, much of the focus on patient safety has been the bedside approach with strategies focused on checklists and multi-disciplinary rounds (Henneman et al., 2012). However other nursing strategies and interventions have been demonstrated to be highly effective in the recognition, management and importantly the interruption of adverse events (Henneman et al., 2012). The role of

the advanced practice nurse has been demonstrated to be an integral aspect of ensuring patient safety (Henneman et al., 2006, Henneman et al., 2010, Kutney-Lee et al., 2009). The nursing workforce are an essential component of the patient journey and having knowledge of risk factors and procedural aspects of care that may cause a complication is of critical importance in all contemporary cardiac catheterisation laboratories. Importantly, it is now mandated via position statements that knowledge, recognition and management of adverse events and complications are requirements for the contemporary nurse (White et al., 2018). A nursing led model of reporting outcomes informs nursing practice, and provides meaningful data to improve the patient experience and importantly patient outcomes (Henneman et al., 2010). Contemporary issues and outcomes of cardiology nursing practice has significance for an international audience. Data that examines clinical outcomes using a nursing model would be an important contributor to the body of knowledge and would assist in refining patient safety policy, informing wider policy development and improving patient care. Upon completion of this program of research the candidate hopes to provide detailed, evidenced based answers to the research aims. Advanced practice nurses have demonstrated that a nursing led model of adverse event monitoring focusing on outcome data can be adopted with ease into their system of care to monitor and reduce complications (Leeper, 2004, Spruce and Butler, 2017, White et al., 2018). Gaining a greater understanding of this broad issue will enable this data to be translated in to contemporary nursing practice. Findings from this thesis can be used as a platform for other institutions or health services wishing to implement a system of adverse event monitoring to enable the nursing workforce to lead the utilisation of current and emerging technology.

Chapter 2:

Missed Acute Myocardial Infarction in a rural and regional setting

This chapter is published as an original research article in the peer reviewed journal International Journal of Cardiology: Heart & Vasculature. The final Word version is included here, with references included at the end of the thesis. A PDF version of the publication is included in the Appendices.

Citation: Williams T, Savage L, Whitehead N, Orvad H, Cummins C, Faddy S, Fletcher P, Boyle A, Inder K. Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting. International Journal of Cardiology: Heart & Vasculature. 22 (2019) 177-180. https://doi.org/10.1016/j.ijcha.2019.02.013

2.1 Preamble

This first study presented in Chapter 2 provided the framework to collect outcome data that incorporated admissions to facilities throughout the whole local health district which covers a large geographical area. Establishing data linkage systems enabled refinement of data collection for the remaining studies in this thesis. These systems are now integrated into routine standard practice.

The overarching theme of this study was to examine adverse events associated with acute admissions to hospital with acute myocardial infarction. This chapter identifies the causes and outcomes of missed diagnosis of myocardial infarction with a focus on the burden of this event in the rural population associated with the local health district. Clinical data collection systems were developed as the basis for the detection of adverse events.

The reasons why patients who present with clinical characteristics and ECG evidence of acute myocardial infarction do not receive evidence based treatment is under reported within the literature, despite the impact on morbidity and mortality. Delay in receiving treatment and/or failure to provide timely reperfusion in ST-segment elevation myocardial infarction (STEMI) can have significant impacts on morbidity and mortality.

There is limited literature concerning the factors that contribute to a missed diagnosis of acute myocardial infarction. This study examines demographic, clinical, ECG and organisational factors associated with patients presenting with STEMI who were eligible for reperfusion therapy but did not receive it in a rural and regional area.

Findings indicate that a missed diagnosis of STEMI is associated with longer length of hospital stay, readmission and mortality and primarily occurs in smaller rural hospitals. Common contributing factors include failure to correctly interpret the ECG

and treatment indecision. This study highlights the need for system improvements to reduce missed diagnosis of this high risk population.

2.2 Abstract

Background: Delay in treatment and/or failure to provide reperfusion in ST-segment elevation myocardial infarction (STEMI) has impacts on morbidity and mortality. Differing clinical presentations and organisational factors make the diagnosis of STEMI challenging**.** This study aimed to describe factors associated with missed diagnosis of acute myocardial infarction (MAMI).

Methods: Retrospective cohort design. Patients who presented with STEMI and failed to receive reperfusion therapy within four hours were identified as MAMI. Univariate analysis was undertaken to identify differences in clinical characteristics between the treated STEMI group and the MAMI group. Length of hospital stay, 30-day readmission rates and mortality were included.

Results: Of 100 patients identified as MAMI (70 male and 30 female), 24 died in hospital. MAMI patients have similar demographics and time from symptom onset to treated STEMI patients. Of the MAMI patients who died, rural hospitals recorded the highest inpatient mortality (69.6% p=0.008). MAMI patients had higher 30 day readmission compared to treated STEMI (31.6% vs 3.3%, p=0.001) and longer length of stay (5.5 vs 4.3 days p=0.029). Causes of MAMI were inaccurate identification of STEMI on electrocardiogram (ECG) (72%) and diagnostic uncertainty (65%). The Glasgow algorithm to identify STEMI was utilised on 57% of occasions, with 93% accuracy.

Conclusion: Mortality following MAMI is high and indicates a need for system improvement, particularly in smaller rural hospitals. MAMI results in increased length of stay and readmission rate. ECG interpretation and diagnostic accuracy require improvement.

2.3 Introduction

The burden of heart disease is 20% greater in rural populations compared to metropolitan populations, with a higher rate of mortality and multiple hospital transfers often required to access specialised care (Brieger and Redfern, 2013). Appropriate and timely clinical care of patients presenting with Acute Coronary Syndrome (ACS), including acute myocardial infarction, is the subject of comprehensive guidelines nationally and internationally (Roffi et al., 2016, Chew et al., 2016b). Timely access to evidence-based management of ST segment elevation myocardial infarction (STEMI) is imperative for optimal clinical outcomes (Savage et al.).

For patients presenting with STEMI in non-metropolitan hospitals the reperfusion treatment is predominantly thrombolysis. If thrombolysis is delivered in a timely fashion, followed by transfer to a percutaneous coronary intervention (PCI) capable hospital, this provides outcomes similar to primary PCI, which is recommended where facilities are available (Khan et al., 2016). The impact of delay in treatment and failure to provide reperfusion doubles mortality, and impacts on morbidity outcomes (Farshid et al., 2016). However differing clinical presentations and organisational factors can make the diagnosis of ACS a challenge for clinicians, resulting in some patients not receiving the appropriate standard of care (Pride et al., 2012). Internationally, the experience of failure to treat STEMI has been documented (Schull et al., 2006, Tricomi et al., 2008). Australian data has shown that more than one third of people presenting with STEMI (who were eligible for treatment) did not

receive recommended reperfusion therapy (Chew et al., 2013). This rate is higher outside the metropolitan environment, and the reasons for this are unclear (Farshid et al., 2016). The purpose of this study was to assess the demographic, clinical, ECG and organisational factors associated with patients presenting with STEMI who were eligible for reperfusion therapy but did not receive timely treatment in a rural and regional area.

2.4 Materials and Methods

A retrospective medical record review of patients presenting to hospital with STEMI to identify those with a missed diagnosis of acute myocardial infarction (MAMI) was conducted from 2011 to 2016 by two senior cardiology medical staff, four nursing staff, and one ambulance staff member.

2.4.1 Setting:

The LHD services a population of 950,000 and covers an area of 131,785 square kilometres, covering major cities, inner regional, outer regional and remote populations (ABS, 2018). The district has seen a 3% cumulative increase per year in presentations to Emergency Departments, with approximately 15,000 chest pain presentations across the LHD annually. The district comprises 37 hospitals, including general practitioner run hospitals (n= 27), general physician on site/ Fellow Australasian College of Emergency Medicine (FACEM) hospitals (n=7), nurse only hospitals (n=2), and tertiary referral centres (n=1).

The local health district's reperfusion strategy for patients presenting with ACS was implemented in 2010 utilising a computer algorithm for identification of STEMI on electrocardiograph (ECG). All hospitals and ambulances in the LHD have ECG machines equipped with the Glasgow algorithm (Macfarlane et al., 2005). This has been shown to have acceptable diagnostic accuracy in the interpretation of STEMI (4, 12). Integrated within this system is the ability to electronically transmit ECGs for

expert review by a cardiologist when STEMI is detected by the algorithm. Under this reperfusion strategy more than 500 acute STEMI patients are identified and treated per annum across the district. These ECGs are electronically stored and form part of the patient's medical record.

2.4.2 Sample

We reviewed the medical records of patients who presented to any hospital in the region with STEMI and failed to receive timely reperfusion therapy, when not contraindicated, from 2011 to 2016. For this analysis timely reperfusion therapy was defined as treatment of patients who exhibited a clinical presentation and changes on ECG consistent with STEMI. ECG confirmation of STEMI was adjudicated by a senior Cardiologist. Patients were required to meet criteria for standard reperfusion therapy (Chew et al., 2016b). Patients who presented with a STEMI and who were not identified and treated within a four-hour period were included in this review as Missed Acute Myocardial Infarction (MAMI). We excluded five patients who had end stage disease processes, including cancer and dementia who were treated using a palliative approach.

2.4.3 Data Sources

A database of patients identified as MAMI was developed and populated using information from medical records, online clinical databases, including pathology and an ECG STEMI database, ambulance service data, and organisational patient

tracking databases. Ethical approval was obtained from the institutional human research ethics committee (AU201711-02). Patients were identified as MAMI through examination of ECG databases, clinical databases (including ACS and STEMI databases), routine audit of transfer to other hospitals reports, inpatient death audits, and clinician notifications via the organisational adverse event reporting mechanisms.

2.4.4 Factors of interest

- Patient demographic factors; including age, gender, and aboriginality; cardiovascular disease (CVD) risk factors including hypertension, dyslipidaemia, diabetes, smoking; and previous CVD including prior myocardial infarction, prior coronary artery bypass graft surgery (CABG) and prior percutaneous coronary intervention (PCI) were included in the dataset.
- Hospitalisation-related factors; including MAMI inpatient mortality, length of hospital stay and 30-day-readmission; and details of the clinical presentation including type of myocardial infarction were collected. Time of presentation to hospital, and time between onset of symptoms to time of hospital presentation were also recorded.
- ECG factors and STEMI characteristics; Timing of ECG, usage of Glasgow ECG interpretation algorithm and appropriate recognition of STEMI using the algorithm, delays in diagnosis, accuracy of interpretation of ECG clinical staff, and diagnosis uncertainty.

- Definitions of factors associated with MAMI; Inaccurate ECG interpretation was defined as failure to make diagnosis of STEMI despite ECG criteria indicating STEMI. This was regardless of whether the Glasgow algorithm was used. Diagnostic uncertainty was defined as delay in access to expert clinical support and confusion around the correct treatment and referral processes. Treatment indecision is defined as where a STEMI was identified yet reperfusion therapy was not given despite an absence of contraindication.
- Organisational factors; Hospitals were classified as: tertiary hospital (bed capacity >500), metropolitan hospital (bed capacity >200 and ≤ 500), rural referral hospital (bed capacity >100 and ≤200) and small rural hospital (bed capacity ≤100). The majority of hospitals were classified under the Australian Statistical Geography Standard (ASGS, 2011) as being in inner or outer regional Australia.

2.4.5 Statistical methods:

Data analysis was conducted using IBM SPSS Statistics (version 22, Chicago, IL, USA). Descriptive statistics are presented by counts and percentages for categorical variables and means and standard deviation (SD) for continuous variables. The patient demographics of the MAMI group were contrasted against the dataset kept for STEMI presentations to the local referral hospital. The two groups are heterogeneous and should be viewed for presentation demographics only. Univariate analyses to identify any differences in clinical characteristics were performed on data comparing two groups. Categorical variables were analysed using a chi-square test, while continuous variables such as age were analysed via analysis of variance

(ANOVA). Planned comparisons were performed using Bonferroni corrections and statistical significance level was set to $p<0.05$.

2.5 Results

Over the five-year period approximately 1,392 patients presented with a STEMI to the hospitals in the region. Of these, 100 patients were identified as missed acute myocardial infarctions (MAMI); 24 of the MAMI patients died in hospital.

Table 2.1: Characteristics of MAMI patients compared to treated STEMI from 2011 to 2016

Variable	Treated STEMI n=1292	MAMI Patients n=100	p-value
Male Gender n (%)	950 (73.5)	70 (70)	0.465
Age (years) m (SD)	63.9 (12.9)	66.3 (12.4)	0.302
Indigenous n (%)	47 (3.6)	4 (4)	0.776
Hypertension n (%)	796 (61.6)	42 (42)	0.076
Dyslipidaemia n (%)	496 (38.4)	38 (38)	1.000
Diabetes n (%)	314 (24.3)	33(34)	0.081
Prior smoking n (%)	693 (53.6)	42(42)	0.039
Prior Myocardial Infarction n (%)	231 (17.9)	26 (26)	0.072
Prior CABG n (%)	37 (2.9)	9 (9)	**0.008**
Prior PCI n (%)	130 (10.1)	14 (14)	0.291
Presentation to hospital m (SD)			
7am-3pm	707 (54.7)	62 (62)	0.190
3pm-11pm	377 (29.2)	21(21)	0.115
11pm-7am	204 (15.8)	17 (17)	0.767
Symptom onset to presentation (minutes) m (SD)	150.5 (144.4)	155.6 (131.4)	0.903
Anterior Infarction n (%)	528 (41)	67 (67)	**0.000**
Length of Stay; m (SD)	4.3 (3.7)	5.5 (4.5)	**0.029**
30-day Readmission n (%)	43 (3.3)	24 (24)	**0.001**

CABG: Coronary Artery Bypass Graft; M: Mean; PCI Percutaneous Coronary Intervention; SD: standard deviation; STEMI: ST segment Myocardial Infarction

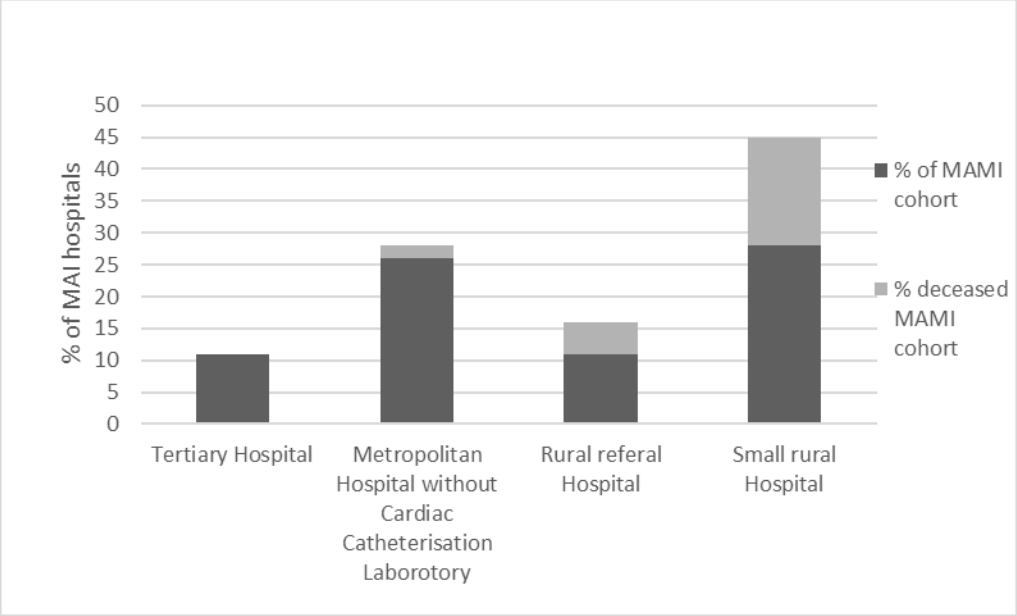
Characteristics of the treated STEMI and MAMI groups are presented in Table 2.1. Compared with the treated STEMI group, demographics of the MAMI group were similar in terms of age, comorbidities and time from symptom onset to presentation. MAMI patients were more likely to have previous CABG (9% vs 2.9%; p=0.008) and present with anterior infarction (67% vs 41%; p<0.001). MAMI patient presentations were common on weekends (50%) and were less likely if patients arrived to hospital via Ambulance (25% vs 50% treated STEMI cohort).

Patients who survived MAMI had a significantly higher thirty-day readmission rate compared with treated STEMI (24% vs 3.3%, p=0.001). The MAMI cohort showed a longer length of stay when compared with the treated STEMI group (5.5 days versus 4.3 days, p=0.029). MAMI patients who survived hospitalisation (n=76) were of similar age to treated STEMI patients. The MAMI patients who died in hospital (n=24) had a higher proportion of women compared with the MAMI group that survived to discharge (46% versus 25%) and a higher proportion presented to hospital after 3pm.

MAMI patients most commonly presented to small rural hospitals (Figure 2.1). Approximately one third of MAMI patients (37%) presented to metropolitan hospitals the remaining to rural hospitals. Of the patients with MAMI who died, smaller rural hospitals recorded the highest inpatient mortality (69.6% p=0.008). There was no in-hospital mortality of patients who had MAMI in the large tertiary referral hospital (Figure 2.1).

In MAMI cases, failure to identify the STEMI on ECG (72%) and diagnostic uncertainty (65%) were the most common contributing factors. The MAMI group had multiple contributors which relates to the complexity of presentation in this group and the multiple contributors to MAMI. Diagnostic uncertainty appeared common in patients with presentations labelled as “atypical symptoms”. In a number of cases a diagnosis of gastrointestinal reflux was made based on limited parts of the presenting complaint. This diagnosis was not altered despite evidence of STEMI, e.g. clear ECG changes. Treatment indecision contributed to delayed therapy in nearly 25% of cases, and resulted in no reperfusion therapy in a number of others.

Clinicians frequently failed to both independently correctly analyse the ECG, or to act on the machine ECG interpretation (Glasgow algorithm). Of the MAMI patients, 57% had an ECG performed on a machine equipped with the Glasgow algorithm. Where the Glasgow algorithm was utilised, it correctly identified STEMI in 93% of occasions. Despite correct machine identification of STEMI in these cases, reperfusion therapy was not given in a timely manner.



The majority of patients presented to rural hospitals. Higher mortality was seen with MAMI in these locations.

Figure 2.1: Initial Presentation Hospital and outcomes for patients presenting with MAMI

2.6 Discussion

This paper describes the patient characteristics and the clinical factors associated with the missed diagnosis of acute myocardial infarction in a rural and regional setting. Patients who had MAMI had a three- fold higher mortality when compared to the regions published mortality rate (Khan et al., 2016). In addition there was a 20% increased LOS, and eight times the readmission rate compared to treated STEMI patients. Alarmingly anterior infarction was the most represented infarct type. These clinical factors place the patients and the healthcare system under unnecessary stress. Understanding the problem more deeply will assist in informing clinicians and policy makers.

The high proportion of STEMI patients not receiving reperfusion therapy is widely described in the literature and has been examined over a long period of time (Masoudi et al., 2006, Welsh et al., 2016). Previous reasons for not receiving reperfusion when indicated included late presentation, atypical symptomatology, gender and co-morbidity factors, in addition to clinician performance issues and system issues (van der Ende et al., 2017, Singer et al., 2017, Schull et al., 2006, Welsh et al., 2016). In our study, there were no clinically meaningful demographic differences in the MAMI cohort. We found several system reasons for failure to treat STEMI by the agreed clinical pathway. A clinical pathway in each facility is underpinned by state health policy for the treatment of STEMI (Health, 2011). There has been previously reported barriers in the usage of guidelines which may impact on widespread compliance with this pathway (Kinsman et al., 2012). The barriers to the utilisation of guidelines maybe a useful source of further research.

Interpretation of the ECG, diagnostic uncertainty and treatment indecision all play a role in the in the increase in mortality (Pride et al., 2012). The use of an interpretive algorithm in assisting with ECG interpretation has been embedded in the NSW health reperfusion strategy for acute myocardial infarction since 2012. While it is uncertain how prevalent MAMI was before this strategy, it is clear that the availability of an algorithm has not eliminated the failure to treat STEMI. The algorithm was triggered in more than half the patients with STEMI who were not treated. Despite correct machine identification of STEMI in these cases, reperfusion therapy was not given. In some cases, it appeared the machine interpretation was not read or noted by treating clinicians, in others cases it appears that the machine interpretation was

disregarded or not believed. The reasoning behind either the clinical failure to interpret the ECG or the operational failure to accept the algorithm interpretation is unclear from the medical record. Further evaluation of this aspect of MAMI is essential to better understand the phenomenon.

A central support hub and spoke for clinical guidance exists in the catchment of this group of patients. This model consists of the tertiary centre being the hub and the rural and regional sites being the spoke (Elrod and Fortenberry, 2017). There appears to be a lack of a clear clinical framework or tool to ensure that communication between hub and spoke is effective and accurate and this may contribute to the incidence of MAMI. The overrepresentation of patients who had MAMI after hours may reflect on the capacity of the “hub” to appropriately support the “spoke” during these times.

The preponderance of MAMI in rural sites compared to metropolitan hospitals reflects the difficultly of practice away from a tertiary centre in the treatment of STEMI (Katzenellenbogen et al., 2012). Previous contributing reasons reported include the complex clinical presentation of ACS (Pride et al., 2012). The difficulties maintaining a viable clinical roster with scarce resources and potentially long distances remain a challenge in the rural and regional setting (Katzenellenbogen et al., 2012). Interpretation of complex ECGs when this is not the core clinician’s role or expertise remains challenging, although the availability of algorithm should minimise this (Savage et al.). Support for smaller facilities particularly in the evening and weekends is essential to improving the outcome of patient with STEMI in the rural environment and reduce the variation in clinical practice. It would be enticing to

speculate on the impact a centralised ECG reading service would have on rural and regional health districts. This approach needs to be tested in a prospective research trial.

The small number of patients who have arrived by Ambulance to hospital and subsequently had MAMI may reflect an important protective role that the Ambulance service plays in the early detection and subsequent treatment of STEMI(Savage et al., 2014). Similar reductions in mortality and enhanced service delivery have been noted by other Ambulance services who have become involved in STEMI management (Mannsverk et al., 2017).

2.7 Limitations

This is an observational study on a sample of patients with data collected from a variety of sources, therefore the denominator of missed MI cannot be accurately ascertained. However, all potential data sources were utilised to minimise missing relevant patients. Data obtained from medical record review carries limitations as it is reliant on the accuracy and interpretation of documentation of care. The MAMI group was a relatively small sample so statistical comparisons need to be interpreted with caution.

2.8 Conclusion

MAMI results in increased mortality, longer LOS, and higher rate of hospital readmission. The most common contributing factors are failure to correctly interpret the ECG and diagnostic difficulty. MAMI occurs more in smaller rural hospitals. Future effects should be directed toward preventing MAMI.

Chapter 3:

Factors associated with Femoral Vascular complications following cardiac catheterisation

This chapter is published as an original research article in the peer reviewed journal British Journal of Cardiac Nursing. The final Word version is included here, with references included at the end of the thesis. A PDF version of the publication is included in the Appendices.

Citation: Williams T, Khan A, Savage L, Condon J, Boyle A, Collins N, Inder K. Femoral vascular complications following cardiac catheterisation. British Journal of Cardiac Nursing 2018 Vol 13, No 12. https://doi.org/10.12968/bjca.2018.13.12.593

3.1 Preamble

This chapter identifies risk factors for the development of femoral vascular complications. This complication is a significant source of adverse health outcomes in a cardiology setting. This study sought to identify those patients at higher risk of developing this complication.

The research methods including, detection of at risk populations, data linkage systems and data collection methods, implemented in study 1 (Chapter 2) prompted

further investigation into a significant contemporary cardiac issue of femoral vascular complications. Accurate data registries of complications are recommended by guidelines and consensus statements from leading bodies to improve care (Klein et al., 2011). Implementing routine data systems can be challenging and continue to be of upmost importance to facilities.

Bleeding complications, including vascular complications have significant impacts on morbidity and mortality outcomes of patients. Femoral vascular complications are a significant contributor to bleeding complications and as a consequence significantly impact on poor health outcomes in patients undergoing investigation and treatment for heart disease (Jolly et al., 2011b).

While trans-radial access has emerged as the default method of arterial access, mandated by the leading guidelines, femoral vascular access is still the preferred method in many centres for structural disease programmes, for complex PCI intervention, and for cardiac catheterisation. Establishing methods of detection of femoral vascular complications remains relevant for the contemporary clinical workforce. Increasing knowledge of risk factors of potential adverse health outcomes will help inform clinical practice and hospital policy for all centres.

This study reviews the risk factors in the development of major femoral complications in a contemporary, consecutive cohort of patients using a case control design over a

five-year period. Findings suggest that gender, cardiovascular disease risk factors, and procedural factors remain important in the development of femoral vascular complications.

3.2 Abstract

Aim: To examine factors associated with femoral vascular complications (FVC) following cardiac catheterisation.

Methods: Using a case-control study design patients with a FVC (pseudoaneurysm or retroperitoneal bleed) were examined over five years. Multivariable logistic regression was used to determine associations with FVCs. Results are reported as adjusted odds ratios (AOR) and 95% confidence intervals (CIs).

Results: Seventy eight (0.65%) patients experienced FVCs (mean age 65 years, 50% female gender) Factors that increased odds of FVC were female gender (AOR 2.9, 95%CI 1.3-6.1), smoking (AOR 7.4, 95%CI 3.5-16), diabetes mellitus (AOR 7.5, 95%CI 3.4-16), hypertension (AOR 2.9 95%CI 1.2-6.9) anticoagulant medication (AOR 16 95%CI 5.5-45) elevated BMI (AOR 1.1, 95% CI 1.0-1.2), and use of vascular closure devices (AOR 3.4 95%CI 0.61-19). Use of a compression device reduced the odds of FVC (AOR 0.6, 95%CI 0.3–1.0).

Conclusion: Gender, cardiovascular disease risk factors, and procedural factors remain important in the development of FVCs

3.3 Introduction

Femoral vascular complications (FVCs) are an infrequent yet serious complication of cardiac catheterisation with significant morbidity, mortality and cost implications (Cox, 2008, Dencker et al., 2016, Yatskar et al., 2007). Each year, approximately 7 million cardiac catheterisation procedures are performed internationally with a reported access site complication rate of up to 6% (Patel et al., 2010). FVCs range from the more minor complications including haematomas, through to the more clinically significant pseudoaneurysm and retroperitoneal bleed, which may have the greatest impact on bleeding and subsequent adverse events (Applegate et al., 2008).

3.3.1 Background

Risk factors for FVC are well established and include female sex, older age, obesity and higher femoral artery puncture (Farouque et al., 2005). With the emergence of complex procedures in structural heart disease such as trans-catheter aortic valve replacement (TAVR), addressing issues pertinent to femoral vascular access and associated complications is timely and important.

The increasing use of the trans-radial vascular access approach in particular, in addition to the use of fluoroscopic landmarks and vascular ultrasound, may reduce the incidence of FVC (Levine et al., 2011). However, some studies have shown the high uptake of trans-radial access has resulted in a higher proportion of femoral access complications in the patients who do have femoral access reported (Azzalini

et al., 2015). Knowledge of risk factors for these potentially significant clinical problems remains important for the contemporary nursing workforce.

3.4. Aims

The aims of this paper are to:

1) Examine the risk factor profile of consecutive patients who sustain an FVC, defined as a pseudoaneurysm or retroperitoneal bleed, following cardiac catheterisation or percutaneous coronary intervention (PCI) at a large tertiary referral hospital.

2) Describe the specific risk factors for femoral pseudoaneurysm and retroperitoneal bleeding groups. This will help to identify patients at increased risk of FVCs and identify strategies that may help to prevent FVCs.

3.5 Methods and methodology

3.5.1 Research design

The study was performed using a case control design.

3.5.2 Study setting

The tertiary referral centre used in this study is based in a region of New South Wales in Australia with a population of 910, 436 people. The cardiac catheterisation laboratory is staffed by 20 specialist nurses, as well as senior interventional cardiologists, fellows and training resident staff trainee doctors, undertaking approximately 2000 cardiac catheterisation procedures and 850 PCIs annually.

3.5.3 Ethical approval

The need for formal ethical approval was waived after review by the institutional human research ethics committee as it was a retrospective examination of registry data.

3.5.4 Selection of cases

Patients who sustain an FVC have clinical, demographic and procedural data recorded prospectively in a separate procedural complication registry. The authors reviewed all medical records of patients who underwent cardiac catheterisation or PCI using femoral artery access who had been diagnosed with an FVC over a 5-year period. All adults in the procedural complication register who experienced a retroperitoneal bleed or a pseudoaneurysm were used in this study as cases. The two databases were linked using three identifiers: sex; date of birth; and unique medical record number. This sample included all diagnostic cardiac catheterisation

procedures and PCIs performed over the study time frame including emergent cases.

3.5.5 Selection of controls

Details of consecutive patients who undergo cardiac catheterisation or PCI are prospectively recorded in a central database, including demographic, clinical and procedural data. The control group was randomly selected from the central database at a ratio of four controls to one case to increase statistical confidence. Controls were adults who had undergone coronary angiography or PCI using femoral artery access and did not develop an FVC.

For the purposes of this study, FVC is defined as any patient who was diagnosed with a pseudoaneurysm or retroperitoneal haemorrhage using doppler ultrasound or computerised tomography after undergoing invasive assessment and treatment.

3.5.6 Statistical methods

Descriptive statistics are presented in counts and percentages for categorical variables, and means and standard deviation (SD) for continuous variables. Comparison of categorical variables was performed using the c^2 test; and continuous variables using t-tests or Mann-Whitney U tests, depending on distribution.

Associations between demographic, disease-specific, procedural and medical management characteristics and FVCs were examined using binary logistic regression. Collinearity of variables in the model was checked using variance inflation factors, and linearity assumption for continuous variables and the log (outcome) were examined. Age and body mass index (BMI) were analysed as continuous variables; all other variables were analysed as categorical variables. Variables included in the model were selected based on clinical relevance, and model selection was performed to create the final model.

Where necessary, because of the low number of patients who experienced an FVC, variables were removed if non-significant in adjusted modelling. The degree of association of each variable in the model was taken into account with the outcome and it was ensured that the inclusion or removal of each variable did not grossly affect either the fit of the model (measured by likelihood ratio test and Akaike information criterion) or the estimates for remaining variables. For outcomes with very low numbers, multivariate modelling was not performed. Crude and adjusted odds ratios (ORs), 95% CIs and Wald *P*-values are presented for the logistic regression modelling.

The variables examined in the model included age, sex, BMI, diabetes, hypertension, smoking status, peripheral vascular disease (PVD), previous coronary artery bypass graft (CABG), cardiogenic shock, anticoagulant/anti-platelet medication, renal failure, vascular closure device and the use of a femoral compression device based on clinical significance. For this analysis, the authors adjusted for age and sex. Multivariate analyses were not performed to examine the

association of variables with retroperitoneal bleed/haematoma because the number of patients was small. All analyses were programmed using SAS v9.4 (SAS Institute, Cary, North Carolina, US).

3.6 Results

3.6.1 All femoral vascular complications:

Within a total of 12, 005 procedures performed over a 5-year period, 78 patients sustained an FVC (0.65%). Characteristics of the sample who did and did not sustain an FVC are shown (Table 1). Fifty-five patients sustained a pseudoaneurysm, while 23 experienced a retroperitoneal bleed/haematoma. Of this group of 78 patients, 50% were male and the mean age was 65 years. Thirteen patients (16.7%) required surgery to manage their FVC. These cases were matched with 250 controls who had undergone a procedure using femoral vascular access and did not sustain a FVC. The mean age (SD) of the controls was 62 (±13) years; 61% were male.

Baseline characteristics of the non-complication group to those who sustained an FVC (Table 3.1). BMI was higher in the FVC complications group than in the group without FVC complications (29.2 [SD ±5.9] vs 27.2 [SD ±3.9]; $p<0.001$). Those who sustained an FVC were more likely to have diabetes (14.8% vs 53.8%, $p<0.0001$), have hypertension (63.6% vs 82%, p=0.002) and smoke (31.6% vs 70.5% $P<0.001$). Patients who sustained an FVC had a higher mean blood pressure at the time of puncture than the non-FVC group (151 mmHg vs 133 mmHg $p<0.0001$). Those who

had been administered clexane within 12 hours of an arterial puncture were more likely to have an FVC than those who did not have a FVC (15.4% vs 0.8%, $p<0.0001$).

The procedural indications within the overall patient sample were diversely distributed with no statistical significance (outpatient diagnostic cardiac catheterisation, 26%; inpatient cardiac catheterisation, 56%; rescue PCI 2.4%; and primary PCI 6.1%). A 6 Fr arterial sheath was used in 98% of cases, while intra-aortic balloon pumps were used in 1.5% of patients. During the procedure, 26 patients (7.9%) received abciximab and one (0.3%) received bivalirudin. Eighteen patients (5.5%) had a CABG procedure with no statistical difference between groups. A higher rate of vascular closure device use was found in the FVC group than in the non-FVC group (10.4% vs 2.8%, p=0.006).

Table 3.1 Characteristics of patients who sustained femoral vascular complication versus those who did not; n=328

Femoral Vascular Complications				
Characteristic	**No (n=250)**	**Yes (n=78)**	**Total (n=328)**	**p-value**
Demographics				
Age in years (Mean, SD)	62 (13)	65 (14)	63 (13)	0.121
Gender (Female)	90 (36%)	39 (50%)	129 (39%)	0.027
CVD Risk Factors				
BMI (Mean, SD)	27.2 (3.9)	29.2 (5.9)	27.7 (4.5)	0.001
Diabetes (Yes)	37 (14.8%)	42 (53.8%)	79 (24%)	<0.0001
Hypertension (Yes)	159 (63.6%)	64 (82%)	223 (68%)	0.002
Smoker (Yes)	79 (31.6%)	55 (70.5%)	134 (41%)	<0.001
PVD (Yes)	26 (10.4%)	18 (23.1%)	44 (13%)	0.004
Procedural factors				
Systolic BP on Puncture (Mean, SD)	133 (26)	151 (18)	137 (25)	<0.0001
Creatinine - Pre procedure (Mean, SD)	90 (21)	101 (57)	92 (34)	0.007
Creatinine group (Normal <=104)	212 (79%)	55 (21%)	267 (81%)	0.005
Inpatient Angiogram	136 (54.4%)	47 (60.4%)	183 (56%)	0.363
Rescue PCI	3 (1.2%)	5 (6.4%)	8 (2.4%)	0.009
Primary PCI	17 (6.8%)	3 (3.8%)	20 (6.1%)	0.341
Previous CABG	14 (5.6%)	4 (5.1%)	18 (5.5%)	0.873
Cardiogenic shock	10 (91%)	1 (9.1%)	11 (3.4%)	0.784
Medical Management pre procedure				
Acetylsalicylic acid (ASA)	73 (29.2%)	68 (87.2%)	141 (43%)	<0.001
Clopidogrel	77 (30.8%)	37 (47.4%)	114 (35%)	0.007
Pre Procedure Enoxaparin within 12hrs of procedure (No)	2 (0.8%)	12 (15.4%)	14 (4.3%)	<0.0001
Warfarin within 24 hrs	0	6 (100%)	6 (1.8%)	<0.001
Haemostasis Method				
Closure device used	7 (2.8%)	8 (10.4%)	15 (4.6%)	0.006
Digital Pressure removal	126 (50.4)	44 (56.3%)	170 (52%)	0.504
Femoral compression device	117 (46.8%)	26 (33.3%)	143 (44%)	0.036

BMI: Body Mass Index; BP: Blood Pressure; CABG: Coronary Artery Bypass Surgery; PCI: Percutaneous Coronary Intervention; PVD: Peripheral Vascular Disease; SD: Standard Deviation

Using logistic regression analysis, the unadjusted results for the development of an FVC showed that being female (OR 1.8, 95% CI 1.1–3.0), having diabetes mellitus (OR 6.7, 95% CI 3.8–12), having hypertension (OR 2.6, 95% CI 1.4–4.9), being a current smoker (OR 5.2, 95% CI 3.0–9.0), having PVD (OR 2.6, 95% CI 1.3–5.0), having an elevated creatinine level (OR 2.3, 95% CI 1.3–4.2) and taking antiplatelet or anticoagulant medication (OR 8.6, 95% CI 3.8–20) significantly increased the odds of an FVC. A one-point increase in BMI was associated with a 10% increase in the odds of experiencing an FVC (OR 1.1, 95% CI 1.0–1.2). The use of a vascular closure device (OR 4.0, 95% CI 1.4–11) increases the likelihood of FVC but the use of a femoral compression device (OR 0.6, 95%CI 0.3–1.0) reduced the odds of an FVC. Age (OR 1.0, 95% CI 1.0–1.03) and previous CABG (OR 0.9, 95%, CI 0.3–2.9) were not associated with FVC in this sample (*Table 3.2*).

After adjusting for age and sex (Table 3.2), results showed that women were three times more likely to develop an FVC than men (AOR 2.9, 95% CI 1.3-6.1), and that elevated BMI (AOR 1.1, 95% CI 1.0–1.2), diabetes mellitus (AOR 7.5, 95% CI 3.4–16), hypertension (AOR 2.9, 95% CI 1.2–6.9), smoking (AOR 7.5, 95% CI 3.5-16) and taking anticoagulant or antiplatelet medications (AOR 16, 95% CI 5.5–45) increased the odds of FVC. The presence of an elevated creatinine level >104 mmol/litre (AOR 2.5, 95% CI 1.1–5.7) was also significantly associated with the development of vascular complications. The use of a vascular compression device during sheath removal reduced the odds of an FVC by 60% (AOR 0.4, 95% CI 0.2–0.9). Age, cardiogenic shock and the use of a vascular closure device were not independently associated with FVC in this adjusted analysis. Because numbers were low, it was not possible to adjust for PVD and previous CABG in the analysis.

Table 3.2 Crude and adjusted odds ratios for development of femoral vascular access complication (retroperitoneal bleed or pseudoanuerysm)

	Unadjusted			Adjusted		
Characteristic	**Odds Ratio**	**95%CI Lower**	**95%CI Upper**	**Odds Ratio**	**95%CI Lower**	**95%CI Upper**
Age (in years)	1.0	0.99	1.0	1.0	0.98	1.0
Gender (Female vs Male)	**1.8**	**1.1**	**3.0**	**2.9**	**1.3**	**6.1**
Body Mass Index	**1.1**	**1.0**	**1.2**	**1.1**	**1.0**	**1.2**
Diabetes (Yes vs No)	**6.7**	**3.8**	**12**	**7.5**	**3.4**	**16**
Hypertension (Yes vs No)	**2.6**	**1.4**	**4.9**	**2.9**	**1.2**	**6.9**
Smoker (Yes vs No)	**5.2**	**3.0**	**9.0**	**7.4**	**3.5**	**16**
Peripheral Vascular Disease (Yes vs No)	**2.6**	**1.3**	**5.0**	.	.	.
Previous CABG (Yes vs No)	**0.9**	**0.3**	**2.9**	.	.	.
Cardiogenic Shock (Yes vs No)	**4.1**	**1.2**	**14**	**4.3**	**0.8**	**24**
Anti-coagulant/Anti-platelet medication (Yes vs No)	**8.6**	**3.8**	**20**	**16**	**5.5**	**45**
Creatinine Group (>104 vs Normal <=104)	**2.3**	**1.3**	**4.2**	**2.5**	**1.1**	**5.7**
Closure Device Used (Yes vs No)	4.0	1.4	11	3.4	0.61	19
Femoral compression device (Yes vs No)	**0.57**	**0.33**	**1.0**	**0.40**	**0.2**	**0.9**

CABG: Coronary Artery Bypass Surgery

3.6.2 Factors associated with the development of pseudoaneurysm

Further analysis was undertaken to determine the risk profile of patients sustaining pseudoaneurysm and retroperitoneal bleed, adjusted for age and sex. The adjusted odds for pseudoaneurysm development (*n*=55) compared with patients who did not sustain a pseudoaneurysm were reported. For every one point increase in BMI, there

was a 10% increased odds of a pseudoaneurysm (AOR 1.1, 95% CI 1.0–1.2). Having diabetes mellitus (AOR 4.1, 95% CI 2.0–8.5), smoking (AOR 4.1 95%, CI 2.0–8.5) or having peripheral vascular disease (AOR 3.3, 95% CI 1.3–7.9) and taking anticoagulant and antiplatelet medication (AOR 7.5, 95%, CI 2.8–20) were shown to increase the likelihood of pseudoaneurysm development. The use of a femoral compression device was shown to reduce the odds of vascular complications (AOR 0.4 95%, CI 0.2–0.9).

3.6.3 Factors associated with the development of retroperitoneal bleed

Demographics, disease-specific characteristics for patients who had a retroperitoneal bleed (*n*=23) compared with those who did not were examined. A logistic regression model was used to predict the likelihood of retroperitoneal bleed developing in this small group. The model considered sex, age, BMI, diabetes, smoking status, hypertension, PVD, previous CABG, cardiogenic shock, closure device used, femoral compression device removal, renal impairment, heparin dose, and anticoagulation and antiplatelet use.

While the number of patients affected was small (*n*=23), in this model, sex and smoking significantly predicted the development of retroperitoneal bleed (*P*<0.05). Results indicated that male sex conferred a reduced risk of developing retroperitoneal bleed (AOR 0.28, p=0.17, 95% CI 0.10–0.80), while smoking (AOR 4.7, p=0.005, 95% CI 1.56–13) was associated with the development of a retroperitoneal haemorrhage.

3.7 Discussion

This study, conducted at a large regional tertiary referral centre, examined factors associated with the development of FVCs, specifically pseudoaneurysm and retroperitoneal haemorrhage following cardiac catheterisation and PCI. Female sex, elevated BMI, diabetes mellitus, the use of a vascular closure device, hypertension, smoking and renal impairment were associated with an increased likelihood of any FVC. For pseudoaneurysm development, high BMI, diabetes mellitus, smoking, peripheral vascular disease and anticoagulant use were shown to be contributors. For retroperitoneal bleed, female sex and smoking were risk factors in a small group of patients.

The use of vascular closure devices was associated with an increased likelihood of FVC in this sample, while the application of a femoral compression device was shown to reduce the odds of FVC. A meta-analysis of randomised control trials, which included 4000 patients, showed closure devices may increase the risk of FVCs, with a caveat of poor methodological structure of some included studies (Koreny et al., 2004). A meta-analysis comparing vascular closure devices with manual compression involving 7,528 patients reported increases in FVCs with vascular closure devices in a low-risk group of people having cardiac catheterisation only (Biancari et al., 2010). Conversely, vascular closure devices have been shown to reduce the risk of vascular and bleeding complications, when used in combination with intraprocedure medication use such as bivalirudin (Marso et al., 2010). In a large, registry-based study of 1 522 935 patients undergoing PCI, vascular closure

device use and bivalirudin were associated with a significantly lower incidence of bleeding, particularly in a group with a high risk of bleeding complications.

A further benefit of the use of vascular closure devices was shown in the reduction of bleeding including haematocrit loss (a marker for bleeding) in the PCI group. (Romaguera et al., 2012). Overall, 7,718 patients who had undergone PCI through femoral access were evaluated for FVCs and the consequent effect of the degree of blood loss on long-term mortality. Femoral closure devices were shown to be an independent predictor in a reduction in bleeding and FVCs. Definitive conclusions regarding the overall safety of vascular closure devices may be difficult to make without randomised control data comparing the variety of arterial closure methods in a large sample (Schulz-Schüpke et al., 2014). Given that experience with these devices in the management of vascular closure in structural heart disease procedures is increasing, continued improved results in their use could be anticipated in patients undergoing coronary interventions (Toggweiler et al., 2013).

The risk factors for FVCs are well established and our results demonstrate that, despite advances in vascular access techniques, the profile of patients, especially women, at risk of such complications remains unchanged (Levine et al., 2011). As operators increasingly use trans-radial artery access for coronary procedures, resulting in less procedural experience in femoral artery access, and with the emergence of structural interventions requiring a large calibre sheath (using femoral access), femoral vascular complications remain clinically relevant. Recognition that patients with particular characteristics remain at a higher risk, despite presumed

awareness, should reinforce the need to direct approaches to minimise the likelihood of vascular complications.

The data in this study are consistent with those in previous studies, confirming female sex is a strong independent risk factor in the development of FVCs (Piper et al., 2003, Tiroch et al., 2008, Farouque et al., 2005). Potential contributors to the increased risk noted in women (Farouque et al., 2005, Schnyder et al., 2001) includes a smaller diameter femoral artery, the underappreciated effects of oestrogen on arterial structures (Celermajer et al., 1994) and the effect of smaller body size compared with males, which may impair recognition of standard landmarks that may make arterial puncture more problematic (Farouque et al., 2005). In addition, female sex in combination with smoking and its reduction in the thickness of the arterial walls, is thought to be implicated in the development of FVC (Suggs et al., 2013).

This sample suggests that a higher BMI is associated with the development of FVC. Previously published literature has demonstrated that obesity and a high body surface area or BMI are significant risk factors in the development of an FVC (Ates et al., 2006, Kassem et al., 2013). Compared to a trans-radial approach, the femoral approach has a significantly higher incidence of procedural-related morbidity, related to bleeding and vascular complications in the high BMI group for cardiac catheterisation and PCI (Hibbert et al., 2012). The present study supports the need for continued vigilance among nursing staff, even in the trans-radial era, in identifying patients who undergo cardiac catheterisation with a high BMI as a high-risk group.

Hypertension is an important patient-related risk factor for the development of an FVC. This may relate to the presence of hypertension at the time of arterial puncture as well as a documented history of hypertension (Cox et al., 2004, Popovic et al., 2010, Ricci et al., 1994, Tiroch et al., 2008). Measures to prevent hypertension at the time of vascular access, such as pharmacological approaches to sedation and blood pressure management, are important. Renal insufficiency—even when mild—has been shown to be a risk factor in the development of vascular complications (Applegate et al., 2008, Tiroch et al., 2008). The association of renal impairment with vascular complications may be attributed to several clinical factors, including the likely platelet and arterial walls changes that patients with uraemia exhibit; or renal impairment may be associated with comorbidities associated with bleeding complications (Prada-Delgado et al., 2012). This dataset supports previously described research findings (Osten et al., 2008).

This study shows a significant association between the use of combination anticoagulant including the use of heparin, oral anticoagulants, GP IIb/IIIa inhibitors and the incidence of FVCs. The use of GP IIb/IIIa inhibitors has previously been shown to be an independent risk factor in the development of both bleeding and FVCs in several studies (Horwitz et al., 2003, Tiroch et al., 2008). This study population was varied in terms of acute and outpatient populations and the subsequent use of GP IIb/IIIa inhibitors can be considered low.

Furthermore, in patients considered to be at high risk, vascular access procedures may be carried out by a more experienced operator, thereby reducing the risk associated with aggressive antithrombotic therapy (Ammann et al., 2003). More

experienced operators have been shown to have lower complication rates, and a higher procedural volume may be a protective factor in the development of complications (Levine et al., 2011); this could well be used to generate further hypotheses for future study, particularly in the realm of structural heart disease.

The centre in this study relies on predominantly a 6 Fr arterial access system for cardiac catheterisation. While the sample of patients who received a larger size sheath is small, a larger sheath size has been shown to increase the likelihood of an FVC (Uhlemann et al., 2012).

3.7.1 Strengths and limitations

The main strength of this study is that the dataset consists of consecutive, prospectively obtained clinical data and allows vascular complications to be assessed in a diverse patient sample, including in people undergoing rescue PCI and treatment for cardiogenic shock.

This study was a case control design so traditional limitations of unintentional bias and the difficulties of matching may be apparent in this sample (Mann, 2003)(Mann, 2003). However, given that the outcome of FVC is relatively uncommon, this was the only feasible and efficient approach and may be helpful in generating hypotheses that can be tested using stronger designs. The data are from a single centre and the authors were not able to report the experience level of the operator undertaking vascular access as this was not routinely recorded. High experience level and

procedural volume has been associated with a reduction in FVCs in previous studies (Levine et al., 2011).

3.8 Conclusion

Several modifiable and non-modifiable risk factors are associated with the development of FVC, including being female, smoking and having a high BMI, diabetes mellitus or hypertension, as well as clinical issues such as anticoagulant use and renal impairment.

While these risk factors are well established, the persisting increased risk experienced by these patients reflects the continued need for improvements in approaches to femoral vascular access. Continued vigilance around modifiable procedural aspects, including anticoagulation and haemostasis method, remain an important aspect of nursing care.

Chapter 4:

A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction

This chapter comprises a manuscript submitted for peer review as an original research article to the International Journal of Nursing Practice. References are included at the end of the thesis.

4.1 Preamble

As chapter 3 demonstrated, femoral vascular access is a safe and widely used method for cardiac catheterisation and PCI. Femoral vascular access was the standard method of arterial access for patients undergoing cardiac catheterisation for a long period of time. The technical methods are well known and enhancements of methods to reduce femoral vascular complications were implemented, including fluoroscopy and ultrasound (Seto et al., 2010, Abu-Fadel et al., 2009, Gedikoglu et al., 2013).

This chapter follows on from the previous study by further evaluating vascular access complications. This chapter explores the inpatient and long term clinical outcomes during the transition period from femoral to radial access and expands on the systems in place to review and detect adverse events. The institution examined in this study adopted the trans-radial approach, firstly in non-urgent patient cohorts,

than transitioned to the emergent STEMI population of patients. Internationally, there is an increased uptake of trans- radial access over the traditional femoral access.

This chapter reports a real world examination of clinical factors and outcomes, and may be of high interest to staff from institutions who are contemplating a change in arterial access site. Given the burden of heart disease and the large number of cardiac catheterisation procedures performed around the world, a real world examination of the transition from arterial access methods in an acute patient group is timely and important.

This study examines demographic, clinical, procedural, and outcome measures associated with patients presenting with STEMI who underwent acute Percutaneous Coronary Intervention via trans-radial or femoral access. Findings from this study highlight that transition from femoral to radial access in patients presenting with STEMI is a safe option, with reduced bleeding complications, reperfusion times and blood transfusions. This study supports the need for a contemporary nursing workforce to have knowledge of patient outcomes, particularly in regards to bleeding outcomes.

4.2 Abstract

Aim To compare the health outcomes for patients presenting with ST segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) using femoral access or trans-radial access.

Design: A retrospective cohort study.

Background: Internationally there is a trend towards the adoption of trans-radial access over femoral access due to well described benefits in reduced bleeding complications.

Method: We assessed a consecutive cohort of patients presenting with STEMI over a four-year period. Univariate analyses were performed to examine the association of vascular access site with end point outcomes. The primary outcome was Net Adverse Clinical Events (NACE), a composite of 30-day mortality, 30-day readmission and in hospital bleeding events. Secondary endpoints were one- year mortality, one-year readmission and 30-day readmission for stroke. The STROBE checklist was completed.

Results: During the study period there were 552 STEMI patients, comprising 219 who underwent PCI via femoral access and 333 (60%) via trans-radial access. Demographics were comparable in both groups. Body mass index was significantly higher in the trans-radial access group and prior hypertension, dyslipidaemia and prior CABG were significantly higher in the femoral access group. There were differences in NACE; femoral access had significantly higher 30-day mortality, higher transfusion rate, higher rate of bleeding, and higher one year mortality in the unadjusted analysis. After adjustment there was no statistical difference in endpoint outcomes. There was a reduced diagnostic ECG to device time in the trans-radial access group compared to the femoral access group.

Conclusion: A transition from femoral to radial access in patients presenting with STEMI is a safe option with reduced bleeding complications, reperfusion times and blood transfusions.

4.3 Introduction

Cardiac catheterisation is performed approximately seven million times across the world each year (Patel et al., 2010), and was traditionally performed via femoral arterial access (Azzalini et al., 2014). Trans-radial access (TRA) in cardiac catheterisation and percutaneous coronary intervention (PCI) has well described benefits in terms of reduced vascular complications, mortality, bleeding, and length of stay when compared to the traditional approach of femoral access (FA) (Tayeh and Ettori, 2014, Jolly et al., 2009, Agostoni et al., 2004, Cantor et al., 2011, Eikelboom et al., 2006, Brener et al., 2017, Jolly et al., 2011b, Ferrante et al., 2016).

4.4 Background

Vascular complications have been shown to be an independent predictor for increased morbidity and ischaemic events in patients undergoing PCI (Jolly et al., 2009, Baklanov et al., 2013, Eikelboom et al., 2006, Rao et al., 2005). The advantages of using TRA over FA include the compressible, smaller calibre nature of the vessel which reduces the potential for bleeding complications, plus the benefits of early mobilisation and increased patient comfort (Agostoni et al., 2004, Cooper et al., 1999). Due to these advantages, the European Society of Cardiology has recommended TRA as the access site of choice for PCI (Roffi et al., 2016).

Barriers to the use of TRA in ST-segment elevation myocardial infarction (STEMI) include the more technically challenging nature of TRA for operators when compared to FA during the transition phase, a higher rate of failure to cross the culprit lesion, increased diagnostic electrocardiograph (ECG) to device times, increase in the proceduralist's radiation exposure, and increased procedural time (Tayeh and Ettori, 2014, Jolly et al., 2009, Hamon and Coutance, 2009, Dauerman et al., 2011). These barriers may lead to the under-utilisation of TRA in patients presenting with STEMI and may therefore have a negative impact on morbidity and mortality. Given the adoption of trans-radial access, documenting the experience of transitioning arterial access methods is of importance to the contemporary international nursing workforce.

The importance of nurses recognising adverse events is now articulated in nursing position statements and guidelines (White et al., 2018). Nurses play a key role in understanding the causes of procedural complications and adverse events (White et al., 2018, Henneman et al., 2010), and the positive impact nurses have on enhancing patient outcomes in interventional cardiology is now well described (Leeper, 2004, Spruce and Butler, 2017)

This study aimed to evaluate a single centre's experience of transitioning from a traditional FA approach to a TRA approach in patients presenting with STEMI, in terms of bleeding complications, procedural parameters, 30-day and one year clinical outcomes.

4.5 Methods

4.5.1 Study design and population

A retrospective cohort study, using prospectively collected data from 552 consecutive patients admitted to a large regional tertiary referral hospital following STEMI between January 1 2009 and December 31 2013 was undertaken. FA was the preferred access method in this hospital's catheterisation laboratory until July 2010. This centre transitioned to TRA after this period.

4.5.2 Participants

Consecutive patients aged 18 years and older, with a confirmed STEMI who were referred to the cardiac catheterisation laboratory for primary PCI. There were no exclusions.

4.5.3 Measures

Demographic characteristics (age and gender), cardiovascular disease risk factors, medications for cardiovascular disease, relevant procedural timing and clinical timing parameters were examined for association with the primary outcome. Total ischaemic time was measured from the time of chest pain onset to time of PCI. The primary outcome was defined as Net Adverse Clinical Event (NACE) which is a composite of death at 30 days, readmission at 30 days, and in hospital bleeding

events using the Bleeding Academic Research Consortium measure (BARC 2-5). Secondary endpoints were one- year mortality, one-year readmission and 30-day readmission for stroke.

4.5.4 Data sources

Data was obtained by accessing available patient records and clinical databases. All admission related information was obtained from the hospital's inpatient tracking systems. The patient's cardiovascular risk factors and history were sourced from the patient's medical records. Fluoroscopy times were sourced from the patient's individual radiation record verified by a senior radiographer; the patient's procedural time was obtained from the haemodynamic reporting system within the cardiac catheterization laboratory. Clinical data including diagnostic ECG to device time, procedural data, and vascular access were sourced from the hospitals prospectively maintained STEMI database. Mortality and hospital readmission data were sourced from the health district's Cardiac and Stroke Outcomes Unit database, where data is linked from the NSW Register of Births, Deaths and Marriages quarterly. This prospectively collected and maintained registry data is automatically generated based on clinical coding and logging of patients in a retrievable database which enables contemporary collection of outcome data.

Ethics approval was obtained from the Hunter New England Human Research Ethics Committee (AU 201807-12). The study was performed in accordance with the Declaration of Helsinki (Forster et al., 2001).

4.5.5 Statistical methods

Data was cleaned and check for implausible errors and all analyses were programmed using STATA Version 14 (StataCorp LLC, Texas, USA). Descriptive statistics are presented by counts and percentages for categorical variables and means (standard deviation) or median (interquartile range) for continuous variables. Prevalence of outcomes are reported with 95% confidence intervals (CI). Comparison of categorical variables was performed using Pearson's Chi squared test; for continuous variables t-tests or Mann-Whitney u tests were used, distribution dependant.

Univariate and multivariate logistic regression analyses were performed to examine the association of vascular access location with end point outcomes. Crude and adjusted odds ratios with 95% CI are shown; statistical significance is set at $p<0.05$. The multivariate model was adjusted for age and gender and clinical variables where the p-value was <0.250 on univariate analysis. The adjusted odds ratios were calculated with adjustment for: ECG balloon time, age, gender, BMI (Body Mass Index), cardiogenic shock, prior PCI, prior Coronary Artery Bypass Graft (CABG), and baseline mean creatinine

The number of STEMI patients undergoing primary PCI annually during the transition period and the corresponding proportion of the previously traditionally planned femoral approaches for PCI each year are reported. The cross over rate from TRA to FA is also be reported.

4.6 Results

A total of 552 consecutive patients with STEMI were referred for primary PCI at the study centre from 2009 to 2013 of whom 219 patients (39.7%) had femoral arterial access and 333 had radial artery access. The mean age was 64 years (SD 12.56) and 73.6% were male. There were no demographic and medication differences between vascular access site groups. A significantly higher proportion of patients in the FA group recorded a history of hypertension, dyslipidaemia and previous coronary artery bypass surgery (CABG). The mean BMI was higher in the TRA group compared to the femoral access group (30.0 vs 28.7 p=0.007). Smoking history, diabetes, prior myocardial infarction and prior PCI were similar in both groups. A profile of this cohort is detailed in Table 4.1.

The median diagnostic ECG to balloon time was significantly shorter in patients undergoing TRA compared to FA (87 min vs 98 min; p=0.003). The mean total ischemic time was higher in the TRA group (210 minutes (IQR 145-300) compared to the FA group (189 minutes (IQR 135-280), however the difference was not statistically significant (p=0.27). When comparing FA to TRA during this transition period there was a preference to use the more familiar FA in those patients with cardiogenic shock on arrival (16.4% vs 3.0% p< 0.001), and those requiring inotrope use (22.8 % vs 6.3 %, p=0.000). There was a 2.5% (n=14) crossover from radial access to femoral access, indicating unsuccessful radial

access due to uncontrollable patient factors such as arterial tortuosity, radial spasm or the inability to adequately position catheters for the diagnostic and interventional procedure.

In terms of bleeding outcomes, the femoral access group included four computerised tomography scan confirmed retroperitoneal bleeds, one pseudoaneurysm and eight femoral haematomas. There were no vascular complications in the TRA group. There were significant differences in transfusion rates between femoral access and radial (9.1% vs 3.0% p=0.002).

Table 4.1 Baseline Characteristics of patients referred for primary PCI post STEMI by vascular access site

Variable	Femoral n=219	Radial n=333	p-value
Demographics			
Age mean (SD)	63.7 (12.6)	64.6 (12.8)	0.401
Male sex n (%)	248 (74.3)	158 (72.5)	0.644
CVD risk factors and history			
BMI (kg/m2) mean (SD)	28.7 (4.3)	30.0 (6.1)	**0.007**
Dyslipidemia n (%)	107 (48.9)	104 (31.3)	**< 0.001**
Hypertension n (%)	161 (73.5)	179 (54.4)	**<0.001**
Diabetes n (%)	48 (21.9)	85 (25.7)	0.313
Smoking History n (%)	115 (52.5)	190 (57.2)	0.276
Prior MI n (%)	44 (20.1)	55 (16.6)	0.290
Prior CABG n (%)	13 (5.9)	3 (0.9)	**0.001**
Prior PCI n (%)	17 (7.8)	39 (11.8)	0.130
Regular CVD Medications			
Angiotensin-converting enzyme (ACE) inhibitors n (%)	55 (25.1)	63 (19.0)	0.086
Beta blocker n (%)	31 (14.2)	39 (11.7)	0.399
HMG-CoA reductase inhibitors (Statin) n (%)	44 (20.1)	69 (20.7)	0.858
Acetylsalicylic acid n (%)	56 (25.7)	72 (21.7)	0.250
Clinical procedural timing parameters			
Diagnostic ECG to device, minutes (median + IQR)	98 (75-120)	87 (63-117)	**0.003#**
Chest pain to device time (median +IQR)	210 (145-300)	189 (135-280)	0.270#
Clinical Parameters			
SBP on arrival	129 (29.1)	129 (22.1)	0.990
Baseline Creatinine mean (SD) (µmol/L)	99.7 (36.5)	94.5 (33.2)	0.089
Baseline Hb mean (SD) (g/L)	140.1 (18.6)	140.4 (16.2)	0.874
Thrombolysis given (eg. Rescue PCI) n (%)	28 (12.9)	59 (17.7)	0.13
Inotropes used n (%)	50 (22.8)	23 (6.9)	**< 0.001**
Cardiogenic shock on arrival n (%)	36 (16.4)	10 (3.0)	**< 0.001**

BMI: Body Mass Index; MI Myocardial Infarction BP: Blood Pressure; CABG: Coronary Artery Bypass Surgery; PCI: Percutaneous Coronary Intervention; SD: Standard Deviation: ACE: Angiotensin converting enzyme inhibitors; IQR: Inter Quartile Range; # Wilcoxon Rank Sum Test

Important clinical procedural elements of cardiac catheterisation showed fluoroscopy dose (2571 mGy vs 2530 mGy, p=0.836), and contrast dose (195 mls vs 189 mls, p=0.326) were similar in the TRA group compared to the FA group. There was no penalty in the transition phase of increasing procedural time in the radial group compared to the femoral access group (54.3 minutes vs 55.4 minutes, p=0.608). Similar rates of Glycoprotein IIb/IIIa inhibitor usage

were noted between the two arterial access groups (FA 49.1% vs TRA 47.9% p=0.785).

The unadjusted analysis of the primary endpoint showed that NACE was almost two times greater in the femoral group compared to the radial group (31% vs 18.9%, OR 1.93 95% CI 0.91-2.38, p=0.001). The secondary endpoints showed a higher one-year mortality in the femoral group compared with the radial group (14.2% vs 5.7%, OR 2.72, 95% CI 1.50 – 4.96, p=0.001). In the unadjusted analysis, there was a significant increase in 30 day mortality in the FA group compared to the TRA group (11.4 % vs 3.3%, OR 3.77 p=0.001). Refer to Table 4.2.

NACE was almost one and half times greater in the FA group compared with the TRA group. When adjusted for the following variables: age > 75 years, gender, hypertension, BMI >25, diabetes, creatinine > 100, cardiogenic shock on arrival, prior MI, prior PCI, NACE was no longer significant (Table 4.2). The one-year readmission and 30-day stroke readmission rates were similar between access sites, this was no longer significant in the adjusted model.

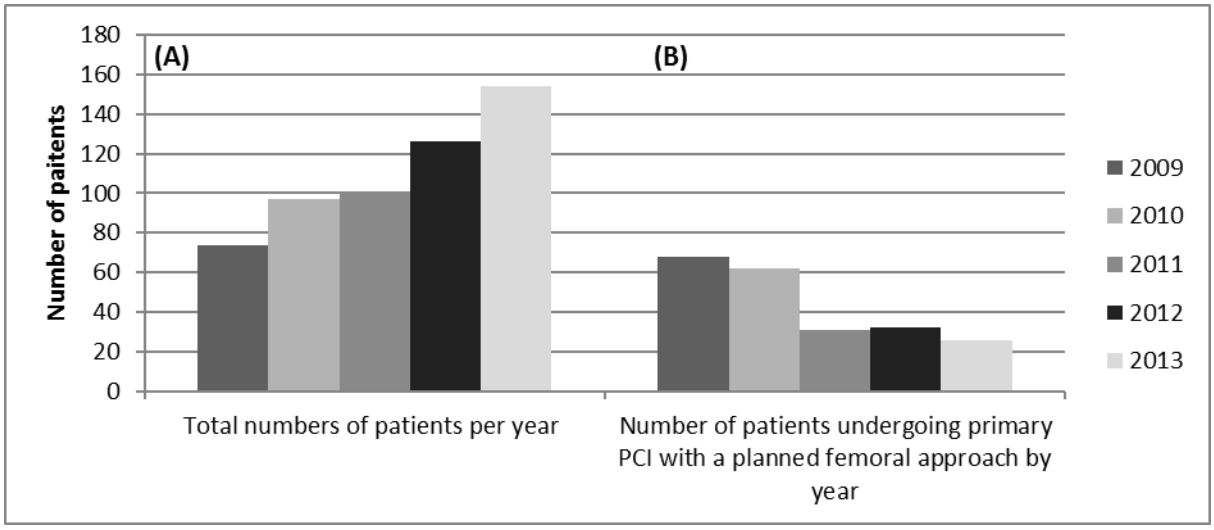
Table 4.2 Logistic regression analyses for primary and secondary endpoints: Femoral access vs Trans- Radial access

	Femoral n = 219 n (%)	Radial n = 333 n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Primary Endpoint						
NACE	68 (31)	63 (18.9)	1.93 (1.29 – 2.87)	0.001	1.47 (0.91 – 2.38)	0.118
Secondary Endpoints						
30 day mortality	25 (11.4)	11 (3.3)	3.77 (1.81 – 7.83)	< 0.001	2.11 (0.81 – 5.51)	0.124
30 day readmission	34 (15.5)	47 (14.1)	1.12 (0.69 – 1.80)	0.647	1.21 (0.70 – 2.09)	0.500
BARC 2-5 bleed	19 (8.7)	13 (3.9)	2.34 (1.13 – 4.84)	0.022	1.74 (0.63 – 4.84)	0.288
1 year mortality	31 (14.2)	19 (5.7)	2.72 (1.50 – 4.96)	0.001	1.74 (0.83 – 3.70)	0.145
1 year readmission	76 (34.7)	111 (33.3)	1.07 (0.74 – 1.52)	0.739	1.15 (0.76 – 1.73)	0.512
30 day stroke readmission	7 (3.2)	11 (3.3)	0.97 (0.37 – 2.53)	0.945	0.79 (0.27 – 2.32)	0.675

NACE: Net Adverse Clinical Event; BARC: Bleeding Academic Research Consortium

Trends during the study period in terms of the annual number of primary PCI cases following STEMI and the corresponding number of planned femoral approaches are illustrated in Figure 4.1. There is a reduction in the proportion of femoral cases from approximately 65% in 2009 to 25% in 2013, as radial access became the preferred arterial access method. Additionally, there was an increasing number of procedures performed during the study period. See Figure 4.1

Figure 4.1 (A) Total number of STEMI presentations to the facility (B) Total number of planned trans-femoral approaches to PCI



Legend: There was an increasing number of procedures performed, with a corresponding decrease in the use of trans-femoral approach for PCI for STEMI patients

4.7 Discussion

This paper aimed to compare clinical outcomes following a change in arterial access route in a high - risk cohort of patients with STEMI undergoing PCI in a tertiary referral centre. The experience of institutional change of practice from FA to TRA is reported. The results indicate the benefits that can be achieved with this change in practice. The TRA approach offers advantages in clinical outcomes over the FA approach including reduced bleeding complications and transfusion rates, despite the operator's preference for FA in more complex presentations. This benefit comes without penalty in the important clinical parameters of increasing contrast dose or procedural time.

The use of TRA has been associated with improved outcomes in terms of mortality, myocardial infarction, bleeding complications and vascular injury (Cantor et al., 2015, Brener et al., 2017, Ferrante et al., 2016, Jolly et al., 2011b). Similarly, the need for timely reperfusion in STEMI patients is definitively established and requires a time sensitive approach (Ezad et al., 2018, Khan et al., 2016). Of particular note, this dataset showed a reduced time from diagnostic ECG to device time in the TRA group. Two important caveats are, firstly the higher procedural acuity in the femoral group, illustrated by a higher rate of cardiogenic shock and inotrope usage, which may delay critical aspects of the procedure due to case complexity. Secondly, in the TRA era there was significantly more patients admitted under the paramedic initiated pre hospital ECG strategy which has shown benefits in reducing diagnostic ECG time (Savage et al., 2014)

An important perceived barrier to the use of the TRA approach is the potential for increased procedure duration. The data presented is reassuring that TRA can be adopted without penalty in terms of procedural duration. Additional concerns regarding the use of TRA is the previously described increase in radiation screening times for radial access (Mercuri et al., 2011, Brueck et al., 2009, Hirshfeld Jr et al., 2004). While there was an increase in fluoroscopy times in the radial group, this was not statistically significant, noting this metric reflects the radiation dose for the patient and not operator exposure. Operator exposure to radiation remains a significant issue for all cardiac catheterisation employees and the adoption of new techniques should include review of appropriate safety measures (Naidu et al., 2016).

There are clear benefits in reduced bleeding complications and reduced rates of transfusion in the radial access group, noting a higher rate of post thrombolysis patients in the radial access group. Post thrombolysis patients appear to benefit from radial access, reflecting favourable bleeding outcomes (Andò et al., 2016). From an organisational standpoint the benefits of utilising the radial artery in appropriate patients are important considerations.

The crossover rate from radial access to femoral access in this group compares favourably to other published data (Azzalini et al., 2015). The operators had experience with radial artery access in non-urgent cases before transitioning to radial access in primary PCI following STEMI. This may have allowed increased proficiency under less acute conditions allowing operators to gain experience in radial access. Institutions contemplating a change in arterial access method should be reassured by this data.

The strength of this dataset is that it reflects a prospectively collected real-world analysis of a change in vascular access approach in a high-risk, diverse patient group (Davies et al., 2017). The limitations of this dataset are that it is an observational study and therefore potential confounders of the relationship between vascular access route and outcomes of interest cannot be completely accounted for in the analysis, particularly during a transition period. There are limitations of using medical record data; for this study some information was sourced directly from the

patient and then recorded in the medical notes, which has previously been described as having potential inadvertent inaccuracies (Kaji et al., 2014).

4.8 Conclusion

A change in practice from femoral to radial access for patients admitted for STEMI who underwent emergency PCI experienced a positive impact during the transition period on transfusion rates and vascular complications. Previously documented concerns regarding significant increase in time to reperfusion and fluoroscopy times were not apparent in this study. STEMI presentations should not be considered a barrier to utilisation of TRA in centres contemplating a change of this important clinical parameter.

Chapter 5

Nursing led ultrasound to aid in trans-radial cardiac catheterisation: A feasibility study

This chapter comprises a manuscript submitted for peer review as an original research article to the Journal of Research in Nursing. References are included at the end of the thesis.

5.1 Preamble

The benefits conferred by radial arterial access were examined in the previous chapter. An innovative model of care was introduced to detect radial artery occlusion, an adverse event post cardiac catheterisation for patients undergoing radial artery access. The previous chapter articulated the clinical and organisational benefits conferred by trans-radial access in the transition phase of a change in arterial access method.

With the emergence of trans-radial access there is an imperative to monitor the adverse events associated with the change in clinical practice. One of the emerging areas of research is the examination of radial artery occlusion after cardiac catheterisation. While radial artery occlusion does not have the prognostic impact of femoral complications, there are several important complications which may occur in trans-radial access. Radial artery occlusion, in most cases renders the radial artery

unusable, thereby requiring operators to use femoral access, conferring a higher risk to patients.

The nursing workforce plays an important role in the care of patients undergoing cardiac catheterisation at all facets of the patient's journey including the pre, intra, post procedure, and follow up care of patients (White et al., 2018). A nursing workforce equipped to monitor and record radial artery occlusion offers clinical benefits to the wider cardiology community.

This chapter provides original research into the clinical feasibility of implementing a nursing-led program to measure radial artery diameter before and after cardiac catheterisation using ultrasound, in addition to identifying potential causes of complications. This chapter describes this key policy change within this clinical environment. This study is timely due to notable uptake of radial artery access in the widely performed cardiac catheterisation and PCI procedures. Knowledge of the key facets of this procedure and the subsequent clinical management issues that this study addresses are important and may be readily translatable and scalable to any cardiac catheterisation laboratory.

The study presented in this chapter is a prospective cohort study of a consecutive patient group which assess radial artery occlusion, radial artery diameter and the feasibility of setting up this programme.

5.2 Abstract

Background: Trans-radial access is increasingly common for cardiac catheterisation. Benefits include reduced bleeding complications, length of hospital stay and costs for the institution.

Aims: To 1) Evaluate the clinical feasibility of implementing a nursing-led program to measure radial artery diameter before and after cardiac catheterisation using ultrasound, 2) Determine radial artery occlusion (RAO), 3) Determine risk factors for RAO and 4) Determine predictors of radial artery diameter.

Method: A prospective observational cohort study design was used to collect imaging data on 100 consecutive patients undergoing cardiac catheterisation or percutaneous coronary intervention using radial artery access. Pre and post-procedural radial artery diameter were measured using ultrasound undertaken by trained nurses. Logistic regression analysis was performed to determine risk factors for RAO and predictors of radial artery diameter with results reported as Odds Ratios (OR) and 95% confidence intervals (CI).

Results: Nurse led ultrasound programmes are safe and feasible with no adverse events. A 4% (n =4) rate of occlusion was observed immediately following compression band removal from access site. A haemostasis device application time

of greater than 190 minutes was a predictor of RAO (OR 3.12 95% CI 0.31-31.1). Male gender and height were predictors for a radial artery diameter of >2.2mm.

Conclusions: Trained nurses can safely lead the assessment of radial artery occlusion within a cardiac catheterisation laboratory to enhance planning and care, including the monitoring of compression times to reduce RAO.

5.3 Introduction

Trans-radial access (TRA) for cardiac catheterisation has become an increasingly used method of arterial access in many centres throughout the world (Santos et al., 2012, Masoudi et al., 2017, Fech et al., 2012). This has been driven by the well-described benefits of TRA compared with trans-femoral access, particularly in patients undergoing percutaneous coronary intervention (PCI) (Dharma et al., 2017). The main benefits of TRA are the reduction of adverse bleeding events, vascular complications, decreased length of stay, improved patient comfort, and cost savings compared to a trans-femoral approach (Amin et al., 2017, Koutouzis et al., 2016, Jolly et al., 2011b). Given these benefits, the European Society of Cardiology has recommended TRA as the preferred access site for PCI (Roffi et al., 2016).

Radial artery occlusion (RAO) following cardiac catheterisation and PCI occur in approximately 5% to 30% of patients (Beyer et al., 2013). Such complications can have a significant impact on patients undergoing this procedure (Uhlemann et al., 2012). A major clinical implication of RAO is that the radial artery (RA) will be unable to be used for further procedures (Pancholy et al., 2012). Major contributors to RAO after cardiac catheterisation include anticoagulation use, compression device application time, and reduced arterial sheath size in comparison to the patient's RA diameter (Saito et al., 1999).

A nurse led approach to ultrasound is widely described among other specialities, including renal, urology, and peripheral cannula teams (Oliveira and Lawrence, 2016, Moore, 2013, Giles et al., 2015). There is evidence of the benefit of nurse led ultrasound initiatives in improving patient care, reducing complications, reducing hospital costs and promoting patient comfort (Steinwandel et al., 2017, Baumann et al., 2008). From a cardiology nursing perspective, a nurse led approach to the performance of ultrasound examination of arterial access has not reported within the literature.

5.4 Aims

This paper describes a single centre experience using a prospective observational cohort study design of a nursing-led model with four main aims: 1) to determine the feasibility of implementing a nursing-led ultrasound program to measure radial artery diameter before and after cardiac catheterisation; 2) to determine radial artery occlusion (RAO) rates; 3) to determine risk factors for RAO, and 4) to determine predictors of radial artery diameter.

This study involved training specialist nurses to perform basic ultrasound measurements and quantify the radial artery diameter in the pre and post procedure phases of cardiac catheterisation.

5.5 Materials and Methods

The study was conducted from 30th November 2016 to 21st December 2016. Ethical approval was obtained from the institutional human research ethics committees (AU201702-05). Verbal consent was obtained from all patients. The investigation conforms with the principles outlined in the Declaration of Helsinki (Rickham, 1964).

5.5.1 Participants

Consecutive adult patients who underwent a cardiac catheterisation or PCI (n=100) during the study period, using a radial artery approach in a regional tertiary referral centre; patients were not randomised.

5.5.2 Inclusion and Exclusion criteria

All patients undergoing cardiac catheterisation or PCI procedures using a radial artery approach were eligible for inclusion. Patients with ST-segment myocardial infarction (STEMI) were excluded as were patients where a trans-femoral approach was used for the procedure (n=26). Included within this group were (n=7) patients who had a crossover arterial access from radial to femoral access. In addition, ST segment myocardial infarction patients (STEMI) were excluded (n=19).

5.5.3 Research Design

The study was performed using a prospective observational cohort study design.

5.5.4 Study Setting

The tertiary referral hospital used in this study is located in regional NSW Australia. The referral base is approximately 131,785 square kilometres with a population of 950,000 people on the east coast of Australia. The cardiac catheterisation laboratory is staffed by senior interventional cardiologists, fellows and training resident staff, in addition to nursing, radiography and cardiac technical staff. This cardiac catheterisation laboratory performs approximately 2200 cardiac catheterisations and PCIs each year, in addition to treating approximately 400 patients with STEMI each year (Khan et al., 2016).

5.5.5 Protocol and Procedures

Radial artery occlusion was defined as the absence of flow using doppler after undergoing invasive assessment and treatment. Radial artery diameter was examined to define sheath to artery ratio.

Prior to commencement of the study routine ultrasound to quantify measurements of the radial artery prior to a procedure, were not current practice in this group of

patients. To undertake this study the following protocol using a standardised approach was conceived and developed by a clinical nurse specialist (TW) and reviewed by a professor of cardiology (AB). Four senior nursing staff employed as clinical nurse specialists were selected to undergo training in ultrasound measurements limited to radial artery diameter and flow dynamics. Staff were selected based on having more than 5 years cardiac catheterisation experience and post graduate qualifications in cardiac nursing. Initial training of the technique to be used by the specialist nurses was undertaken by a professor of cardiology with extensive experience in this area. Further training involved a review of current literature, training in the recording of information to ensure standardisation of data collection, and a didactic educational presentation.

The specialist nurses were accredited to undertake the procedure when examination of the radial artery diameter and patency were accurately recorded against a known radial artery assessment result. To ensure accuracy of performance of the ultrasound, inter-observer reliability assessments were undertaken during this training period, assessed using “percentage of agreement”. All trained specialist nurses achieved the required 90-95% to establish inter observer reliability (Burns, 2014). Once inter-observer reliability was achieved on 20 patients, the trained nurse specialist commenced independently measuring and recording the radial artery diameter. Patency flow images were recorded immediately before the procedure-and after haemostatic device removal post procedure. Images that indicated RAO were reviewed by the interventional cardiologist on duty during the training period.

Trained specialist nurses who performed the ultrasound were rostered in the pre procedure and recovery areas of the catheterisation laboratory to avoid any disruptions to work flow. Prior to cardiac catheterisation all patients had an ultrasound performed to the radial artery using the Sonosite S-ICU machine using a 10 hertz probe (Sonosite Inc, Bothell USA) by the trained nurses. Longitudinal and cross sectional images were obtained for each patient. An arm board was used on each patient for bracing hand extension to ensure consistent angle of measurement. The diameter of the radial artery (RA) was obtained by measuring one centimetre proximal to the styloid process and then measuring internal diameter of the RA. Calliper measurements were performed and images were stored. The longitudinal view was then obtained and doppler flow was assessed to determine artery flow post procedure recorded in this view to the mid-forearm. Radial artery measurements were recorded in millimetres.

Radial artery access was obtained by the attending proceduralist, which included senior interventional cardiologists, interventional fellows and training cardiologists. Lidocaine 1% was administered prior to radial artery sheath insertion. Patients routinely received intra-arterial glyceryl trinitrate and heparin with varying doses depending on the proceduralist's preference. The arterial sheaths were removed from all patients immediately post procedure. Haemostasis was achieved using a commerically available radial haemastasis device.

Ultrasound measurements were repeated following haemostasis device removal undertaken by the same trained nurses who took the pre-procedure measurements. No adverse events related to the ultrasound procedure were recorded in this group of patients. Ultrasound equipment is easily accessible in most cardiac catheterisation environments. The training and supervision of nurses allowed easy adoption of this low risk, non-invasive adjunct to patient care.

5.5.6 Other Measures

Demographic information, cardiovascular disease risk factors and medical management information were obtained by accessing patient's medical records. The procedural time, procedural characteristics and radial artery measurements were obtained from both the patient's medical records and the haemodynamic reporting system within the cardiac catheterisation laboratory. Admission related information was obtained from the hospital's inpatient tracking systems. Variables were selected according to clinical relevance. Data was stored on a password protected database.

5.5.7 Statistical methods

All statistical analyses were programmed using SAS v9.4 (SAS Institute, Cary, North Carolina, USA). Baseline descriptive statistics are presented by counts and percentages for categorical variables and means (standard deviation) or median (min, max) for continuous variables. Based on medium effect size and predictor

variables and 80% power the required sample size to detect population associations is approximately n=98 using 0.05 significance level tests.

Logistic regression was performed to determine the factors associated with RAO (yes or no) following cardiac catheterisation. The variables examined in the model selected on clinical relevance were sex (male vs females), age (categorised as greater than 65 years or less than or equal to 65 years) and obesity (BMI > 25). Procedural data included anticoagulant dosage of Heparin, the dosage of sedation, the number of punctures, sheath to artery ratio of >1, presence of RA spasm, radial diameter <2.2mm, TR application time of > 190 minutes and procedural length >30 minutes.

Logistic regression was performed to determine factors associated with radial artery diameter of 2.2mm or greater based on the mean diameter of the patient group. Variables examined in this model were sex (male or female), age (greater than 65 years or less than or equal to 65 years), Body Mass Index (BMI) greater than 25 or less than or equal to 25, current smoker (yes or no), diabetes (yes or no), hypertension (yes or no), dyslipidaemia (yes or no) and systolic blood pressure (greater than 140mmHg). Height was dichotomised based on the mean height of 1.72 metres (less than or equal to 1.72 metres or above 1.72 metres) and weight was dichotomised based on the mean weight of 88kg (greater than 88kg or less than or equal to 88kg).

Results of the logistic regressions are reported as odds ratios (OR) or adjusted ORs (AORs) with 95% confidence intervals (CI). Statistical significance is set at $p < 0.05$. Due to the low number of patients with unfavourable procedural outcomes, only age and gender were adjusted for in the regression model.

5.6 Results

Of the 145 patients who underwent a cardiac catheterisation or PCI in the study period, 26 patients were excluded as a trans-femoral approach, including patients requiring cross-over to femoral artery access. Additionally, 19 patients with STEMI were excluded due to the time sensitive approach required for reperfusion therapy. Therefore there were 100 consecutive patients following TRA included in this study, and of these 4 patients (4%) experienced an in-hospital RAO. Patient demographic information, risk factor status, procedural characteristics, medical management and radial artery access data are summarised in Table 5.1. The mean age of the group was 64 years, and 71% were male; 78% were overweight (mean BMI 29.3, SD 6.4). This patient group had a background of significant coronary heart disease, including prior myocardial infarction (36%), prior coronary artery bypass graft (CABG) (11%) and aortic stenosis (15%). Cardiovascular risk factors included hypertension in 75% and a history of tobacco consumption in 62%.

Table 5.1: Characteristics of consecutive patients undergoing trans-radial access for coronary catheterisation or percutaneous coronary intervention (n=100)

Variable	Characteristic	Characteristic n (%)
Demographics		
Sex	Male	71 (71%)
Age in years	mean	63.7
Height	mean (SD)	172 (10.1)
Weight	mean (SD)	88.3 (21.8)
Body Surface Area	Metres^2	2.02 (0.29)
Cardiovascular Disease Risk Factors		
Hypertension (>140mmHg)	Yes	75 (75%)
Dyslipidaemia	Yes	70 (70%)
Diabetes	Yes	40(40%)
Body Mass Index	Mean (SD)	29.3 (6.4)
Creatinine	mean	87.5
Smoking	Current	40 (40%)
	Ex- smoker	22 (22%)
Previous cardiovascular disease	Prior AMI	36 (36%)
	Prior CABG	11 (11%)
	Aortic stenosis	15 (15%)
	PVD	1 (1%)
Procedural Characteristics		
Cardiac Catheterisation	Outpatient	32 (32%)
	Inpatient	25 (25%)
Percutaneous Coronary Intervention	Outpatient	11 (11%)
	Inpatient	32 (32%)
Prior radial access	Yes	14 (14%)
Systolic BP at arterial puncture	mean (SD)	137.3 (24.2)
Disease severity	No coronary disease	9 (9%)
	Minor disease	29 (29%)
	Single or multi-vessel disease	62 (62%)
Number of catheters used	Median	3 (range 1-5)
Upgrade 5Fr sheath to 6Fr Sheath	Yes	5 (5%)
Medical Management pre/intra procedure		
Intra-arterial glyceryl trinitrate usage		100 (100%)
Intra-arterial glyceryl trinitrate dose	100mcg 150mcg 200mcg 250mcg 300mcg	20 (20%) 19 (19%) 54 (54%) 1 (1%) 5 (5%)

	400mcg	1 (1%)
Heparin dose (units)	median	3000
Fentanyl dose (mcg)	median	25
Midazolam dose (mg)	median	1
Prior Acetylsalicylic acid	Yes	74 (74%)
Prior Clopidogrel	Yes	43 (43%)
Radial artery access specifics		
Spasm	Yes	4 (4%)
Initial amount of air in radial compression device (ml)	mean	13.2 (1.1)
Procedure time (minutes)	mean	34 (17.5)
Hydrophilic wire use	Yes	6 (6%)
TRA Pre Diameter (mm)	mean	2.20
TRA Post Diameter (mm)	mean	2.47
Radial artery occlusion	Yes	4 (4%)
Forearm complication requiring admission	Haematoma Dissection	1(1%) 1(1%)

BMI: Body Mass Index; BP: Blood Pressure; CABG: Coronary Artery Bypass Surgery; PCI: Percutaneous Coronary Intervention; PVD: Peripheral Vascular Disease; SD: Standard Deviation

Diagnostic cardiac catheterisation was performed more commonly than PCI (57% vs 43%), with right radial artery (91%) and 6 French sheaths (78%) favoured in the majority of patients. Most patients required a single site of vascular access, with 7% requiring cross-over to femoral artery access who were subsequently excluded from this study. Pre or intra-procedural sedation (fentanyl and midazolam) was used in 71% of cases, with 29% receiving no sedation, only local anaesthetic. Reassuringly on 94% of occasions, arterial access was achieved on the first puncture. The mean duration of the radial compression device band application was 211 minutes (SD 76.6 minutes) which was more than the protocol recommendation of 180 minutes, with a difference noted depending on patient location following the procedure. Higher acuity areas such as Coronary Care, recorded lower compression times than the

less acute cardiology medical wards. Procedural characteristics are outlined in Table 1.

The mean initial radial artery measure was 2.20mm. A total of 53 patients had a radial artery diameter measure of greater than 2.20mm. There was a mean increase in radial diameter from 2.20mm in the pre procedural measurement compared with 2.47mm in the post procedural measurement (p=0.005). On univariate analysis a haemostasis device application time of greater than 190 minutes increased the odds of development of RAO (OR 3.12, 95% CI 0.31-31.1 p=0.007) in this group of patients. Due to the small number of patients with RAO further significant associations were unable to be determined and therefore multivariate analysis was not performed.

Logistic regression was undertaken to determine the predictors of radial artery diameter of greater than 2.20mm, adjusting for age and sex. This showed male gender (AOR 4.54, 95%CI 1.76 – 11.7 p=0.02) and height of greater than 1.74m (AOR 2.91, 95%CI 1.29 – 6.57 p=0.01) were significant predictors of increased radial artery diameter in this patient group.

5.7 Discussion

This study aimed to determine the clinical feasibility of implementing a nursing-led program to measure RA diameter before and after coronary intervention procedures, to determine RAO rates, risk factors for RAO and predictors of RA diameter. The results suggest that a nurse led model of using ultrasound to measure diameter of the radial artery is safe and feasible with no adverse events associated with the implementation of this programme reported. It offers valuable clinical data to assist in detecting early RAO and enhancing patient care in a cardiology setting.

Nursing led performance of pre and post procedural ultrasound measurement and colour doppler flow utilisation in a cardiac catheterisation environment has not been previously described in the literature to our knowledge. Nursing staff are important elements in the early detection of procedural complications and are a key element in interventional nursing standards (White et al., 2018). This research addresses a previously underreported complication from a nursing perspective, and this innovative approach can be easily and safely adopted in any cardiac catheterisation laboratory, offering a valuable adjunct to clinical care.

The RAO and vascular complication rates were relatively low (4%), which is comparable to previously published data on RAO (Kotowycz et al., 2014, Uhlemann et al., 2012). While the complications related to RAO do not have the prognostic implications of femoral access complications, RAO may result in pain, readmission,

the need for surgery, and will prevent future radial artery access (Pancholy et al., 2016). Nursing adoption of any measures that can reduce RAO is timely and important.

The utilisation of ultrasound measurements and colour doppler may translate to a range of clinical benefits. The optimisation of patient selection for radial artery approach for cardiac catheterisation and PCI, particularly for patients perceived to be at higher risk of radial artery access failure. Equipment selection may also be guided by ultrasound derived radial artery diameter prior to attempted arterial access (Chugh et al., 2015). For example, appropriate sheath and catheter size may be more accurately selected, allowing for improved patient centred procedures and potential reduction in access site injury. Evidence suggests that ensuring a ratio of the radial artery internal diameter to external sheath diameter greater than 1 may reduce the incidence of RAO (Saito et al., 1999). Avoidance of vessel trauma may limit the risk of radial artery spasm and reduce the rate of crossover from TRA to trans-femoral access (Beyer et al., 2013).

The thrombotic mechanism of RAO ensures that both anticoagulation dose and compression time remain important considerations of TRA (Goswami et al., 2016). A Heparin dose of 5000 units maybe protective of RAO while it has been well established that lower doses may be predictive of RAO (Bazemore, 2005). Arterial occlusion and time to haemostasis remains a pertinent issue for interventional nursing staff delivering post procedural care (Fech et al., 2012). Increased

compression time has been demonstrated to be a significant contributor to RAO resulting in future inability to utilise TRA (Kiemeneij and Boink, 2016). Solutions to reduce haemostasis time include; patent haemostasis which refers to allowing controlled radial artery bleeding after sheath removal, and allowing antergrade blood flow which avoids occlusive compression. This can be confirmed by plethysmography or alternatively if bleeding occurs (Wilson et al., 2017). Our data showed that compliance with the compression time could be improved. It maybe enticing to speculate that our RAO rate could be improved with improved protocol adherence. This would be a useful area of further research by collaborating with other centres.

There is emerging data supporting ulnar artery occlusion (allowing increased flow through the radial artery via antergrade flow) which has been demonstrated to reduce RAO immediately post procedure (Koutouzis et al., 2016), and at 30 days (Pancholy et al., 2016). This advanced technique can be adopted in those centres seeking to reduce the incidence of RAO. As nursing is predominantly responsible for the care of the TRA site post procedure, increasing nurses' knowledge of RAO has practical clinical benefits, and maybe an area for further nursing led research. Data collected in this study showed higher compression times in less acute wards. Continued vigilance by cardiology nurses around adherence to, or development of protocols designed to reduce RAO through education, training, and research will be a positive step to RAO reduction.

One of the recognised complications of TRA is that the radial artery is prone to spasm causing tight vascular constriction, pain, loss of palpable pulse and transient entrapment of the arterial sheath and/or catheter (Ho et al., 2012). This study group showed a low radial artery spasm rate. Our study demonstrated high usage of intra-arterial glyceryl trinitrate usage after sheath insertion and high usage of intra venous sedation. This may be associated with a subsequent quantified increase in radial artery diameter recorded post-procedurally and maybe linked to a reduced likelihood of radial artery vasospasm (Boyer et al., 2013). The use of sedation has been shown to reduce pain and anxiety, promote a more positive patient experience, and reduce radial artery spasm (Deftereos et al., 2013). An additional explanation for increased artery diameter recorded post procedure could include the effect of the sheath stretching the radial artery during the procedure (Dharma et al., 2017).

The benefits of pre-procedure doppler imaging assessment of radial arteries to minimise sheath artery mismatch has been well described (Chugh et al., 2015). In this group of patients predictors of a higher radial diameter were being tall and being a male. The sheath to artery diameter plays a significant role in radial RAO with a clear association of smaller diameter sheaths producing less RAO (Saito et al., 1999), (Dahm et al., 2002). In the era of chronic total occlusion and complex PCI , these procedures may require large access site catheters, and more specialised equipment to aid in the performance of these procedures (Galassi et al., 2014). The ability to accurately measure radial artery diameter becomes increasingly important to inform radial access (Seto et al., 2010). Specialised cardiac catheterisation nurses who perform ultrasound are well positioned to support this.

There are clearly described benefits of utilising ultrasound guided assistance to aid arterial access compared with palpation (Tang et al., 2014). These benefits centre on reducing multiple punctures and reduction in haematoma rate (Tang et al., 2014). Quantifying pre-procedural measurements of the radial artery diameter via ultrasound measurement is a useful planning tool (Chugh et al., 2015). Results should be incorporated into standard cardiac catheterisation admission documentation which may inform practice improvements and policy change for cardiac nurses. Further research for nursing may involve testing long the term impacts that this innovative change in nursing policy has on nursing job satisfaction, the nursing experience of translating this change into practice, and patient outcomes.

5.8 Conclusion

A nurse led approach to ultrasound in interventional cardiology is safe and feasible and offers a range of clinical benefits including pre procedural planning, allowing early identification of potential complications for patients who undergo radial artery access for cardiac catheterisation. This first step in establishing the safety and feasibility of this programme will lead to prospective nurse led trials in both inpatient and outpatient setting to determine efficacy and allow long term follow up of cardiac catheterisation patients.

5.9 Limitations

The limitations of this study include that this is an observational study in a single centre with a small sample size. Patients were not randomised and the design lacked long-term follow-up and did not include primary PCI so definitive conclusions regarding the implications of ultrasound assessment in emergent cases cannot be made. From this study the feasibility of nursing-led ultrasound measurement pre and post cardiac catheterisation procedures has been established, however future research using a randomised controlled trial design is needed to establish efficacy and to build on these findings.

Chapter 6

Contemporary trends in stroke complicating cardiac catheterisation

This chapter comprises a manuscript submitted for peer review as an original research article to the Internal Medical Journal. References are included at the end of the thesis.

6.1 Preamble

The previous two chapters described the clinical impacts of trans- radial access with a focus on clinical outcomes and the introduction of an easily adoptable radial occlusion monitoring method. This chapter describes a study that examines the serious procedural complication of stroke within cardiology. This chapter focuses on the occurrence of this potentially disabling and catastrophic complication in the context of a number of changes within local and international interventional cardiology. An examination of patient outcomes and the key elements of adverse event detection is undertaken.

Severe strokes have been reported by patients as having a similar viewed consequence as death, in addition to being the post procedural complication that is feared most (Pandit et al., 2014, Solomon et al., 1994). The diagnosis of stroke has immediate health consequences to patients and caregivers. Given the burden of

heart disease and stroke throughout the world, the high prevalence of cardiac catheterisation and the adverse immediate and long term effects of stroke, examining this issue makes an important contribution to the literature.

This aim of this study was to determine the functional impact of post procedural stroke using the Modified Rankin Score, in the context of atrial fibrillation, procedural anti-coagulation and enhanced procedural complexity. The Modified Rankin Score measures the degree of disability and dependence after a stroke. Stroke post cardiac catheterisation is an infrequent, although serious, complication which has a significant impact on early and late mortality. Contemporary changes in procedural practice may predispose patients to an increased risk of post-procedural stroke. While the incidence of post procedural stroke has been reported as low, any exploration of this potentially catastrophic consequences is important. This study was undertaken in a noteworthy period within cardiology in the local district, during a period of transition from femoral to trans-radial access and the widespread use of a thrombectomy catheter in the treatment of STEMI. In addition, this period saw the introduction of a structural disease interventional programme, and a doubling of the STEMI activity within five years.

This study demonstrates a stable annual incidence of stroke despite changing patterns of procedural practice. Stroke continues to confer an increased mortality risk despite advances in stroke therapy. Functional impairment was not significantly different between those with a history of atrial fibrillation compared to those without a

history of atrial fibrillation, offering mechanistic insight to the aetiology of stroke complicating cardiac catheterisation.

6.2 Abstract

Background: Stroke remains an important complication of diagnostic cardiac catheterisation and percutaneous coronary intervention and is associated with high rates of in-hospital mortality.

Aims: We sought to evaluate the incidence of stroke over a ten-year period and assess the long-term influence of stroke following cardiac catheterisation and percutaneous coronary intervention (PCI) on functional outcomes, based on modified Rankin score (mRS), and mortality.

Methods: The study was performed using a case control design in a single tertiary referral centre. Patients were identified by correlating those patients undergoing cardiac catheterisation between October 2006 and December 2016 with patients who underwent neuroimaging within 7 days to identify possible cases of suspected stroke or TIA.

Results: A total of 21510 patients underwent cardiac catheterisation during the study period. Sixty patients (0.28%) experienced stroke or TIA. Compared to control patients, those who patients who did experience cerebral ischaemic events were older (70.5 vs 64 years; $p<0.001$), with higher rates of atrial fibrillation, hypertension and diabetes mellitus. Stroke complicating cardiac catheterisation was associated

with an increased risk of readmission, with a significantly higher hazard of readmission for stroke noted. Despite minimal functional impairment based on mRS, stroke was associated with a significant risk of early and cumulative mortality. Stroke incidence remained stable over the study period despite changes in procedural practice.

Conclusions: The incidence and functional severity of stroke remains low despite evolving procedural practice with a stable incidence over time despite changes in procedural practice, however, post-procedural stroke confirms an increased mortality hazard.

6.3 Background

Stroke remains an important complication of diagnostic cardiac catheterisation and percutaneous coronary intervention with a reported incidence of 0.1% to 0.37% (Korn-Lubetzki et al., 2013, Dukkipati et al., 2004, Hoffman et al., 2011) and is associated with high rates of in-hospital mortality. Several novel risk factors have been implicated for stroke following cardiac catheterisation procedures, including increased rates of radial artery access, rotational atherectomy and aspiration thrombectomy (Hoffman et al., 2012, Jolly et al., 2015a, Jurga et al., 2011, Secemsky et al., 2019). In addition, the presence of an aging population with an increasing burden of atrial fibrillation (AF), further contributes to increased stroke risk in such patients undergoing diagnostic catheterisation (Chao et al., 2018). However, while stroke remains a feared complication of cardiac catheterisation, prevention and treatment of acute stroke has improved with the availability of novel anticoagulant agents, thrombolytic therapy and endovascular treatment.

We aimed to evaluate the incidence and predictors of stroke over a contemporary ten-year period and assess the long-term influence of stroke occurring following cardiac catheterisation and percutaneous coronary intervention (PCI) on outcome. We also aimed to describe any changes in incidence and document the severity of stoke complicating cardiac catheterisation, particularly with reference to the effect of co-existing AF.

6.4 Methods

6.4.1 Study design

The study was performed using a case control design in a single tertiary referral centre. Patients were identified by correlating neuroimaging with those undergoing cardiac catheterisation. Patients undergoing cardiac catheterisation and PCI, incorporating primary and rescue PCI, performed between October 2006 and December 2016 were identified. Details of consecutive patients undergoing cardiac catheterisation and PCI were prospectively recorded in a central database, including demographic, clinical and procedural data. A complete list of neuroimaging performed during this same period was also obtained from the institutional central clinical database, including computed tomography (CT) and magnetic resonance imaging (MRI). These two cohorts were then cross-referenced using three identifiers (gender, date of birth and unique medical record number) to establish those patients who underwent cardiac catheterisation followed by neuroimaging within 7 days to identify possible cases of suspected stroke or TIA.

Identified subject's medical records were reviewed and clinical, demographic and procedural data were recorded prospectively in a separate procedural complication registry. Two neurologists provided independent adjudication to confirm stroke or TIA following cardiac catheterisation. Patients considered to have suffered stroke or TIA comprised the stroke group for statistical analysis. The control group comprised inpatients with a complete record of relevant co-morbid conditions prospectively

maintained on the institutional database and underwent cardiac catheterisation during the study period that did not develop cerebral ischemia post procedure.

Outcome data was sourced from the institutional Cardiac and Stroke Outcomes Unit database, which has previously been described (Marsden et al., 2010) and included hospital readmission within 30 days, death in hospital, and all-cause mortality until censored at August 2017. In brief, the institutional database prospectively has recorded all cardiac and stroke admissions to public hospitals within the area health service (>98% stroke admissions) based on ICD codes since 1995 (Marsden et al., 2010, Heller et al., 2000). Readmission with subsequent episodes of stroke or TIA were recorded to determine if procedural stroke places an individual at a higher risk of further cerebral ischaemic events compared to control population.

Patient Modified Rankin scores (mRS) of the stroke group were extracted from medical records and from access to the institutional clinical stroke database. Procedural characteristics including indication for procedure, presence of cardiogenic shock, use of intra-aortic balloon pump (IABP) insertion, arterial access site and cross over rate, use of thrombectomy devices, anticoagulation/antiplatelet medication, number of catheters used, and procedural duration were recorded for those patients experiencing documented cerebral ischemia.

During this time frame, the cardiac catheterisation laboratory transitioned from predominantly femoral artery access for procedures (2006-2010) to predominately radial artery access (2010-2016).

6.4.2 Statistical methods

The baseline patient characteristics and procedural data of the post procedural stroke group and the control group are presented. Continuous variables are presented as means and medians utilising ANOVA. Categorical variables were presented as frequencies and percentages utilising Chi Square tests. In addition, a pre-planned subgroup analysis of stroke group patients was performed comparing those who had documented AF and those without previously documented AF.

Stroke trends are presented using a segmented Poisson regression. Stroke trends were analysed in two periods, 2006-2010 a predominantly femoral arterial access era, and 2010-2016, when the institution transitioned to a predominantly trans-radial access centre. The immediate effect of years from 2010 and the long-term effect of admission year, with an offset by the number of catheterisations conducted in each year. Incident rate ratio (IRR), 95% confidence intervals and P values are presented.

The recorded mRS on admission, discharge, and at 90 days was compared between subject groups experiencing stroke with and without a prior diagnosis of AF. These groups were compared using ordinal logistic regression with robust variance and

inverse probability of treatment weighting (IPTW) utilising age, year of admission, co-morbidities, and pre-morbid mRS. Odds ratio (OR), 95% confidence intervals and p-values are presented.

Cox regression was used to model time from discharge to readmission and time from discharge to death. These patient groups were modelled adjusting for age, sex, year of admission, and the number of co-morbidities. This is presented as a cumulative incident function graph.

Statistical analysis was conducted using SAS version 9.4 (SAS institute Inc., Cary, NC, USA).

6.5 Results

A total of 21,510 patients underwent cardiac catheterisation during the study period between October and December 2016. Sixty patients (0.28%) experienced stroke or TIA within 7 days of the index procedure. Of the entire cohort, 8352 (including 1573 undergoing primary percutaneous coronary intervention for ST elevation myocardial infarction) underwent percutaneous coronary intervention, with 13,158 patients undergoing cardiac catheterisation alone. In patients undergoing cardiac catheterisation alone, the incidence of stroke and TIA was 0.24% (32/13158). The incidence of cerebral ischemia in patients treated with PCI was 0.34% (28/8352). Compared to control patients who did not experience cerebral ischemia (n=10,279),

those who did experience cerebral ischaemic events were older (70.5 vs 64 years; p<0.001), with higher rates of AF, hypertension and diabetes mellitus (Table 6.1). Stroke complicating cardiac catheterisation was associated with an increased risk of readmission, with a significantly higher hazard of readmission for stroke noted. Stroke was also associated with a significant risk of early and cumulative mortality (Figure 6.1).

Table 6.1: Baseline clinical characteristics

Variable	Control patients (n=10279)	Procedural stroke (n=60)	P value
Demographics			
Age mean (SD)	63.97 (12.8)	70.48 (10.4)	<0.0001
Male sex n (%)	6794 (66)	31 (52)	0.019
Co-morbidities			
Prior Dyslipidemia n (%)	520 (5.1)	2 (4.2)	0.778
Prior Hypertension n (%)	4079 (40)	47 (78)	0.0001
Prior AF n (%)	744 (7.2)	17 (28)	0.0001
Prior Diabetes n (%)	1731 (17)	15 (31)	0.008
Prior chronic renal disease n (%)	625 (6.1)	6 (13)	0.064
Smoking History n (%)	2363 (23)	9 (19)	0.486
Prior Heart Failure n (%)	781 (7.6)	7 (15)	0.069
Outcome measures			
Number of readmissions since procedure median (IQR)	3 (1,6)	1 (0,4)	<0.0001
Days from discharge till first readmission median (IQR)	90 (70,90)	90 (13,90)	0.084
Stroke readmission n (%)	410 (5.9)	12 (20)	<0.0001
Inpatient Mortality n (%)	182 (1.8)	8 (13)	<0.0001
*Subsequent mortality n (%)	2092 (20)	27 (45)	<0.0001

AF - Atrial Fibrillation. IQR - Inter Quartile Range. SD - Standard Deviation.* Patient recorded as died at any time after discharge

Figure 6.1: Survival estimates of mortality in patients following cardiac catheterisation comparing post procedural stroke to absence of stroke.

Relevant demographic and clinical variables in the stroke cohort are outlined in table 6.2, with patients with a history of AF more likely to have documented previous cerebral ischemia. Of the patients experiencing cerebral ischemia in this cohort, 4 were treated with thrombolytic therapy, 1 patient underwent endovascular therapy

with the remainder managed with medical therapy alone. No difference in rates of haemorrhagic stroke were seen between patients with and without a history of AF.

Table 6. 2: Clinical characteristics patients with stroke according to atrial fibrillation status

Variable	No prior AF status (n=43)	Confirmed prior AF (n=17)	P value
Demographics			
Age mean (SD)	70.07 (11.1)	73.35 (8.34)	0.276
Male sex n (%)	19 (44)	12 (71)	0.065
Comorbidities and CVD risk factors			
Prior Dyslipidemia n (%)	16 (37)	8 (47)	0.483
Prior Hypertension n (%)	34 (79)	13 (76)	0.826
Diabetes n (%)	11 (26)	5 (29)	0.762
Prior chronic renal impairment n (%)	5 (12)	1 (5.9)	0.504
Current Smoker n (%)	9 (21)	6 (35)	0.247
Ex-Smoker n (%)	12 (28)	2 (12)	0.183
Prior stroke n (%)	9 (21)	5 (29)	0.484
Prior TIA n (%)	0	3 (18)	0.005
Prior Heart Failure n (%)	4 (9.3)	6 (35)	0.015
BSA mean (SD)	1.87 (0.26)	1.86 (0.24)	0.287
BMI (kg/m2) mean (SD)	29.17 (8.95)	24.96 (5.37)	0.075
Prior MI n (%)	15 (35)	3 (18)	0.189
Prior CABG n (%)	3 (7)	4 (24)	0.072
Prior PCI n (%)	9 (21)	3 (18)	0.774
Pre Morbid MRS mean (SD)	0.31 (0.87)	0.38 (1.02)	0.808
Clinical and procedural characteristics			
Elective cardiac catheterization n (%)	15 (35)	6 (35)	0.976
STEMI n (%)	16 (37)	2 (12)	0.053
Post thrombolysis n (%)	3 (7)	0	0.263
PCI n (%)	22 (51)	6 (35)	0.267
Cardiogenic shock n (%)	4 (9.3)	3 (18)	0.364
GP IIb/IIIa Inhibitor use n (%)	8 (19)	0	0.056
IABP n (%)	2 (4.7)	0	0.366
Trans-radial access n (%)	19 (44)	4 (24)	0.138
Crossover trans-radial access to femoral access n (%)	3 (7)	0	0.264
Use of thrombectomy catheter n (%)	5 (12)	1 (5.9)	0.504
Length of procedure mean mins (SD)	50.09 (32.34)	50.65 (22.67)	0.949
Number of catheters used mean (SD)	2.35 (0.87)	2.24 (1.35)	0.700

BMI - Body Mass Index; BSA - Body Surface Area; CABG - Coronary Artery Bypass Surgery; GP - Glycoprotein; IABP - Intra-Aortic Balloon Pump; MI - Myocardial Infarction; mRS - Modified Rankin Score; PCI - Percutaneous Coronary Intervention; SD - Standard Deviation; TIA - Transient Ischaemic Attack

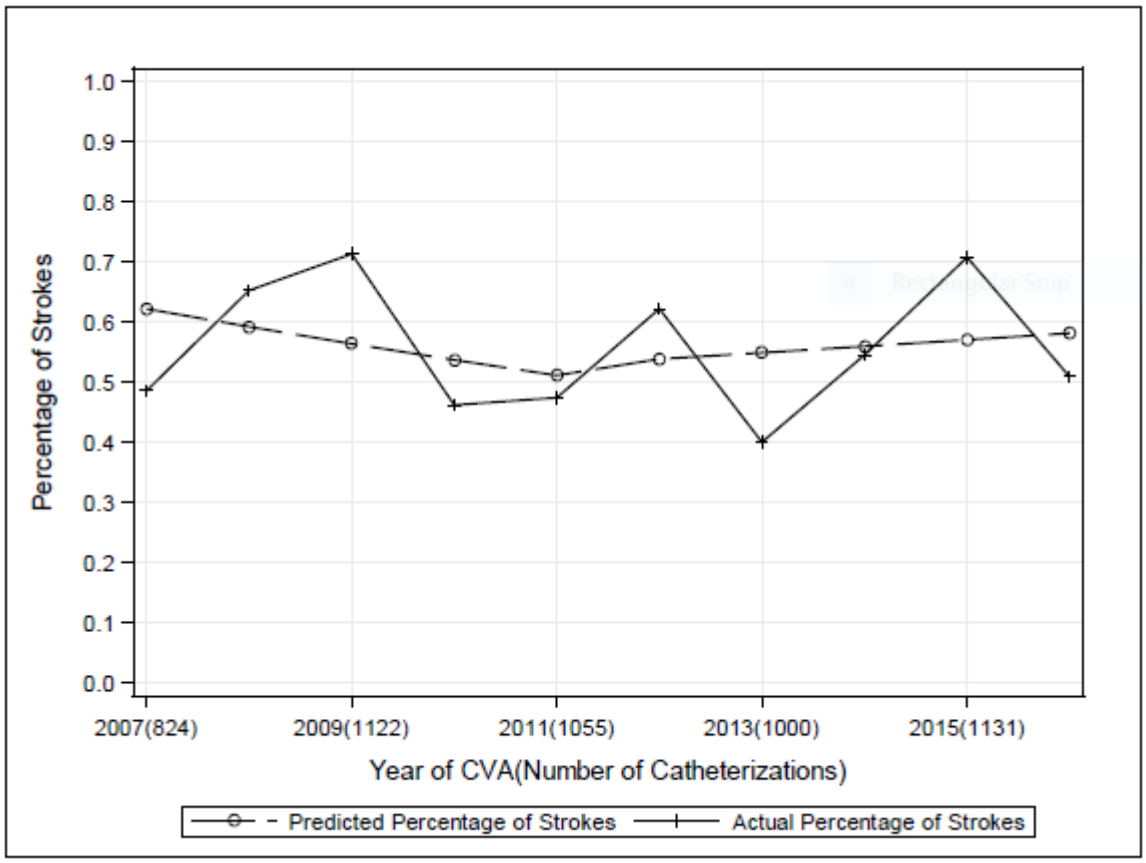


Figure 6.2: Annual Incidence of Stroke Events after Cardiac Catheterisation 2007- 2016

No significant difference was seen in procedural annual stroke incidence over the study period which incorporated different eras reflecting transition from predominantly femoral to radial artery access (Figure 6.2).

The presence of AF did not influence outcome in terms of readmission and subsequent mortality (Table 6.3). Functional impairment was low, with the majority of patients having mRS 0 at 90 days; there was no difference in mRS between those patients with and without AF at 90 days (Figure 6. 3).

Table 6.3: Stroke type and outcome measures by atrial fibrillation status

Variable		No prior AF (n=43)	Confirmed prior AF (n=17)	P value
Stroke type				
Ischaemic stroke n (%)		29 (67)	13 (76)	0.491
Hemorrhagic stroke n (%)		2 (4.7)	1 (5.9)	0.844
Outcome measures				
Readmission status n (%)	Alive and no readmission	8 (19)	3 (18)	0.990
	Readmission	27 (63)	11 (65)	
	Died	8 (19)	3 (18)	
Cardiac cause readmission n (%)		15 (35)	8 (47)	0.382
Stroke cause readmission n (%)		9 (21)	3 (18)	0.744
Inpatient mortality n (%)		6 (14)	2 (12)	0.822
Post discharge mortality (%)		17 (40)	10 (59)	0.176

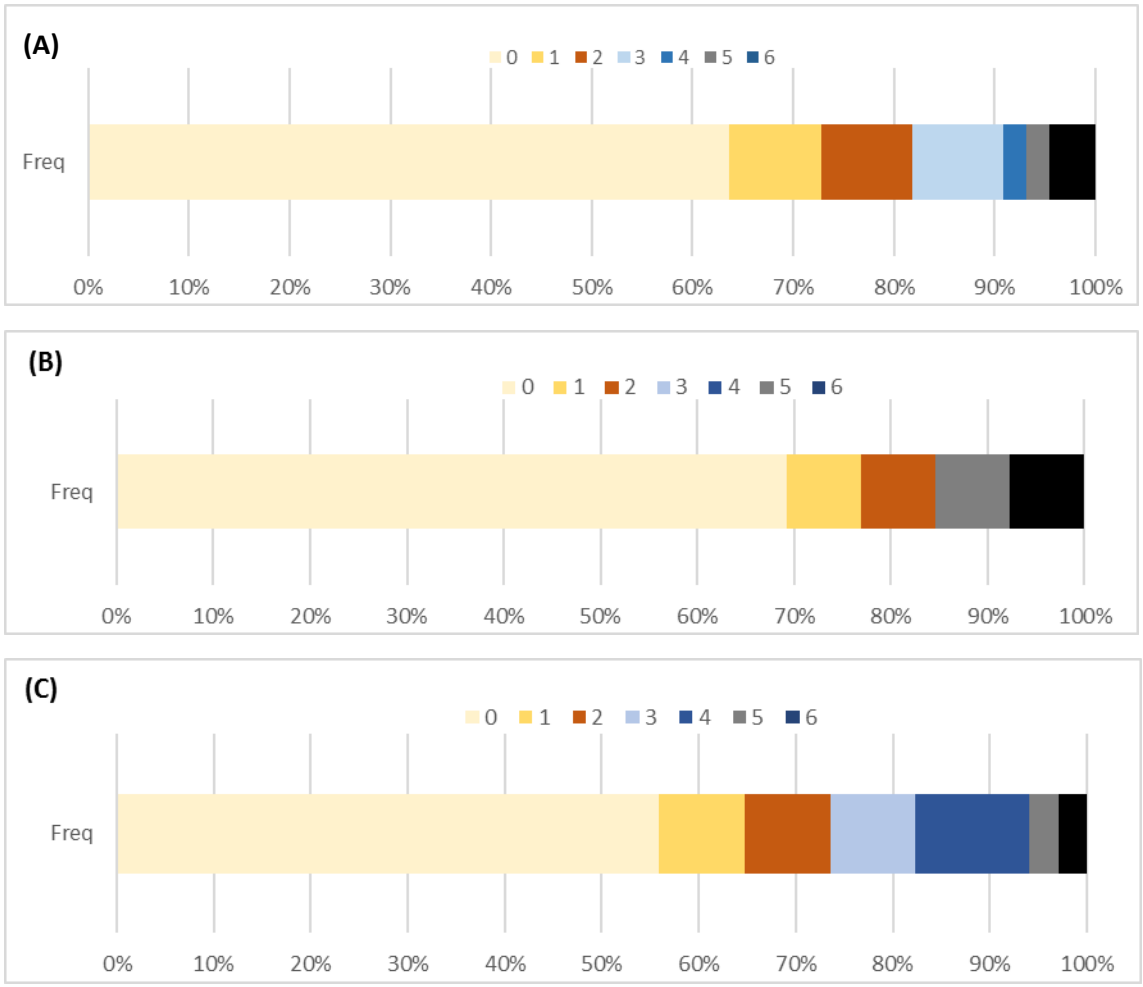


Figure 6.3: Modified Rankin Score (mRS) assessed at 90 day follow up, including total patient group (A), those patients with prior atrial fibrillation (B) and those without atrial fibrillation (C)

6.6 Discussion

We report an incidence of 0.28% of stroke and TIA up to 7 days following cardiac catheterisation in a contemporary patient cohort, with a stable annual incidence of stroke or TIA despite evolving patterns of procedural practice. While functional disability following stroke in patients undergoing cardiac catheterisation is low, stroke

following cardiac catheterisation was associated with important early mortality hazard despite advances in stroke therapy. AF was not associated with an increased risk of haemorrhagic stroke. Assessment of stroke severity using mRS suggested low rates of significant functional disability with no difference seen between those patients with AF and those maintained in sinus rhythm. This is in contrast to the large body of literature demonstrating worse stroke outcomes in those in whom the aetiology is AF (Tu et al., 2010, Jorgensen et al., 1996). This suggests that suggesting the aetiology of stroke following cardiac catheterisation is not a function of AF.

While stroke is an uncommon complication of cardiac catheterisation, with a significantly lower incidence compared to coronary artery bypass graft surgery (Head et al., 2018, Devgun et al., 2018), it is associated with considerable morbidity and mortality. Stroke complicating percutaneous coronary intervention results in increased mortality risk (Dukkipati et al., 2004, Aggarwal et al., 2009), particularly when complicated by haemorrhagic stroke (Kwok et al., 2015), with in-hospital mortality rates up to 30% previously described (Aggarwal et al., 2009). Previous studies are consistent with our findings, and have suggested an annual stroke incidence of between 0.1% and 0.37%, noting this study included events up to 7 days post procedure, a limitation of previous studies; increasing age, previous stroke, hypertension, diabetes mellitus, renal impairment and urgent procedures are associated with increased risk (Korn-Lubetzki et al., 2013, Dukkipati et al., 2004, Hoffman et al., 2011, Head et al., 2018, Kwok et al., 2015). The use of mechanical thrombectomy, rotational atherectomy, large calibre guide catheter use and

potentially the use of radial artery access have been implicated in increasing stroke risk (Hoffman et al., 2012, Jolly et al., 2015b, Jurga et al., 2011). The use of radial artery access has been associated with improved outcomes in terms of mortality, myocardial infarction, bleeding complications and vascular injury (Jolly et al., 2011b, Brener et al., 2017, Cantor et al., 2015, Ferrante et al., 2016). While there is observational data suggesting an increased propensity to cerebral emboli complicating radial access (Jurga et al., 2011), several large-scale series have suggested the radial approach is not associated with increased stroke risk, as reflected in this study (Ratib et al., 2013, Sirker et al., 2016a). In addition, multiple series have also reported an increase in incident stroke risk over time, attributed to patient complexity and co-morbidity, independent of vascular access site (Kwok et al., 2015, Raposo et al., 2015).This observation may in part reflect access to contemporary neuroimaging. This cohort did not demonstrate a significant change in stroke incidence despite the transition to radial artery access and despite any change in patient complexity and age encountered over time.

The presumed mechanism of stroke in the post cardiac catheterisation cohort may offer prognostic value, with embolisation of atherosclerotic debris the presumed mechanism in the absence of AF (Devgun et al., 2018). Stroke complicating AF is reported to typically be associated with more extensive deficits (Jorgensen et al., 1996, Tu et al., 2010), however, the mRS was not significantly different between patients with a background of AF compared to those without a history of AF. This implies a similar mechanism of stroke complicating cardiac catheterisation irrespective of underlying cardiac rhythm. This is supported by the observation of

similar prognosis of patients in this cohort experiencing cerebral ischemia irrespective of AF status. The mortality hazard seen in those experiencing previous cerebral ischemia, despite minimal functional impairment, may be a consequence of the extent of underlying atherosclerotic burden which may predispose to both peri-procedural stroke and subsequent adverse vascular sequelae.

Age is recognised as an important risk factor for both stroke complicating both cardiac catheterisation and AF (Aguilar et al., 2012, Chao et al., 2018), reflected in age being associated with higher likelihood of post-procedural stroke in this study. While patients with AF were more likely to have experienced a previous episode of cerebral ischemia, an increased the risk of adverse outcomes and neurological recovery was not noted in our cohort.

Approaches to anticoagulation during cardiac catheterisation vary, with interruption to anticoagulation theoretically contributing to stroke risk in the peri-procedural period. Performing procedures using the radial approach, continuing anticoagulation and avoiding bridging may limit this risk. Our data suggest atheroemboli may be more likely to precipitate cerebral ischemia, with interruption of anticoagulation potentially less contributory to ischaemic events, in keeping with previously published randomised data (Douketis et al., 2015).

This study is limited by the lack of detailed procedural data for the control cohort. While limited by the small number of events, reinforcing that procedural-related

stroke risk is low, it is difficult to confirm differences between those patients with and without AF.

6.7 Conclusions

The incidence of stroke in this contemporary patient cohort is low with a stable incidence over time and is associated with traditional cardiovascular risk factors. Despite previous concerns regarding stroke risk in the context of radial artery access and an increasingly complex, aging patient population, we did not observe a change in stroke incidence over time. The presence of AF did not influence the severity and outcome of procedure related stroke, offering mechanistic insights. While the incidence and functional severity of stroke complicating cardiac catheterisation appears low, post-procedural stroke nonetheless confirms an increased mortality hazard, indicating strategies to avoid procedure related stroke are important.

Chapter 7

7.1 Conclusion and Future Directions

The burden of heart disease is significant and the need to provide safe optimum evidenced based management to patients hospitalised with heart disease is imperative. Reviewing systems of care and enhancing research methods to improve health outcomes for patients undergoing investigations and treatment for heart disease remains important.

The aim of this thesis was to investigate the outcomes obtained by a nurse led programme in identifying, managing and reporting major adverse events associated with cardiovascular nursing. This thesis had its genesis through an identified need to address a deficit in formal structured reporting and identification of adverse events following an admission to a large, tertiary referral hospital for heart disease, in a geographically diverse health district. This thesis has described the nature of adverse events in patients with cardiac disease, particular those undergoing invasive diagnostic and treatment procedures and outlines the potentially catastrophic consequences for the immediate and long term health outcomes of this patient population. This thesis has illustrated identifiable factors, both patient and non-patient related, which are implicated in the aetiology of adverse events. Understanding these factors is crucial to inform clinical practice and policy development to improve patient outcomes.

The purpose of this final chapter is to synthesise the work presented, highlighting the relevant contributions of this thesis to the literature. Initially, the background of this thesis will be reviewed to outline the motives behind this body of work. The topics covered in this thesis can be translatable to similar institutions and health services with the aim of utilising routine clinical data collection and data linkage to document and monitor the nature of adverse cardiac procedural outcomes with the ultimate aim of improving care for people hospitalised with heart disease.

The key findings of each area study will be summarised, the immediate contributions this work outlined, and the future directions of research will be discussed.

7.1.1 Summary of aims and findings

This thesis presented a series of studies designed to inform cardiology outcomes through the description of significant adverse events and changes in practice. By adopting this approach, this thesis (1) provided a review of the literature in regards to heart disease, acute coronary syndromes (ACS), interventional cardiology, and associated adverse health outcomes; (2) described the co-morbidity and risk factor profile of a diverse patient group with established cardiac disease; (3) examined the factors associated with adverse health outcomes; and (4) discussed the immediate and long-term health outcomes of adverse events in the context of change in practice

This wider purpose of this thesis was to contribute new knowledge to the body of literature in regards to the identification and outcomes of adverse events within a large tertiary institution serving a populous health district. This has been achieved by the exploration of major adverse events, changes to practice, and examination of the health outcomes in this group. This thesis is divided into 7 categories. The first section of the thesis contains an introduction, which provided a broad overview of heart disease, its management, clinical presentations, and potential adverse health outcomes associated with a presentation to hospital for heart disease. This was followed by five chapters, each providing contemporary data on patient outcomes using innovative models of examination into patient outcomes. This thesis, rather than using the rigid selection criteria seen in randomised controlled trials, provides a real-life examination of cardiology data in a diverse patient group undergoing usual care.

The first study in this thesis “Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting” described the high incidence of misdiagnosis of STEMI in smaller, rural hospitals with a consequent increase in mortality. This first study allowed for the development of systems to adequately investigate important clinical outcomes associated with cardiology, reflected in the subsequent papers contained within this thesis. This study allowed for real time morbidity and mortality data linkages to be populated, across an area the geographical size of England. This study examined demographic, clinical, ECG and organisational factors associated with patients presenting with STEMI who were eligible for reperfusion therapy but did not receive timely treatment in a rural and regional area, comparing this to outcomes

in major regional referral centre. The examination of geographical differences in outcome, has international relevance to centres with similar challenging geography and diverse populations. The missed acute myocardial infarction (MAMI) data indicates that failure to interpret the ECG and inadequate clinical judgment are the most frequent causes of failure to accurately diagnose and treat STEMI, occurring in 70% and 65% of missed STEMI cases respectively. MAMI patients had higher 30-day readmission compared to treated STEMI patients with an associated longer length of stay and higher rate of death.

The second study assessed predictors of vascular access complications following cardiac catheterisation/PCI, with a secondary aim to determine the prevalence of vascular complications following cardiac catheterisation or percutaneous intervention/PCI. The occurrence of femoral vascular access complications was found to be similar to that reported from other tertiary centres. The results showed a higher body mass index (BMI) and anti-coagulant/anti-platelet medications were significant in the development of this complication. Documented vascular disease risk factors, including diabetes mellitus, hypertension, smoking and elevated creatinine were shown to be statistically significant in the development of vascular complications. Complications were less likely with use of the Femstop® removal device. With the emergence of structural disease programmes, which rely on femoral access, in particular transcatheter aortic valve implantation (TAVI), and complex PCI programmes, continued monitoring and understanding of factors associated with this complication continue to remain of the upmost importance.

The third study in this thesis “A comparison of outcomes during a transition from femoral to radial access in patients presenting with ST segment elevation myocardial infarction” described the change in vascular access complications during a period of transition from femoral access to radial access in the STEMI population. Demographics were comparable in both groups. This study supports the reduced adverse bleeding outcomes reported when using the radial approach in this contemporary cohort. One of the perceived barriers to adoption of the radial access approach is a concern that this access route may increase the important key performance indicator of door to balloon time (DTB). Data from this study suggested a reduced DTB in the radial group compared to the femoral group. While definitive conclusions cannot be drawn from this result, it suggests that radial access may not obviously increase DTB in a high-risk group.

The important end points of patient length of stay (LOS) and 28 day readmission showed a clear reduction in LOS. The significantly lower readmission rate for the radial access group may be as result of their being less patients with cardiogenic shock patients and minimal vascular and bleeding complications in the radial group.

While the benefits conferred by trans-radial access are established, the incidence and predictors of radial artery occlusion are emerging. Study four, “Nursing led ultrasound to aid in trans-radial cardiac catheterisation: A feasibility study”, sought to address ultrasound monitoring of radial access pre and post post-procedurally. The aim was to (1) evaluate the clinical feasibility of implementing a nursing-led program

to measure radial artery diameter before and after cardiac catheterisation using ultrasound, (2) determine incidence of radial artery occlusion (RAO), (3) determine risk factors for RAO and (4) determine predictors of radial artery diameter. Using a prospective observational study a nurse led ultrasound programmes was found to be safe and feasible with no adverse events reported. A low rate of occlusion (4%) was observed immediately following compression band removal from access site. A haemostasis device application time of greater than 190 minutes was a predictor of RAO. Male gender and height were predictors for a radial artery diameter of >2.2mm, which is associated with reduced occlusion. This study, the first of its kind reported within the literature, confirmed nursing staff can safely lead the assessment of radial artery dimensions and occlusion within a cardiac catheterisation laboratory to enhance planning and care, including the monitoring of compression times to reduce RAO.

This thesis concluded with an analysis of stroke after cardiac catheterisation. It aimed to evaluate the occurrence of stroke after cardiac catheterisation and PCI. In addition, it aimed to determine the immediate and functional outcomes of this group of patients based on modified Rankin score. This was achieved using a case control design conducted over a 10 year period, during which time there were 21,510 cardiac catheterisation procedures performed and 0.28% of patients experienced a stroke. Those that suffered a post procedural stroke were older, had a higher incidence of atrial fibrillation and cardiac risk factors including diabetes mellitus and hypertension. The occurrence of a post procedural stroke resulted in a higher risk of readmission and a higher hazard risk for future stroke. The functional impact of

stroke remains low as demonstrated by modified Rankin score. Importantly, this study demonstrated a post procedural stroke confirms an increase mortality risk for patients.

7.1.2 Immediate effects of this thesis

Findings from this thesis have had a significant immediate impact on health delivery, research, system improvement, and information technology enhancement within the local health district. One of the themes of this thesis is the implementation of methods of monitoring these adverse events across a large geographical area encompassing a number of different health facilities. The large geography of the health district requires the use of innovative approaches for research and clinical system enhancement, while also permitting and promoting the opportunity for future research collaborations. Furthermore, components of the individual studies have been presented at peak body international conferences and local cardiac conferences.

Health care delivery

This thesis articulated significant clinical variation in the diagnosis of ACS in rural populations, particularly in missed diagnosis of myocardial infarction. This thesis demonstrated that missed acute myocardial infarction resulting from failure to

correctly interpret ECG and serum markers does occur, leads to increased mortality and morbidity and is overrepresented in rural hospitals that are maintained by general practitioners.

Utilising data from this thesis on missed myocardial infarction, the Candidate as part of a team from the local health district was successful in obtaining a translational research grant for $600,000 to improve identification and management of patients with ACS. This grant aims to provide ACS treatment guidance in rural hospitals across three local health districts by implementing and evaluating an ongoing ACS management system using a prospective, cluster randomised controlled trial (RCT) design. Patients allocated to the treatment arm who present to an intervention hospital will have an ECG and serum troponin level result transmitted to a central nursing-based reporting service based at a metropolitan hospital supported by the tertiary referral cardiology service. Staff with clinical expertise from the central reporting service will review the ECG and serum troponin level and determine the likelihood of an acute coronary syndrome. This grant is a direct result of data contained in this thesis.

This thesis has generated practice change within this large health service and has driven grant income to address the adverse health outcomes articulated in this thesis; this project has potential to be translatable and scalable to similar health services.

7.1.3 Research collaborations

The treatment of stroke following cardiac catheterisation is under reported. Further research collaboration involving an additional large tertiary referral hospital has resulted from this study. This new project will examine the effects of reperfusion therapies, including thrombolysis and endovascular clot retrieval, after cardiac catheterisation on health outcomes. This study will aim to explore thrombus density and its effect on thrombolysis for treatment of stroke, and will aim to determine if endovascular clot retrieval is a more effective option for treatment of stroke following cardiac catheterisation. This collaboration involves senior interventional cardiologists, neurologists, neuro-radiologists, radiologists, junior medical staff, and the candidate of this thesis. Additional to this study, a case report is currently being prepared for publication providing an overview of stroke post cardiac catheterisation. This clinically focused paper will add important clinical perspectives to enhance knowledge of this complex disease process.

Information technology developments and data linkage

This thesis implemented real time data collection of relevant serious post procedural complications and outcomes. Prospective data linkages are now being implemented for all interventional procedures with outcome data. In particular, data from pathology results, emergent visits to theatre, transfusion, length of hospitalisation, readmission

and 30-day mortality are now prospectively collected and linked with hospital and clinical data systems.

The paucity of data regarding rural and regional outcomes, with respect to both inpatient and post discharge care, was identified as an area which required enhancement. The candidate and supervisors led the design, implementation and rollout of an ACS database that prospectively populates all chest pain presentations, inpatient outcomes, pathology, transfer data and post discharge outcomes. This thesis generated this immediate service enhancement through the implementation of real time data collection to guide service development and clinical care of patients presenting with chest pain.

7.2 Future Directions

There are several important directions for further research that will build upon the work and findings from this thesis. This local health district, with its unique geography (rural and metropolitan), and reperfusion strategies (prehospital thrombolysis, nurse initiated thrombolysis, pre hospital assessment of primary angioplasty, inter-facility STEMI patients, and emergency department presentations of STEMI) provides a diverse patient cohort to examine. This cohort allows exploration of a range of outcomes from each of these groups, particularly with reference to bleeding complications, long term follow up, barriers to evidence based management and the influence of vascular access.

Recommendations for future research and development include:

1) A qualitative examination of barriers for clinicians that limit the accurate diagnosis of Acute Coronary Syndrome
2) Examination of cardiology and neuro-interventional treatment and outcomes, including the role of Trans Aortic Valve Implantation and complex PCI in neurological outcome after cardiac catheterisation procedures.
3) Evaluation of strategies to reduce radial artery occlusion as newer methods of haemostasis become available which may aid in the reduction of the complications of trans-radial access; this would be perfectly suited for cross institutional collaborations.

7.3 Final Conclusions

The aim of this thesis was to examine complications and health outcomes associated with a cardiology admission to a health district. This was achieved by using a nurse-led system to identify and manage adverse events over a large geographical area, utilising routinely collected clinical “real world” data. This thesis has demonstrated that serious adverse events following a cardiology admission are relatively rare; however they are associated with significant impacts on long term health outcomes including morbidity and mortality.

This thesis has demonstrated that patient’s co-morbidities, presenting clinical history and organisational factors each may have a role to play in negatively impacting health outcomes for patients. Understanding these issues and incorporating systems to identify at risk patients has considerable benefits to patients and their families, clinicians, managers of health organisations and policy developers. In particular, this work has shown that organisational systems, both clinical and non-clinical, remain important factors in predicting outcomes. This thesis has highlighted the importance of monitoring systems of care, change within those systems, such as change in vascular access, and reinforces the need for continued review of any change in practice.

The innovative methods of data collection and linkage detailed within each study ensures this research is translatable and scalable to other cardiology services, particularly those with a rural and regional population.

Within the current local health district, improvements have been made and further research has commenced, and it is anticipated future guideline development will be enhanced that will permit large scale evaluation projects.

References

ABS. 2018. *Australian Statistical Geography Standard (ASGS)* [Online]. Australian Bureau of Statistics. Available: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS) [Accessed 01/03/2018 2018].

ABU-FADEL, M., SPARLING, J., ZACHARIAS, S., ASTON, C., SAUCEDO, J., SCHECHTER, E. & HENNEBRY, T. 2009. Fluroscopy vs Traditional guided femoral arterial access and the use of closure devices: A randomised controlled trial. *Catherisation and Cardiovascualr Interventions,* 74**,** 533-539.

AGGARWAL, A., DAI, D., RUMSFELD, J. S., KLEIN, L. W., ROE, M. T. & AMERICAN COLLEGE OF CARDIOLOGY NATIONAL CARDIOVASCULAR DATA, R. 2009. Incidence and predictors of stroke associated with percutaneous coronary intervention. *American Journal of Cardiology,* 104**,** 349-53.

AGOSTONI, P., BIONDI-ZOCCAI, G. G. L., DE BENEDICTIS, M. L., RIGATTIERI, S., TURRI, M., ANSELMI, M., VASSANELLI, C., ZARDINI, P., LOUVARD, Y. & HAMON, M. 2004. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures: Systematic overview and meta-analysis of randomized trials. *Journal of the American College of Cardiology,* 44**,** 349-356.

AGUILAR, E., GARCIA-DIAZ, A. M., SANCHEZ MUNOZ-TORRERO, J. F., ALVAREZ, L. R., PIEDECAUSA, M., ARNEDO, G., MONREAL, M. & INVESTIGATORS, F. 2012. Clinical outcome of stable outpatients with coronary, cerebrovascular or peripheral artery disease, and atrial fibrillation. *Thrombosis Research,* 130**,** 390-5.

AIHW 2018. Cardiovascular disease snapshot. *Cardiovascular disease snapshot.* Canberra: Australian institute of health and welfare.

AL-LAMEE, R. & NOWBAR ALEXANDRA, N. 2018. Vascular Closure Devices for Transfemoral Angiography. *Circulation: Cardiovascular Interventions,* 11**,** e007085.

ALBARQOUNI, L., DOUST, J. A., MAGLIANO, D., BARR, E. L., SHAW, J. E. & GLASZIOU, P. P. 2019. External validation and comparison of four cardiovascular risk prediction models with data from the Australian Diabetes, Obesity and Lifestyle study. *Medical Journal Australia,* 210**,** 161-167.

AMIN, A. P., PATTERSON, M., HOUSE, J. A., GIERSIEFEN, H., SPERTUS, J. A., BAKLANOV, D. V., CHHATRIWALLA, A. K., SAFLEY, D. M., COHEN, D. J., RAO, S. V. & MARSO, S. P. 2017. Costs Associated With Access Site and Same-Day Discharge Among Medicare Beneficiaries Undergoing Percutaneous Coronary Intervention: An Evaluation of the Current Percutaneous Coronary Intervention Care Pathways in the United States. *JACC: Cardiovascular Interventions,* 10**,** 342-351.

AMMANN, P., BRUNNER- LA ROCCA, ANGEHRN.WALTER., HANS., R., SAGMEISTER., M. & RICKLI.H 2003. Procedural Complications Following Diagnostic Coronary Angiography are related to the operators experience and the catheter size. *Catherisation and Cardiovascualr Interventions,* 59**,** 13-18.

AMSTERDAM, E. A., WENGER, N. K., BRINDIS, R. G., CASEY, D. E., GANIATS, T. G., HOLMES, D. R., JAFFE, A. S., JNEID, H., KELLY, R. F., KONTOS, M. C., LEVINE, G. N., LIEBSON, P. R., MUKHERJEE, D., PETERSON, E. D., SABATINE, M. S., SMALLING, R. W. & ZIEMAN, S. J. 2014. 2014 AHA/ACC Guideline for the Management of Patients With Non–ST-Elevation Acute Coronary Syndromes. *A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines,* 64**,** e139-e228.

ANDERSON, J. L., ADAMS, C. D., ANTMAN, E. M., BRIDGES, C. R., CALIFF, R. M., CASEY JR, D. E., CHAVEY II, W. E., FESMIRE, F. M., HOCHMAN, J. S., LEVIN, T. N., LINCOFF, A. M., PETERSON, E. D., THEROUX, P., WENGER, N. K., WRIGHT, R. S., SMITH JR, S. C., JACOBS, A. K., HALPERIN, J. L., HUNT, S. A., KRUMHOLZ, H. M., KUSHNER, F. G., LYTLE, B. W., NISHIMURA, R., ORNATO, J. P., PAGE, R. L. & RIEGEL, B. 2007. ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction) Developed in Collaboration with the American College of Emergency Physicians, the Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation and the Society for Academic Emergency Medicine. *Journal of the American College of Cardiology,* 50**,** e1-e157.

ANDÒ, G., PORTO, I., MONTALESCOT, G., BOLOGNESE, L., TRANI, C., ORETO, G., HARRINGTON, R. A. & BHATT, D. L. 2016. Radial access in patients with acute coronary syndrome without persistent ST-segment elevation: Systematic review, collaborative meta-analysis, and meta-regression. *International Journal of Cardiology,* 222**,** 1031-1039.

APPLEGATE, R. J., SACRINTY, M. T., KUTCHER, M. A., KAHL, F. R., GANDHI, S. K., SANTOS, R. M. & LITTLE, W. C. 2008. Trends in Vascular Complications After Diagnostic Cardiac Catheterization and Percutaneous Coronary Intervention Via the Femoral Artery, 1998 to 2007. *JACC: Cardiovascular Interventions,* 1**,** 317-326.

ARMSTRONG, P. W., GERSHLICK, A. H., GOLDSTEIN, P., WILCOX, R., DANAYS, T., LAMBERT, Y., SULIMOV, V., ROSELL ORTIZ, F., OSTOJIC, M., WELSH, R. C., CARVALHO, A. C., NANAS, J., ARNTZ, H.-R., HALVORSEN, S., HUBER, K., GRAJEK, S., FRESCO, C., BLUHMKI, E., REGELIN, A.,

VANDENBERGHE, K., BOGAERTS, K. & VAN DE WERF, F. 2013. Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction. *New England Journal of Medicine,* 368**,** 1379-1387.

ARONNE, L. J., BROWN, W. V. & ISOLDI, K. K. 2007. Cardiovascular disease in obesity: A review of related risk factors and risk-reduction strategies. *Journal of Clinical Lipidology,* 1**,** 575-582.

ATES, M., SAHIN, S., KONURALP, C., GULLU, U., CIMEN, S., KIZILAY, M., GUNAY, R., SENSOZ, Y. & AKCAR, M. 2006. Evaluation of risk factors associated with femoral pseudoaneurysms after cardiac catheterization. *Journal of Vascular Surgery,* 43**,** 520-524.

AUSTRALIAN, B. O. S. 2014. Incident Management Policy. *In:* COMMISSION, C. E. (ed.). NSW Health: NSW Health.

AVEZUM, A., MAKDISSE, M., SPENCER, F., GORE, J. M., FOX, K. A. A., MONTALESCOT, G., EAGLE, K. A., WHITE, K., MEHTA, R. H., KNOBEL, E. & PHILIPPE COLLET, J. 2005. Impact of age on management and outcome of acute coronary syndrome: Observations from the global registry of acute coronary events (GRACE). *American Heart Journal,* 149**,** 67-73.

AZZALINI, L., KHAN, R., AL-HAWWAS, M., HATEM, R., FORTIER, A., L'ALLIER, P. L. & LY, H. Q. 2014. Effect of Radial-to-Femoral Access Crossover on Adverse Outcomes in Primary Percutaneous Coronary Intervention. *American Journal of Cardiology,* 114**,** 1165-1173.

AZZALINI, L., TOSIN, K., CHABOT-BLANCHET, M., AVRAM, R., LY, H. Q., GAUDET, B., GALLO, R., DOUCET, S., TANGUAY, J. F., IBRAHIM, R., GREGOIRE, J. C., CREPEAU, J., BONAN, R., DE GUISE, P., NOSAIR, M., DORVAL, J. F., GOSSELIN, G., L'ALLIER, P. L., GUERTIN, M. C., ASGAR, A. W. & JOLICOEUR, E. M. 2015. The Benefits Conferred by Radial Access for Cardiac Catheterization Are Offset by a Paradoxical Increase in the Rate of Vascular Access Site Complications With Femoral Access: The Campeau Radial Paradox. *JACC Cardiovascular Interventions,* 8**,** 1854-64.

BAKLANOV, D. V., KALTENBACH, L. A., MARSO, S. P., SUBHERWAL, S. S., FELDMAN, D. N., GARRATT, K. N., CURTIS, J. P., MESSENGER, J. C. & RAO, S. V. 2013. The Prevalence and Outcomes of Transradial Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: Analysis From the National Cardiovascular Data Registry (2007 to 2011). *Journal of the American College of Cardiology,* 61**,** 420-426.

BALGHITH, M. A., ALGHAMDI, A., ALENEZY, A. & HARB, A. 2011. Op-014: incidence of contrast induced nephropathy in saudi patient after cardiac catherization

International Journal of Cardiology, 147, Supplement 2**,** S41.

BANNING, A. P., BAUMBACH, A., BLACKMAN, D., CURZEN, N., DEVADATHAN, S., FRASER, D., LUDMAN, P., NORELL, M., MUIR, D., NOLAN, J. & REDWOOD, S. 2015. Percutaneous coronary intervention in the UK: recommendations for good practice 2015. *Heart,* 101**,** 1-13.

BATES, E. R. 2016. Balancing the Evidence Base on Coronary Stents. *N Engl J Med,* 375**,** 1286-8.

BAUMANN, B. M., MCCANS, K., STAHMER, S. A., LEONARD, M. B., SHULTS, J. & HOLMES, W. C. 2008. Volumetric bladder ultrasound performed by trained nurses increases catheterization success in pediatric patients. *American Journal of Emergency Medicine,* 26**,** 18-23.

BAZEMORE, A. J. T. M. 2005. Problems and Complications of the Transradial Approach for Coronary Interventions: A Review. *Cath Lab digest,* 13.

BENJAMIN, E. J., VIRANI, S. S., CALLAWAY, C. W., CHAMBERLAIN, A. M., CHANG, A. R., CHENG, S., CHIUVE, S. E., CUSHMAN, M., DELLING, F. N., DEO, R., FERRANTI, S. D. D., FERGUSON, J. F., FORNAGE, M., GILLESPIE, C., ISASI, C. R., JIMÉNEZ, M. C., JORDAN, L. C., JUDD, S. E., LACKLAND, D., LICHTMAN, J. H., LISABETH, L., LIU, S., LONGENECKER, C. T., LUTSEY, P. L., MACKEY, J. S., MATCHAR, D. B., MATSUSHITA, K., MUSSOLINO, M. E., NASIR, K., O'FLAHERTY, M., PALANIAPPAN, L. P., PANDEY, A., PANDEY, D. K., REEVES, M. J., RITCHEY, M. D., RODRIGUEZ, C. J., ROTH, G. A., ROSAMOND, W. D., SAMPSON, U. K. A., SATOU, G. M., SHAH, S. H., SPARTANO, N. L., TIRSCHWELL, D. L., TSAO, C. W., VOEKS, J. H., WILLEY, J. Z., WILKINS,

J. T., WU, J. H., ALGER, H. M., WONG, S. S. & MUNTNER, P. 2018. Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association. *Circulation,* 137**,** e67-e492.

BEYER, A. T., NG, R., SINGH, A., ZIMMET, J., SHUNK, K., YEGHIAZARIANS, Y., PORTS, T. A. & BOYLE, A. J. 2013. Topical nitroglycerin and lidocaine to dilate the radial artery prior to transradial cardiac catheterization: A randomized, placebo-controlled, double-blind clinical trial: The PRE-DILATE Study. *International Journal of Cardiology,* 168**,** 2575-2578.

BHATTY, S. C., RICHARD. SHETTY, RANJITH, JOVIN, ION 2011. Femoral vascular complications in the cardiac catheterisation laboratory: Diagnosis and Management. *Interventional Cardiology* 3**,** 503-514.

BIANCARI, F., D'ANDREA, V., MARCO, C. D., SAVINO, G., TIOZZO, V. & CATANIA, A. 2010. Meta-analysis of randomized trials on the efficacy of vascular closure devices after diagnostic angiography and angioplasty. *American Heart Journal,* 159**,** 518-531.

BLUMENTHAL, R. S., COHN, G. & SCHULMAN, S. P. 2000. Medical therapy versus coronary angioplasty in stable coronary artery disease: a critical review of the literature. *Journal of the American College of Cardiology,* 36**,** 668-673.

BODEN, W. E., O'ROURKE, R. A., TEO, K. K., HARTIGAN, P. M., MARON, D. J., KOSTUK, W. J., KNUDTSON, M., DADA, M., CASPERSON, P., HARRIS, C. L., CHAITMAN, B. R., SHAW, L., GOSSELIN, G., NAWAZ, S., TITLE, L. M., GAU, G., BLAUSTEIN, A. S., BOOTH, D. C., BATES, E. R., SPERTUS, J. A., BERMAN, D. S., MANCINI, G. B. J. & WEINTRAUB, W. S. 2007. Optimal Medical Therapy with or without PCI for Stable Coronary Disease. *New England Journal of Medicine,* 356**,** 1503-1516.

BOGABATHINA, H., SHI, R., SINGIREDDY, S., MORRIS, L., ABDULBAKI, A., ZABHER, H., KATIKANENI, P. & MODI, K. 2018. Reduction of vascular complication rates from femoral artery access in

contemporary women undergoing cardiac catheterization. *Cardiovascular Revascularization Medicine,* 19**,** 27-30.

BOYER, N., BEYER, A., GUPTA, V., DEHGHANI, H., HINDNAVIS, V., SHUNK, K., ZIMMET, J., YEGHIAZARIANS, Y., PORTS, T. & BOYLE, A. 2013. The effects of intra-arterial vasodilators on radial artery size and spasm: implications for contemporary use of trans-radial access for coronary angiography and percutaneous coronary intervention. *Cardiovascular Revascularization Medicine,* 14**,** 321-324.

BRAUNWALD, E. & MORROW, D. A. 2013. Unstable Angina. *Circulation,* 127**,** 2452-2457.

BRENER, M. I., BUSH, A., MILLER, J. M. & HASAN, R. K. 2017. Influence of radial versus femoral access site on coronary angiography and intervention outcomes: A systematic review and meta-analysis. *Catheterization & Cardiovascular Interventions,* 90**,** 1093-1104.

BRIEGER, D. B. & REDFERN, J. 2013. Contemporary themes in acute coronary syndrome management: from acute illness to secondary prevention. *Medical Journal of Australia,* 199**,** 174-8.

BROWN, T. M. & BITTNER, V. 2007. Management of stable patients with coronary heart disease: Clinical implications of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial. *Journal of Clinical Lipidology,* 1**,** 564-574.

BRUECK, M., BANDORSKI, D., KRAMER, W., WIECZOREK, M., HÖLTGEN, R. & TILLMANNS, H. 2009. A Randomized Comparison of Transradial Versus Transfemoral Approach for Coronary Angiography and Angioplasty. *JACC: Cardiovascular Interventions,* 2**,** 1047-1054.

BUCHOLZ, E. M., BUTALA, N. M., NORMAND, S.-L. T., WANG, Y. & KRUMHOLZ, H. M. 2016. Association of Guideline-Based Admission Treatments and Life Expectancy After Myocardial Infarction in Elderly Medicare Beneficiaries. *Journal of the American College of Cardiology,* 67**,** 2378-2391.

BURKE, A. P., FARB, A., MALCOM, G. T., LIANG, Y.-H., SMIALEK, J. & VIRMANI, R. 1997. Coronary Risk Factors and Plaque Morphology in Men with Coronary Disease Who Died Suddenly. *New England Journal of Medicine,* 336**,** 1276-1282.

BURKE, G. M., GENUARDI, M., SHAPPELL, H., D'AGOSTINO, R. B. & MAGNANI, J. W. 2017. Temporal Associations Between Smoking and Cardiovascular Disease, 1971 to 2006 (from the Framingham Heart Study). *The American Journal of Cardiology,* 120**,** 1787-1791.

BURNS, M. K. 2014. How to establish interrater reliability. *Nursing2018,* 44**,** 56-58.

CAIXETA, A., LEON, M. B., LANSKY, A. J., NIKOLSKY, E., AOKI, J., MOSES, J. W., SCHOFER, J., MORICE, M. C., SCHAMPAERT, E., KIRTANE, A. J., POPMA, J. J., PARISE, H., FAHY, M. & MEHRAN, R. 2009. 5-year clinical outcomes after sirolimus-eluting stent implantation insights from a patient-level pooled analysis of 4 randomized trials comparing sirolimus-eluting stents with bare-metal stents. *Journal of American College of Cardiology,* 54**,** 894-902.

CAMM, A., LUSCHER, T. & SERRUYS, P. W. 2006. *The ESC textbook of Cardiovascular Medicine,* France, European Society of Cardiology.

CANTOR, W. J., KO, D. T., NATARAJAN, M., LE MAY, M. R., DZAVI-K, V., VELIANOU, J. L., WIJEYSUNDERA, H., PURDHAM, D. & KINGSBURY, K. 2011. 715 Reperfusion times for radial vs. femoral access in patients with ST-elevation myocardial infarction undergoing primary PCI: Observations from the CCN provincial primary PCI registry. *Canadian Journal of Cardiology,* 27**,** S325.

CANTOR, W. J., MEHTA, S. R., YUAN, F., DŽAVÍK, V., WORTHLEY, M., NIEMELÄ, K., VALENTIN, V., FUNG, A., CHEEMA, A. N., WIDIMSKY, P., NATARAJAN, M., JEDRZEJOWSKI, B. & JOLLY, S. S. 2015. Radial versus femoral access for elderly patients with acute coronary syndrome undergoing coronary angiography and intervention: insights from the RIVAL trial. *American Heart Journal,* 170**,** 880-886.

CASTLE, E. V., RATHOD, K. S., GUTTMANN, O. P., JENKINS, A. M., MCCARTHY, C. D., KNIGHT, C. J., O'MAHONY, C., MATHUR, A., SMITH, E. J., WEERACKODY, R., TIMMIS, A. D., WRAGG, A. & JONES, D. A. 2019. Routine use of fluoroscopic guidance and up-front femoral angiography results in reduced femoral complications in patients undergoing coronary angiographic procedures: an observational study using an Interrupted Time-Series analysis. *Heart Vessels,* 34**,** 419-426.

CASTRO-DOMINGUEZ, Y., DHARMARAJAN, K. & MCNAMARA, R. L. 2018. Predicting death after acute myocardial infarction. *Trends in Cardiovascular Medicine,* 28**,** 102-109.

CELERMAJER, D. S., SORENSEN, K. E., SPIEGELHALTER, D. J., GEORGAKOPOULOS, D., ROBINSON, J. & DEANFIELD, J. E. 1994. Aging is associated with endothelial dysfunction in healthy men years before the age-related decline in women. *Journal of the American College of Cardiology,* 24**,** 471-476.

CHACKO, M., LINCOFF, A. M., WOLSKI, K. E., COHEN, D. J., BITTL, J. A., LANSKY, A. J., TSUCHIYA, Y., BETRIU, A., YEN, M. H., CHEW, D. P., CHO, L. & TOPOL, E. J. 2006. Ischemic and bleeding outcomes in women treated with bivalirudin during percutaneous coronary intervention: A subgroup analysis of the Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events (REPLACE)-2 trial. *American Heart Journal,* 151**,** 1032.e1-1032.e7.

CHAO, T. F., LIP, G. Y. H., LIU, C. J., LIN, Y. J., CHANG, S. L., LO, L. W., HU, Y. F., TUAN, T. C., LIAO, J. N., CHUNG, F. P., CHEN, T. J. & CHEN, S. A. 2018. Relationship of Aging and Incident Comorbidities to Stroke Risk in Patients With Atrial Fibrillation. *Journal of Amercian College of Cardiology,* 71**,** 122-132.

CHEW, D. P., FRENCH, J., BRIFFA, T. G., HAMMETT, C. J., ELLIS, C. J., RANASINGHE, I., ALIPRANDI-COSTA, B. J., ASTLEY, C. M., TURNBULL, F. M., LEFKOVITS, J., REDFERN, J., CARR, B., GAMBLE, G. D., LINTERN, K. J., HOWELL, T. E., PARKER, H., TAVELLA, R., BLOOMER, S. G., HYUN, K. K. &

BRIEGER, D. B. 2013. Acute coronary syndrome care across Australia and New Zealand: the SNAPSHOT ACS study. *Medical Journal of Australia,* 199**,** 185-91.

CHEW, D. P., MACISAAC, A. I., LEFKOVITS, J., HARPER, R. W., SLAWOMIRSKI, L., BRADDOCK, D., HORSFALL, M. J., BUCHAN, H. A., ELLIS, C. J., BRIEGER, D. B. & BRIFFA, T. G. 2016a. Variation in coronary angiography rates in Australia: correlations with socio-demographic, health service and disease burden indices. *Medical Journal of Australia,* 205**,** 114-20.

CHEW, D. P., SCOTT, I. A., CULLEN, L., FRENCH, J. K., BRIFFA, T. G., TIDEMAN, P. A., WOODRUFFE, S., KERR, A., BRANAGAN, M. & AYLWARD, P. E. 2016b. National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the management of acute coronary syndromes 2016. *Medical Journal of Australia,* 205**,** 128-33.

CHUA, T. P., HOWLING, S. J., WRIGHT, C. & FOX, K. M. 1998. Ultrasound-guided compression of femoral pseudoaneurysm: an audit of practice. *International Journal of Cardiology,* 63**,** 245-250.

CHUGH, S. K., CHUGH, Y. & CHUGH, S. 2015. How to tackle complications in radial procedures: Tip and tricks. *Indian Heart Journal,* 67**,** 275-281.

COLHOUN, H. M., BETTERIDGE, D. J., DURRINGTON, P. N., HITMAN, G. A., NEIL, H. A., LIVINGSTONE, S. J., THOMASON, M. J., MACKNESS, M. I., CHARLTON-MENYS, V. & FULLER, J. H. 2004. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. *Lancet,* 364**,** 685-96.

COLLINS, R., REITH, C., EMBERSON, J., ARMITAGE, J., BAIGENT, C., BLACKWELL, L., BLUMENTHAL, R., DANESH, J., SMITH, G. D., DEMETS, D., EVANS, S., LAW, M., MACMAHON, S., MARTIN, S., NEAL, B., POULTER, N., PREISS, D., RIDKER, P., ROBERTS, I., RODGERS, A., SANDERCOCK, P., SCHULZ, K., SEVER, P., SIMES, J., SMEETH, L., WALD, N., YUSUF, S. & PETO, R. 2016.

Interpretation of the evidence for the efficacy and safety of statin therapy. *Lancet,* 388**,** 2532-2561.

COOPER, C. J., EL-SHIEKH, R. A., COHEN, D. J., BLAESING, L., BURKET, M. W., BASU, A. & MOORE, J. A. 1999. Effect of transradial access on quality of life and cost of cardiac catheterization: A randomized comparison. *American Heart Journal,* 138**,** 430-436.

COX, N. 2008. Managing the Femoral Artery in Coronary Angiography. *Heart, Lung and Circulation,* 17**,** S65-S69.

COX, N., RESNIC, F. S., POPMA, J. J., SIMON, D. I., EISENHAUER, A. C. & ROGERS, C. 2004. Comparison of the risk of vascular complications associated with femoral and radial access coronary catheterization procedures in obese versus nonobese patients. *The American Journal of Cardiology,* 94**,** 1174-1177.

DAHM, J. B., VOGELGESANG, D., HUMMEL, A., STAUDT, A., VÖLZKE, H. & FELIX, S. B. 2002. A randomized trial of 5 vs. 6 French transradial percutaneous coronary interventions. *Catheterization and Cardiovascular Interventions,* 57**,** 172-176.

DANCHIN, N., PUYMIRAT, E., STEG, P. G., GOLDSTEIN, P., SCHIELE, F., BELLE, L., COTTIN, Y., FAJADET, J., KHALIFE, K., COSTE, P., FERRIERES, J. & SIMON, T. 2014. Five-year survival in patients with ST-segment-elevation myocardial infarction according to modalities of reperfusion therapy: the French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) 2005 Cohort. *Circulation,* 129**,** 1629-36.

DAUERMAN, H. L., APPLEGATE, R. J. & COHEN, D. J. 2007. Vascular Closure Devices: The Second Decade. *Journal of the American College of Cardiology,* 50**,** 1617-1626.

DAUERMAN, H. L., RAO, S. V., RESNIC, F. S. & APPLEGATE, R. J. 2011. Bleeding Avoidance Strategies: Consensus and Controversy. *Journal of the American College of Cardiology,* 58**,** 1-10.

DAVIES, A. J., NAUDIN, C., AL-OMARY, M., KHAN, A., OLDMEADOW, C., JONES, M., BASTIAN, B., BHAGWANDEEN, R., FLETCHER, P., LEITCH, J. & BOYLE, A. 2017. Disparities in the incidence

of acute myocardial infarction: long-term trends from the Hunter region. *Internal Medicine Journal,* 47**,** 557-562.

DE LUCA, G., DIRKSEN, M. T., SPAULDING, C., KELBAEK, H., SCHALIJ, M., THUESEN, L., VAN DER HOEVEN, B., VINK, M. A., KAISER, C., MUSTO, C., CHECHI, T., SPAZIANI, G., DIAZ DE LA LLERA, L. S., PASCERI, V., DI LORENZO, E., VIOLINI, R., SURYAPRANATA, H. & STONE, G. W. 2013. Impact of diabetes on long-term outcome after primary angioplasty: insights from the DESERT cooperation. *Diabetes Care,* 36**,** 1020-5.

DE MARZO, V., D'AMARIO, D., GALLI, M., VERGALLO, R. & PORTO, I. 2018. High-risk percutaneous coronary intervention: how to define it today? *Minerva Cardioangiol,* 66**,** 576-593.

DEEK, H., NEWTON, P., SHEERIN, N., NOUREDDINE, S. & DAVIDSON, P. M. 2014. Contrast media induced nephropathy: a literature review of the available evidence and recommendations for practice. *Australian Critcal Care,* 27**,** 166-71.

DEFTEREOS, S., GIANNOPOULOS, G., RAISAKIS, K., HAHALIS, G., KAOUKIS, A., KOSSYVAKIS, C., AVRAMIDES, D., PAPPAS, L., PANAGOPOULOU, V., PYRGAKIS, V., ALEXOPOULOS, D., STEFANADIS, C. & CLEMAN, M. W. 2013. Moderate Procedural Sedation and Opioid Analgesia During Transradial Coronary Interventions to Prevent Spasm: A Prospective Randomized Study. *JACC: Cardiovascular Interventions,* 6**,** 267-273.

DENCKER, D., PEDERSEN, F., ENGSTROM, T., KOBER, L., HOJBERG, S., NIELSEN, M. B., SCHROEDER, T. V. & LONN, L. 2016. Major femoral vascular access complications after coronary diagnostic and interventional procedures: A Danish register study. *International Journal of Cardiology,* 202**,** 604-8.

DEVGUN, J. K., GUL, S., MOHANANEY, D., JONES, B. M., HUSSAIN, M. S., JOBANPUTRA, Y., KUMAR, A., SVENSSON, L. G., TUZCU, E. M. & KAPADIA, S. R. 2018. Cerebrovascular Events After Cardiovascular Procedures: Risk Factors, Recognition, and Prevention Strategies. *Journal of Amercian College of Cardiology,* 71**,** 1910-1920.

DHARMA, S., KEDEV, S., PATEL, T., RAO, S. V., BERTRAND, O. F. & GILCHRIST, I. C. 2017. Radial artery diameter does not correlate with body mass index: A duplex ultrasound analysis of 1706 patients undergoing trans-radial catheterization at three experienced radial centers. *International Journal of Cardiology,* 228**,** 169-172.

DOUKETIS, J. D., SPYROPOULOS, A. C., KAATZ, S., BECKER, R. C., CAPRINI, J. A., DUNN, A. S., GARCIA, D. A., JACOBSON, A., JAFFER, A. K., KONG, D. F., SCHULMAN, S., TURPIE, A. G., HASSELBLAD, V., ORTEL, T. L. & INVESTIGATORS, B. 2015. Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation. *New England Journal of Medicine,* 373**,** 823-33.

DUKKIPATI, S., O'NEILL, W. W., HARJAI, K. J., SANDERS, W. P., DEO, D., BOURA, J. A., BARTHOLOMEW, B. A., YERKEY, M. W., SADEGHI, H. M. & KAHN, J. K. 2004. Characteristics of cerebrovascular accidents after percutaneous coronary interventions. *Journal of Amercian College of Cardiology,* 43**,** 1161-7.

EIKELBOOM, J. W., MEHTA, S. R., ANAND, S. S., XIE, C., FOX, K. A. A. & YUSUF, S. 2006. Adverse impact of bleeding on prognosis in patients with acute coronary syndromes. *Circulation,* 114**,** 774-82.

EISEN, A., CANNON, C. P., BLAZING, M. A., BOHULA, E. A., PARK, J. G., MURPHY, S. A., WHITE, J. A., GIUGLIANO, R. P. & BRAUNWALD, E. 2016. The benefit of adding ezetimibe to statin therapy in patients with prior coronary artery bypass graft surgery and acute coronary syndrome in the IMPROVE-IT trial. *European Heart Journal,* 37**,** 3576-3584.

ELROD, J. K. & FORTENBERRY, J. L. 2017. The hub-and-spoke organization design: an avenue for serving patients well. *BMC Health Services Research,* 17**,** 457.

EZAD, S., DAVIES, A. J., CHEEMA, H., WILLIAMS, T. & LEITCH, J. 2018. Keys to Achieving Target First Medical Contact to Balloon Times and Bypassing Emergency Department More Important Than Distance. *Cardiology research and practice,* 2018**,** 2951860-2951860.

FAOUR, A., CHERRETT, C., GIBBS, O., LINTERN, K., RAJARATNAM, R., JUERGENS, C. & FRENCH, J. 2017. The University of Glasgow ECG Analysis Algorithm is Not Specific for the Pre-hospital diagnosis of STEMI in Patients with Bundle Branch Block. *Heart, Lung and Circulation,* 26**,** S236.

FARKOUH, M. E., DOMANSKI, M., DANGAS, G. D., GODOY, L. C., MACK, M. J., SIAMI, F. S., HAMZA, T. H., SHAH, B., STEFANINI, G. G., SIDHU, M. S., TANGUAY, J.-F., RAMANATHAN, K., SHARMA, S. K., FRENCH, J., HUEB, W., COHEN, D. J. & FUSTER, V. 2018. Long-term Survival following Multivessel Revascularization in Patients with Diabetes (FREEDOM Follow-On Study). *Journal of the American College of Cardiology*.

FAROUQUE, H. M. O., TREMMEL, J. A., RAISSI SHABARI, F., AGGARWAL, M., FEARON, W. F., NG, M. K. C., REZAEE, M., YEUNG, A. C. & LEE, D. P. 2005. Risk factors for the development of retroperitoneal hematoma after percutaneous coronary intervention in the era of glycoprotein IIb/IIIa inhibitors and vascular closure devices. *Journal of the American College of Cardiology,* 45**,** 363-368.

FARSHID, A., BRIEGER, D., HYUN, K., HAMMETT, C., ELLIS, C., RANKIN, J., LEFKOVITS, J., CHEW, D. & FRENCH, J. 2016. Characteristics and Clinical Course of STEMI Patients who Received no Reperfusion in the Australia and New Zealand SNAPSHOT ACS Registry. *Heart Lung & Circulation,* 25**,** 132-9.

FECH, J. C., WELSH, R., HEGADOREN, K. & NORRIS, C. M. 2012. Caring for the radial artery post-angiogram: a pilot study on a comparison of three methods of compression. *European Journal of Cardiovascular Nursing,* 11**,** 44-50.

FERNANDEZ-AVILES, F., ALONSO, J. J., CASTRO-BEIRAS, A., VAZQUEZ, N., BLANCO, J., ALONSO-BRIALES, J., LOPEZ-MESA, J., FERNANDEZ-VAZQUEZ, F., CALVO, I., MARTINEZ-ELBAL, L., SAN ROMAN, J. A. & RAMOS, B. 2004. Routine invasive strategy within 24 hours of thrombolysis

versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet,* 364**,** 1045-53.

FERRANTE, G., RAO, S. V., JÜNI, P., DA COSTA, B. R., REIMERS, B., CONDORELLI, G., ANZUINI, A., JOLLY, S. S., BERTRAND, O. F., KRUCOFF, M. W., WINDECKER, S. & VALGIMIGLI, M. 2016. Radial Versus Femoral Access for Coronary Interventions Across the Entire Spectrum of Patients With Coronary Artery Disease: A Meta-Analysis of Randomized Trials. *JACC: Cardiovascular Interventions,* 9**,** 1419-1434.

FOREMAN, K. J., MARQUEZ, N., DOLGERT, A., FUKUTAKI, K., FULLMAN, N., MCGAUGHEY, M., PLETCHER, M. A., SMITH, A. E., TANG, K., YUAN, C.-W., BROWN, J. C., FRIEDMAN, J., HE, J., HEUTON, K. R., HOLMBERG, M., PATEL, D. J., REIDY, P., CARTER, A., CERCY, K., CHAPIN, A., DOUWES-SCHULTZ, D., FRANK, T., GOETTSCH, F., LIU, P. Y., NANDAKUMAR, V., REITSMA, M. B., REUTER, V., SADAT, N., SORENSEN, R. J. D., SRINIVASAN, V., UPDIKE, R. L., YORK, H., LOPEZ, A. D., LOZANO, R., LIM, S. S., MOKDAD, A. H., VOLLSET, S. E. & MURRAY, C. J. L. 2018. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. *The Lancet,* 392**,** 2052-2090.

FORSTER, H. P., EMANUEL, E. & GRADY, C. 2001. The 2000 revision of the Declaration of Helsinki: a step forward or more confusion? *Lancet,* 358**,** 1449-53.

FOX, C., S., GOLDEN, S., HILL, ANDERSON, C., BRAY, G., A., BURKE, L., E., DE BOER, I., H., DEEDWANIA, P., ECKEL ROBERT, H., ERSHOW, A., G., FRADKIN, J., INZUCCHI, S., E., KOSIBOROD, M., NELSON, R., G., PATEL, M., J., PIGNONE, M., QUINN, L., SCHAUER, P., R., SELVIN, E. & VAFIADIS, D., K. 2015. Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus in Light of Recent Evidence. *Circulation,* 132**,** 691-718.

FUCHS, S., STABILE, E., KINNAIRD, T. D., MINTZ, G. S., GRUBERG, L., CANOS, D. A., PINNOW, E. E., KORNOWSKI, R., SUDDATH, W. O., SATLER, L. F., PICHARD, A. D., KENT, K. M. & WEISSMAN,

N. J. 2002. Stroke complicating percutaneous coronary interventions: incidence, predictors, and prognostic implications. *Circulation,* 106**,** 86-91.

GABB, G. M., MANGONI, A. A., ANDERSON, C. S., COWLEY, D., DOWDEN, J. S., GOLLEDGE, J., HANKEY, G. J., HOWES, F. S., LECKIE, L., PERKOVIC, V., SCHLAICH, M., ZWAR, N. A., MEDLEY, T. L. & ARNOLDA, L. 2016. Guideline for the diagnosis and management of hypertension in adults - 2016. *Medical Journal of Australia,* 205**,** 85-9.

GAEDE, P., VEDEL, P., LARSEN, N., JENSEN, G. V., PARVING, H. H. & PEDERSEN, O. 2003. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med,* 348**,** 383-93.

GALASSI, A., GRANTHAM, A., KANDZARI, D., LOMBARDI, W., MOUSSA, I., THOMPSON, C., WERNER, G., CHAMBERS, C. & BRILAKIS, E. 2014. Percutaneous Treatment of Coronary Chronic Total Occlusion Part 2: Technical Approach. *Interventional Cardiology Review,* 9**,** 201-207.

GALLOE, A. M., KELBAEK, H., THUESEN, L., HANSEN, H. S., RAVKILDE, J., HANSEN, P. R., CHRISTIANSEN, E. H., ABILDGAARD, U., STEPHANSEN, G., LASSEN, J. F., ENGSTROM, T., JENSEN, J. S., JEPPESEN, J. L. & BLIGAARD, N. 2017. 10-Year Clinical Outcome After Randomization to Treatment by Sirolimus- or Paclitaxel-Eluting Coronary Stents. *Journal of American College of Cardiology,* 69**,** 616-624.

GANZ, P. & HSUE, P. 2009. Individualised Approach to the Management of Coronary Heart Disease. *Journal of the American College of Cardiology,* 53**,** 331-333.

GEDIKOGLU, M., OGUZKURT, L., GUR, S., ANDIC, C., SARITURK, C. & OZKAN, U. 2013. Comparison of ultrasound guidance with the traditional palpation and fluoroscopy method for the common femoral artery puncture. *Catheterization and Cardiovascular Interventions,* 82**,** 1187-1192.

GERSH, B. J., STONE, G. W., WHITE, H. D. & HOLMES, D. R., JR. 2005. Pharmacological facilitation of primary percutaneous coronary intervention for acute myocardial infarction: is the slope of the curve the shape of the future? *Jama,* 293**,** 979-86.

GERSHLICK, A. H., STEPHENS-LLOYD, A., HUGHES, S., ABRAMS, K. R., STEVENS, S. E., UREN, N. G., DE BELDER, A., DAVIS, J., PITT, M., BANNING, A., BAUMBACH, A., SHIU, M. F., SCHOFIELD, P., DAWKINS, K. D., HENDERSON, R. A., OLDROYD, K. G. & WILCOX, R. 2005. Rescue Angioplasty after Failed Thrombolytic Therapy for Acute Myocardial Infarction. *New England Journal of Medicine,* 353**,** 2758-2768.

GIBBONS, R. J., ABRAMS, J., CHATTERJEE, K., DALEY, J., DEEDWANIA, P. C., DOUGLAS, J. S., FERGUSON, T. B., JR., FIHN, S. D., FRAKER, T. D., JR., GARDIN, J. M., O'ROURKE, R. A., PASTERNAK, R. C., WILLIAMS, S. V., GIBBONS, R. J., ALPERT, J. S., ANTMAN, E. M., HIRATZKA, L. F., FUSTER, V., FAXON, D. P., GREGORATOS, G., JACOBS, A. K. & SMITH, S. C., JR. 2003. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina--summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). *Circulation,* 107**,** 149-58.

GILES, M., WATTS, W., O'BRIEN, A., BERENGER, S., PAUL, M., MCNEIL, K. & BANTAWA, K. 2015. Does our bundle stack up! Innovative nurse-led changes for preventing catheter-associated urinary tract infection (CAUTI). *Healthcare Infection,* 20**,** 62-71.

GLADWELL, T. D. 2002. Bivalirudin: A direct thrombin inhibitor. *Clinical Therapeutics,* 24**,** 38-58.

GOSWAMI, R., OLIPHANT, C. S., YOUSSEF, H., MORSY, M. & KHOUZAM, R. N. 2016. Radial Artery Occlusion After Cardiac Catheterization: Significance, Risk Factors, and Management. *Current Problems in Cardiology,* 41**,** 214-227.

GRUNDY, S. M., STONE, N. J., BAILEY, A. L., BEAM, C., BIRTCHER, K. K., BLUMENTHAL, R. S., BRAUN, L. T., DE FERRANTI, S., FAIELLA-TOMMASINO, J., FORMAN, D. E., GOLDBERG, R., HEIDENREICH, P. A., HLATKY, M. A., JONES, D. W., LLOYD-JONES, D., LOPEZ-PAJARES, N., NDUMELE, C. E., ORRINGER, C. E., PERALTA, C. A., SASEEN, J. J., SMITH, S. C., SPERLING, L., VIRANI, S. S. & YEBOAH, J. 2018. 2018

AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines*.

GRÜNTZIG, A. 1978. TRANSLUMINAL DILATATION OF CORONARY-ARTERY STENOSIS. *The Lancet,* 311**,** 263.

HAHALIS, G., DANGAS, G., DAVLOUROS, P. & ALEXOPOULOS, D. 2010. Revascularization strategies for stable multivessel and unprotected left main coronary artery disease: From BARI to SYNTAX. *International Journal of Cardiology*.

HAMON, M., BARON, J., VIADER, F. & HAMON, M. 2008. Periprocedural Stroke and Cardiac Catheterization. *Circulation,* 118**,** 678-683.

HAMON, M. & COUTANCE, G. 2009. Transradial Intervention for Minimizing Bleeding Complications in Percutaneous Coronary Intervention. *The American Journal of Cardiology,* 104**,** 55C-59C.

HEAD, S. J., MILOJEVIC, M., DAEMEN, J., AHN, J. M., BOERSMA, E., CHRISTIANSEN, E. H., DOMANSKI, M. J., FARKOUH, M. E., FLATHER, M., FUSTER, V., HLATKY, M. A., HOLM, N. R., HUEB, W. A., KAMALESH, M., KIM, Y. H., MAKIKALLIO, T., MOHR, F. W., PAPAGEORGIOU, G., PARK, S. J., RODRIGUEZ, A. E., SABIK, J. F., 3RD, STABLES, R. H., STONE, G. W., SERRUYS, P. W. & KAPPETEIN, A. P. 2018. Stroke Rates Following Surgical Versus Percutaneous Coronary Revascularization. *J Am Coll Cardiol,* 72**,** 386-398.

HEALTH, N. 2011. Chest Pain Evaluation (NSW Chest Pain Pathway). *In:* INNOVATION, A. O. C. (ed.). Sydney: NSW Health.

HELLER, R. F., FISHER, J. D., D'ESTE, C. A., LIM, L. L., DOBSON, A. J. & PORTER, R. 2000. Death and readmission in the year after hospital admission with cardiovascular disease: the Hunter Area Heart and Stroke Register. *Medical Journal of Australia,* 172**,** 261-5.

HENNEMAN, E. A., BLANK, F. S. J., GAWLINSKI, A. & HENNEMAN, P. L. 2006. Strategies used by nurses to recover medical errors in an academic emergency department setting. *Applied Nursing Research,* 19**,** 70-77.

HENNEMAN, E. A., GAWLINSKI, A., BLANK, F. S., HENNEMAN, P. L., JORDAN, D. & MCKENZIE, J. B. 2010. Strategies Used by Critical Care Nurses to Identify, Interrupt, and Correct Medical Errors. *American Journal of Critical Care,* 19**,** 500-509.

HENNEMAN, E. A., GAWLINSKI, A. & GIULIANO, K. K. 2012. Surveillance: A Strategy for Improving Patient Safety in Acute and Critical Care Units. *Critical Care Nurse,* 32**,** e9-e18.

HIBBERT, B., SIMARD, T., WILSON, K. R., HAWKEN, S., WELLS, G. A., RAMIREZ, F. D., LE MAY, M. R., SO, D. Y., GLOVER, C. A., FROESCHL, M., MARQUIS, J.-F., LABINAZ, M., DICK, A. & O'BRIEN, E. R. 2012. Transradial Versus Transfemoral Artery Approach for Coronary Angiography and Percutaneous Coronary Intervention in the Extremely Obese. *JACC: Cardiovascular Interventions,* 5**,** 819-826.

HIGGS, S. M. & SMITH, F. C. T. 2005. Surgical Management of Massive Rectus Sheath Haematoma due to Inferior Epigastric Artery Rupture. *EJVES Extra,* 9**,** 93-95.

HILLIARD, A. A., FROM, A. M., LENNON, R. J., SINGH, M., LERMAN, A., GERSH, B. J., HOLMES, D. R., JR., RIHAL, C. S. & PRASAD, A. 2010. Percutaneous revascularization for stable coronary artery disease temporal trends and impact of drug-eluting stents. *JACC Cardiovascular Interventions,* 3**,** 172-9.

HIRSHFELD JR, J. W., BALTER, S., BRINKER, J. A., KERN, M. J., KLEIN, L. W., LINDSAY, B. D., TOMMASO, C. L., TRACY, C. M., WAGNER, L. K., CREAGER, M. A., ELNICKI, M., LORELL, B. H., RODGERS, G. P. & WEITZ, H. H. 2004. ACCF/AHA/HRS/SCAI clinical competence statement on physician knowledge to optimize patient safety and image quality in fluoroscopically guided invasive cardiovascular procedures: A report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on

Clinical Competence and Training. *Journal of the American College of Cardiology,* 44**,** 2259-2282.

HO, H. H., JAFARY, F. H. & ONG, P. J. 2012. Radial artery spasm during transradial cardiac catheterization and percutaneous coronary intervention: incidence, predisposing factors, prevention, and management. *Cardiovascular Revascularization Medicine,* 13**,** 193-195.

HOFFMAN, S. J., HOLMES, D. R., JR., RABINSTEIN, A. A., RIHAL, C. S., GERSH, B. J., LENNON, R. J., BASHIR, R. & GULATI, R. 2011. Trends, predictors, and outcomes of cerebrovascular events related to percutaneous coronary intervention: a 16-year single-center experience. *JACC Cardiovascular Interventions,* 4**,** 415-22.

HOFFMAN, S. J., ROUTLEDGE, H. C., LENNON, R. J., MUSTAFA, M. Z., RIHAL, C. S., GERSH, B. J., HOLMES, D. R., JR. & GULATI, R. 2012. Procedural factors associated with percutaneous coronary intervention-related ischemic stroke. *JACC Cardiovascular Interventions,* 5**,** 200-6.

HORWITZ, P. A., BERLIN, J. A., SAUER, W. H., LASKEY, W. K., KRONE, R. J. & KIMMEL, S. E. 2003. Bleeding risk of platelet glycoprotein IIb/IIIa receptor antagonists in broad-based practice (results from the Society for Cardiac Angiography and Interventions Registry). *The American Journal of Cardiology,* 91**,** 803-806.

IBANEZ, B., JAMES, S., AGEWALL, S., ANTUNES, M. J., BUCCIARELLI-DUCCI, C., BUENO, H., CAFORIO, A. L. P., CREA, F., GOUDEVENOS, J. A., HALVORSEN, S., HINDRICKS, G., KASTRATI, A., LENZEN, M. J., PRESCOTT, E., ROFFI, M., VALGIMIGLI, M., VARENHORST, C., VRANCKX, P., WIDIMSKÝ, P. & GROUP, E. S. C. S. D. 2018. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevationThe Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal,* 39**,** 119-177.

IQBAL, M. B., NADRA, I. J., DING, L., FUNG, A., AYMONG, E., CHAN, A. W., HODGE, S., ROBINSON, S. D. & SIEGA, A. D. 2016. Long-term outcomes following drug-eluting stents versus bare metal

stents for primary percutaneous coronary intervention: A real-world analysis of 11,181 patients from the british columbia cardiac registry. *Catheter Cardiovascular Interventions,* 88**,** 24-35.

JANSSON, K. & FRANSSON, S. G. 1996. Mortality related to coronary angiography. *Clinical Radiology,* 51**,** 858-860.

JOLLY, S., NIEMELA, K., XAVIER, D., WIDIMSKY, P., BUDAJ, A., VALENTIN, V., LEWIS, B., AVEZUM, A., STEG, P., RAO, S., CAIRNS, J., CHROLAVICIUS, S., YUSUF, S. & MEHTA, S. 2011a. Design and rationale of the RadIal Vs. femorAL access for coronary intervention (RIVAL) trial: A randomized comparison of radial versus femoral access for coronary angiography or intervention in patients with acute coronary syndromes. *American Heart Journal,* 161**,** 254-260.e4.

JOLLY, S. S., AMLANI, S., HAMON, M., YUSUF, S. & MEHTA, S. R. 2009. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: A systematic review and meta-analysis of randomized trials. *American Heart Journal,* 157**,** 132-140.

JOLLY, S. S., CAIRNS, J. A., YUSUF, S., MEEKS, B., GAO, P., HART, R. G., KEDEV, S., STANKOVIC, G., MORENO, R., HORAK, D., KASSAM, S., ROKOSS, M. J., LEUNG, R. C., EL-OMAR, M., ROMPPANEN, H. O., ALAZZONI, A., ALAK, A., FUNG, A., ALEXOPOULOS, D., SCHWALM, J. D., VALETTAS, N., DZAVIK, V. & INVESTIGATORS, T. 2015a. Stroke in the TOTAL trial: a randomized trial of routine thrombectomy vs. percutaneous coronary intervention alone in ST elevation myocardial infarction. *European Heart Journal,* 36**,** 2364-72.

JOLLY, S. S., CAIRNS, J. A., YUSUF, S., MEEKS, B., POGUE, J., ROKOSS, M. J., KEDEV, S., THABANE, L., STANKOVIC, G., MORENO, R., GERSHLICK, A., CHOWDHARY, S., LAVI, S., NIEMELA, K., STEG, P. G., BERNAT, I., XU, Y., CANTOR, W. J., OVERGAARD, C. B., NABER, C. K., CHEEMA, A. N., WELSH, R. C., BERTRAND, O. F., AVEZUM, A., BHINDI, R., PANCHOLY, S., RAO, S. V.,

NATARAJAN, M. K., TEN BERG, J. M., SHESTAKOVSKA, O., GAO, P., WIDIMSKY, P., DZAVIK, V. & INVESTIGATORS, T. 2015b. Randomized trial of primary PCI with or without routine manual thrombectomy. *New England Journal of Medicine,* 372**,** 1389-98.

JOLLY, S. S., YUSUF, S., CAIRNS, J., NIEMELÄ, K., XAVIER, D., WIDIMSKY, P., BUDAJ, A., NIEMELÄ, M., VALENTIN, V., LEWIS, B. S., AVEZUM, A., STEG, P. G., RAO, S. V., GAO, P., AFZAL, R., JOYNER, C. D., CHROLAVICIUS, S. & MEHTA, S. R. 2011b. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *The Lancet,* 377**,** 1409-1420.

JORGENSEN, H. S., NAKAYAMA, H., REITH, J., RAASCHOU, H. O. & OLSEN, T. S. 1996. Acute stroke with atrial fibrillation. The Copenhagen Stroke Study. *Stroke,* 27**,** 1765-9.

JURGA, J., NYMAN, J., TORNVALL, P., MANNILA, M. N., SVENARUD, P., VAN DER LINDEN, J. & SARKAR, N. 2011. Cerebral microembolism during coronary angiography: a randomized comparison between femoral and radial arterial access. *Stroke,* 42**,** 1475-7.

KAJI, A. H., SCHRIGER, D. & GREEN, S. 2014. Looking Through the Retrospectoscope: Reducing Bias in Emergency Medicine Chart Review Studies. *Annals of Emergency Medicine,* 64**,** 292-298.

KANEI, Y., KWAN, T., NAKRA, N., LIOU, M., HUANG, Y., VALVES, L., FOX, J., CHEN, J. & SAITO, S. 2011. Transradial Cardiac Catherization: A review of Access site complications. *Catherisation and Cardiovascualr Interventions,* 78.

KASSEM, H. H., ELMAHDY, M. F., EWIS, E. B. & MAHDY, S. G. 2013. Incidence and predictors of post-catheterization femoral artery pseudoaneurysms. *The Egyptian Heart Journal,* 65**,** 213-221.

KASTRATI, A., NEUMANN, F.-J., MEHILLI, J., BYRNE, R. A., IIJIMA, R., BÜTTNER, H. J., KHATTAB, A. A., SCHULZ, S., BLANKENSHIP, J. C., PACHE, J., MINNERS, J., SEYFARTH, M., GRAF, I., SKELDING, K. A., DIRSCHINGER, J., RICHARDT, G., BERGER, P. B. & SCHÖMIG, A. 2008. Bivalirudin versus Unfractionated Heparin during Percutaneous Coronary Intervention. *New England Journal of Medicine,* 359**,** 688-696.

KATZENELLENBOGEN, J. M., SANFILIPPO, F. M., HOBBS, M. S. T., BRIFFA, T. G., KNUIMAN, M. W., DIMER, L., THOMPSON, P. L. & THOMPSON, S. C. 2012. Complex impact of remoteness on the incidence of myocardial infarction in Aboriginal and non-Aboriginal people in Western Australia. *Australian Journal of Rural Health,* 20**,** 305-311.

KERN, M. J. 2011. *The Cardiac Catherization Handbook,* Philadelphia, Saunders Elsevier.

KHAN, A. A., WILLIAMS, T., SAVAGE, L., STEWART, P., ASHRAF, A., DAVIES, A. J., FADDY, S., ATTIA, J., OLDMEADOW, C. & BHAGWANDEEN, R. 2016. Pre-hospital thrombolysis in ST-segment elevation myocardial infarction: a regional Australian experience. *The Medical Journal of Australia,* 205**,** 121-125.

KHERA, A. V., EMDIN, C. A., DRAKE, I., NATARAJAN, P., BICK, A. G., COOK, N. R., CHASMAN, D. I., BABER, U., MEHRAN, R., RADER, D. J., FUSTER, V., BOERWINKLE, E., MELANDER, O., ORHO-MELANDER, M., RIDKER, P. M. & KATHIRESAN, S. 2016. Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. *New England Journal of Medicine,* 375**,** 2349-2358.

KIEMENEIJ, F. & BOINK, G. J. J. 2016. The PROPHET-II's Prophecy∗. *JACC: Cardiovascular Interventions,* 9**,** 2000-2001.

KING III, S. B., SMITH JR, S. C., HIRSHFELD JR, J. W., JACOBS, A. K., MORRISON, D. A. & WILLIAMS, D. O. 2008. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. *Journal of the American College of Cardiology,* 51**,** 172-209.

KINSMAN, L. D., ROTTER, T., WILLIS, J., SNOW, P. C., BUYKX, P. & HUMPHREYS, J. S. 2012. Do clinical pathways enhance access to evidence-based acute myocardial infarction treatment in rural emergency departments? *Australian Journal of Rural Health,* 20**,** 59-66.

KLAUS, T., ARORA, N., MATHENY, M. E., LIU, C., LEE, T. C. & RESNIC, F. S. 2008. Risk Predictors of Retroperitoneal Hemorrhage Following Percutaneous Coronary Intervention. *The American Journal of Cardiology,* 102**,** 1473-1476.

KOKOLIS, S., CAVUSOGLU, E., CLARK, L. T. & MARMUR, J. D. 2004. Anticoagulation strategies for patients undergoing percutaneous coronary intervention: unfractionated heparin, low-molecular-weight heparins, and direct thrombin inhibitors. *Progress in Cardiovascular Diseases,* 46**,** 506-523.

KONTOPODIS, N., TSETIS, D., TAVLAS, E., DEDES, A. & IOANNOU, C. V. 2016. Ultrasound Guided Compression Versus Ultrasound Guided Thrombin Injection for the Treatment of Post-Catheterization Femoral Pseudoaneurysms: Systematic Review and Meta-Analysis of Comparative Studies. *European Journal of Vascular and Endovascular Surgery,* 51**,** 815-823.

KORENY, M., RIEDMULLER, E., NIKFARDJAM, M., SIOSTRZONEK, P. & MULLNER, M. 2004. Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. *ACC Current Journal Review,* 13**,** 44-44.

KORN-LUBETZKI, I., FARKASH, R., PACHINO, R. M., ALMAGOR, Y., TZIVONI, D. & MEERKIN, D. 2013. Incidence and risk factors of cerebrovascular events following cardiac catheterization. *J Am Heart Assoc,* 2**,** e000413.

KOTOWYCZ, M. A., JOHNSTON, K. W., IVANOV, J., ASIF, N., ALMOGHAIRI, A. M., CHOUDHURY, A., NAGY, C. D., SIBBALD, M., CHAN, W., SEIDELIN, P. H., BAROLET, A. W., OVERGAARD, C. B. & DŽAVÍK, V. 2014. Predictors of Radial Artery Size in Patients Undergoing Cardiac Catheterization: Insights From the Good Radial Artery Size Prediction (GRASP) Study. *Canadian Journal of Cardiology,* 30**,** 211-216.

KOUTOUZIS, M. J., MANIOTIS, C. D., AVDIKOS, G., TSOUMELEAS, A., ANDREOU, C. & KYRIAKIDES, Z. S. 2016. ULnar Artery Transient Compression Facilitating Radial Artery Patent Hemostasis (ULTRA): A Novel Technique to Reduce Radial Artery Occlusion After Transradial Coronary Catheterization. *Journal of Invasive Cardiology,* 28**,** 451-454.

KUTNEY-LEE, A., LAKE, E. T. & AIKEN, L. H. 2009. Development of the Hospital Nurse Surveillance Capacity Profile. *Research in Nursing and Health,* 32**,** 217-28.

KWOK, C. S., KONTOPANTELIS, E., MYINT, P. K., ZAMAN, A., BERRY, C., KEAVNEY, B., NOLAN, J., LUDMAN, P. F., DE BELDER, M. A., BUCHAN, I., MAMAS, M. A., BRITISH CARDIOVASCULAR INTERVENTION, S. & NATIONAL INSTITUTE FOR CARDIOVASCULAR OUTCOMES, R. 2015. Stroke following percutaneous coronary intervention: type-specific incidence, outcomes and determinants seen by the British Cardiovascular Intervention Society 2007-12. *European Heart Journal,* 36**,** 1618-28.

LAKOVOU, I., SCHMIDT, T., BONIZZONI, E., GE, L., SANGIORGI, G. M., STANKOVIC, G., AIROLDI, F., CHIEFFO, A., MONTORFANO, M., CARLINO, M., MICHEV, I., CORVAJA, N., BRIGUORI, C., GERCKENS, U., GRUBE, E. & COLOMBO, A. 2005. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *Jama,* 293**,** 2126-30.

LANCET 2017. 40 years of percutaneous coronary intervention: where next? *The Lancet.* The Lancet.

LANGE, R. A. & HILLIS, L. D. 2003. Diagnostic Cardiac Catheterization. *Circulation,* 107**,** e111-e113.

LEE, I. M., SHIROMA, E. J., LOBELO, F., PUSKA, P., BLAIR, S. N., KATZMARZYK, P. T. & LANCET PHYSICAL ACTIVITY SERIES WORKING, G. 2012. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet (London, England),* 380**,** 219-229.

LEEPER, B. 2004. Nursing outcomes: percutaneous coronary interventions. *Journal of Cardiovascular Nursing,* 19**,** 346-53.

LEVINE, G. N., BATES, E. R., BLANKENSHIP, J. C., BAILEY, S. R., BITTL, J. A., CERCEK, B., CHAMBERS, C. E., ELLIS, S. G., GUYTON, R. A., HOLLENBERG, S. M., KHOT, U. N., LANGE, R. A., MAURI, L., MEHRAN, R., MOUSSA, I. D., MUKHERJEE, D., NALLAMOTHU, B. K. & TING, H. H. 2011. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation,* 124**,** e574-651.

LEVINE, G. N., BATES, E. R., BLANKENSHIP, J. C., BAILEY, S. R., BITTL, J. A., CERCEK, B., CHAMBERS, C. E., ELLIS, S. G., GUYTON, R. A., HOLLENBERG, S. M., KHOT, U. N., LANGE, R. A., MAURI, L., MEHRAN, R., MOUSSA, I. D., MUKHERJEE, D., TING, H. H., O'GARA, P. T., KUSHNER, F. G., ASCHEIM, D. D., BRINDIS, R. G., CASEY, D. E., CHUNG, M. K., DE LEMOS, J. A., DIERCKS, D. B., FANG, J. C., FRANKLIN, B. A., GRANGER, C. B., KRUMHOLZ, H. M., LINDERBAUM, J. A., MORROW, D. A., NEWBY, L. K., ORNATO, J. P., OU, N., RADFORD, M. J., TAMIS-HOLLAND, J. E., TOMMASO, C. L., TRACY, C. M., WOO, Y. J. & ZHAO, D. X. 2016. 2015 ACC/AHA/SCAI Focused Update on Primary Percutaneous Coronary Intervention for Patients With ST-Elevation Myocardial Infarction. *An Update of the 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention and the 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction,* 67**,** 1235-1250.

LIN, C.-F., CHU, K.-C. & WANG, Y.-M. 2010. Acute Ischemic Stroke After Percutaneous Cardiac Intervention in an Elderly Patient. *International Journal of Gerontology,* 4**,** 43-46.

LINCOFF, A. M., BITTL, J. A., KLEIMAN, N. S., SAREMBOCK, I. J., JACKMAN, J. D., MEHTA, S., TANNENBAUM, M. A., NIEDERMAN, A. L., BACHINSKY, W. B., TIFT-MANN, J., PARKER, H. G., KEREIAKES, D. J., HARRINGTON, R. A., FEIT, F., MAIERSON, E. S., CHEW, D. P. & TOPOL, E. J. 2004. Comparison of bivalirudin versus heparin during percutaneous coronary intervention (the Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events [REPLACE]-1 trial). *The American Journal of Cardiology,* 93**,** 1092-1096.

LINCOFF, A. M., CALIFF, R. M. & TOPOL, E. J. 2000. Platelet glycoprotein IIb/IIIa receptor blockade in coronary artery disease. *Journal of the American College of Cardiology,* 35**,** 1103-1115.

LLOYD-JONES, D. M., BRAUN, L. T., NDUMELE, C. E., SMITH, S. C., SPERLING, L. S., VIRANI, S. S. & BLUMENTHAL, R. S. 2018. Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease. *A Special Report From the American Heart Association and American College of Cardiology*.

LLOYD-JONES, D. M., LARSON, M. G., BEISER, A. & LEVY, D. 1999. Lifetime risk of developing coronary heart disease. *The Lancet,* 353**,** 89-92.

MACFARLANE, P. W., DEVINE, B. & CLARK, E. The university of glasgow (Uni-G) ECG analysis program. Computers in Cardiology, 2005, 25-28 Sept. 2005 2005. 451-454.

MAK, K. H., MOLITERNO, D. J., GRANGER, C. B., MILLER, D. P., WHITE, H. D., WILCOX, R. G., CALIFF, R. M. & TOPOL, E. J. 1997. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction. GUSTO-I Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *Journal of Amercian College of Cardiology,* 30**,** 171-9.

MANN, C. J. 2003. Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emergency Medicine Journal,* 20**,** 54-60.

MANNSVERK, J., STEIGEN, T., WANG, H., TANDE, P. M., DAHLE, B. M., NEDREJORD, M. L., HOKLAND, I. O. & GILBERT, M. 2017. Trends in clinical outcomes and survival following prehospital thrombolytic therapy given by ambulance clinicians for ST-elevation myocardial infarction in rural sub-arctic Norway. *Eur Heart J Acute Cardiovasc Care***,** 2048872617748550.

MANSON, J. E., GREENLAND, P. & LACROIX, A. Z. 2003. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. *ACC Current Journal Review,* 12**,** 29.

MARSDEN, D. L., SPRATT, N. J., WALKER, R., BARKER, D., ATTIA, J., POLLACK, M., PARSONS, M. W. & LEVI, C. R. 2010. Trends in stroke attack rates and case fatality in the Hunter region, Australia 1996-2008. *Cerebrovasc Dis,* 30**,** 500-7.

MARSHALL, K. 2011. Acute coronary syndrome: diagnosis, risk assessment and management. *Nursing Standard,* 25**,** 47-58.

MARSO, S. P., AMIN, A. P., HOUSE, J. A. & ET AL. 2010. Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. *JAMA,* 303**,** 2156-2164.

MASOUDI, F. A., MAGID, D. J., VINSON, D. R., TRICOMI, A. J., LYONS, E. E., CROUNSE, L., HO, P. M., PETERSON, P. N. & RUMSFELD, J. S. 2006. Implications of the Failure to Identify High-Risk Electrocardiogram Findings for the Quality of Care of Patients With Acute Myocardial Infarction. *Results of the Emergency Department Quality in Myocardial Infarction (EDQMI) Study,* 114**,** 1565-1571.

MASOUDI, F. A., PONIRAKIS, A., DE LEMOS, J. A., JOLLIS, J. G., KREMERS, M., MESSENGER, J. C., MOORE, J. W. M., MOUSSA, I., OETGEN, W. J., VAROSY, P. D., VINCENT, R. N., WEI, J., CURTIS, J. P., ROE, M. T. & SPERTUS, J. A. 2017. Trends in U.S. Cardiovascular Care: 2016 Report From 4 ACC National Cardiovascular Data Registries. *Journal of the American College of Cardiology,* 69**,** 1427-1450.

MEARS, R., PARDEY, T. M., MCIVOR, D., SAVAGE, L. & FLETCHER, P. 2010. Nurse initiated thrombolysis in rural NSW. *Australasian Emergency Nursing Journal,* 13**,** 162-163.

MERCURI, M., MEHTA, S., XIE, C., VALETTAS, N., VELIANOU, J. L. & NATARAJAN, M. K. 2011. Radial Artery Access as a Predictor of Increased Radiation Exposure During a Diagnostic Cardiac Catheterization Procedure. *JACC: Cardiovascular Interventions,* 4**,** 347-352.

MOHR, F. W., MORICE, M. C., KAPPETEIN, A. P., FELDMAN, T. E., STAHLE, E., COLOMBO, A., MACK, M. J., HOLMES, D. R., JR., MOREL, M. A., VAN DYCK, N., HOULE, V. M., DAWKINS, K. D. & SERRUYS, P. W. 2013. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. *Lancet,* 381**,** 629-38.

MOORE, C. 2013. An Emergency Department Nurse-Driven Ultrasound-Guided Peripheral Intravenous Line Program. *The Journal of the Association for Vascular Access,* 18**,** 45-51.

MOREYRA, A. E., MANIATIS, G. A., GU, H., SWERDEL, J. N., MCKINNEY, J. S., COSGROVE, N. M., KOSTIS, W. J. & KOSTIS, J. B. 2017. Frequency of Stroke After Percutaneous Coronary

Intervention or Coronary Artery Bypass Grafting (from an Eleven-Year Statewide Analysis). *Amercian Journal of Cardiology,* 119**,** 197-202.

MORIARTY, P. M., PARHOFER, K. G., BABIRAK, S. P., CORNIER, M. A., DUELL, P. B., HOHENSTEIN, B., LEEBMANN, J., RAMLOW, W., SCHETTLER, V., SIMHA, V., STEINHAGEN-THIESSEN, E., THOMPSON, P. D., VOGT, A., VON STRITZKY, B., DU, Y. & MANVELIAN, G. 2016. Alirocumab in patients with heterozygous familial hypercholesterolaemia undergoing lipoprotein apheresis: the ODYSSEY ESCAPE trial. *European Heart Journal,* 37**,** 3588-3595.

MOSCA, L., BARRETT-CONNOR, E. & WENGER, N. K. 2011. Sex/Gender Differences in Cardiovascular Disease Prevention. *Circulation,* 124**,** 2145-2154.

MOSER, D. R., BARBARA 2008. *Cardiac Nursing: A Companion to Braunwalds HEART DISEASE,* St Louis, Saunders Elsevier.

MOZAFFARIAN, D., BENJAMIN, E. J., GO, A. S., ARNETT, D. K., BLAHA, M. J., CUSHMAN, M., DE FERRANTI, S., DESPRES, J. P., FULLERTON, H. J., HOWARD, V. J., HUFFMAN, M. D., JUDD, S. E., KISSELA, B. M., LACKLAND, D. T., LICHTMAN, J. H., LISABETH, L. D., LIU, S., MACKEY, R. H., MATCHAR, D. B., MCGUIRE, D. K., MOHLER, E. R., 3RD, MOY, C. S., MUNTNER, P., MUSSOLINO, M. E., NASIR, K., NEUMAR, R. W., NICHOL, G., PALANIAPPAN, L., PANDEY, D. K., REEVES, M. J., RODRIGUEZ, C. J., SORLIE, P. D., STEIN, J., TOWFIGHI, A., TURAN, T. N., VIRANI, S. S., WILLEY, J. Z., WOO, D., YEH, R. W. & TURNER, M. B. 2015. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. *Circulation,* 131**,** e29-322.

MYERS, R. H., KIELY, D. K., CUPPLES, L. A. & KANNEL, W. B. 1990. Parental history is an independent risk factor for coronary artery disease: The Framingham Study. *American Heart Journal,* 120**,** 963-969.

NAIDU, S. S., ARONOW, H. D., BOX, L. C., DUFFY, P. L., KOLANSKY, D. M., KUPFER, J. M., LATIF, F., MULUKUTLA, S. R., RAO, S. V., SWAMINATHAN, R. V. & BLANKENSHIP, J. C. 2016. SCAI expert

consensus statement: 2016 best practices in the cardiac catheterization laboratory: (Endorsed by the cardiological society of india, and sociedad Latino Americana de Cardiologia intervencionista; Affirmation of value by the Canadian Association of interventional cardiology-Association canadienne de cardiologie d'intervention). *Catheterization & Cardiovascular Intervention,* 88**,** 407-23.

NDREPEPA, G., NEUMANN, F. J., DELIARGYRIS, E. N., MEHRAN, R., MEHILLI, J., FERENC, M., SCHULZ, S., SCHOMIG, A., KASTRATI, A. & STONE, G. W. 2012. Bivalirudin versus heparin plus a glycoprotein IIb/IIIa inhibitor in patients with non-ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention after clopidogrel pretreatment: pooled analysis from the ACUITY and ISAR-REACT 4 trials. *Circ Cardiovasc Interv,* 5**,** 705-12.

NELSON, N. J. 2000. Nurses' health study: nurses helping science and themselves. *Journal of National Cancer Institute,* 92**,** 597-9.

NEUMANN, F.-J., SOUSA-UVA, M., AHLSSON, A., ALFONSO, F., BANNING, A. P., BENEDETTO, U., BYRNE, R. A., COLLET, J.-P., FALK, V., HEAD, S. J., JÜNI, P., KASTRATI, A., KOLLER, A., KRISTENSEN, S. D., NIEBAUER, J., RICHTER, D. J., SEFEROVIĆ, P. M., SIBBING, D., STEFANINI, G. G., WINDECKER, S., YADAV, R., ZEMBALA, M. O. & GROUP, E. S. C. S. D. 2018. 2018 ESC/EACTS Guidelines on myocardial revascularization. *European Heart Journal***,** ehy394-ehy394.

NOORI, V. J. & ELDRUP-JØRGENSEN, J. 2018. A systematic review of vascular closure devices for femoral artery puncture sites. *Journal of Vascular Surgery,* 68**,** 887-899.

NSWHF. 2011. *The New South Wales Heart Foundation* [Online]. Available: www.heartfoundation.org.au/information-for-professionals/Clinical-Information/Pages/default.aspx [Accessed May 2011 2011].

O'GARA, P. T., KUSHNER, F. G., ASCHEIM, D. D., CASEY, D. E., JR., CHUNG, M. K., DE LEMOS, J. A., ETTINGER, S. M., FANG, J. C., FESMIRE, F. M., FRANKLIN, B. A., GRANGER, C. B., KRUMHOLZ,

H. M., LINDERBAUM, J. A., MORROW, D. A., NEWBY, L. K., ORNATO, J. P., OU, N., RADFORD, M. J., TAMIS-HOLLAND, J. E., TOMMASO, C. L., TRACY, C. M., WOO, Y. J., ZHAO, D. X., ANDERSON, J. L., JACOBS, A. K., HALPERIN, J. L., ALBERT, N. M., BRINDIS, R. G., CREAGER, M. A., DEMETS, D., GUYTON, R. A., HOCHMAN, J. S., KOVACS, R. J., KUSHNER, F. G., OHMAN, E. M., STEVENSON, W. G. & YANCY, C. W. 2013. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Jornal of American College of Cardiology,* 61**,** e78-140.

OLIVEIRA, L. & LAWRENCE, M. 2016. Ultrasound-Guided Peripheral Intravenous Access Program for Emergency Physicians, Nurses, and Corpsmen (Technicians) at a Military Hospital. *Journal of Military Medicine,* 181**,** 272-6.

ORCHARD, T. J., NATHAN, D. M., ZINMAN, B., CLEARY, P., BRILLON, D., BACKLUND, J. Y. & LACHIN, J. M. 2015. Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *Jama,* 313**,** 45-53.

OSTEN, M. D., IVANOV, J., EICHHOFER, J., SEIDELIN, P. H., ROSS, J. R., BAROLET, A., HORLICK, E. M., ING, D., SCHWARTZ, L., MACKIE, K. & DÅ¾AVÃ-K, V. R. 2008. Impact of Renal Insufficiency on Angiographic, Procedural, and In-Hospital Outcomes Following Percutaneous Coronary Intervention. *The American Journal of Cardiology,* 101**,** 780-785.

PAIVA, L., PROVIDENCIA, R., BARRA, S., DINIS, P., FAUSTINO, A. C. & GONCALVES, L. 2015. Universal definition of myocardial infarction: clinical insights. *Cardiology,* 131**,** 13-21.

PANCHOLY, S. B., BERNAT, I., BERTRAND, O. F. & PATEL, T. M. 2016. Prevention of Radial Artery Occlusion After Transradial Catheterization: The PROPHET-II Randomized Trial. *JACC: Cardiovascular Interventions,* 9**,** 1992-1999.

PANCHOLY, S. B., BERTRAND, O. F. & PATEL, T. 2012. Comparison of A Priori Versus Provisional Heparin Therapy on Radial Artery Occlusion After Transradial Coronary Angiography and

Patent Hemostasis (from the PHARAOH Study). *The American Journal of Cardiology,* 110**,** 173-176.

PANDIT, J., GUPTA, V., BOYER, N., YEGHIAZARIANS, Y., PORTS, T. A. & BOYLE, A. J. 2014. Patient and physician perspectives on outcomes weighting in revascularization. The POWR study. *International Journal of Cardiology,* 177**,** 513-514.

PATEL, M. R., JNEID, H., DERDEYN, C. P., KLEIN, L. W., LEVINE, G. N., LOOKSTEIN, R. A., WHITE, C. J., YEGHIAZARIANS, Y., ROSENFIELD, K., AMERICAN HEART ASSOCIATION, D., INTERVENTIONAL CARDIAC CATHETERIZATION COMMITTEE OF THE COUNCIL ON CLINICAL CARDIOLOGY, C. O. C. R., INTERVENTION, C. O. P. V. D. C. O. C. S., ANESTHESIA & STROKE, C. 2010. Arteriotomy closure devices for cardiovascular procedures: a scientific statement from the American Heart Association.[Erratum appears in Circulation. 2010 Nov 2;122(18):e507]. *Circulation,* 122**,** 1882-93.

PEATE, I. 2011. Caring for the patient with angina: causes and treatment. *British Journal of Healthcare Assistants,* 5**,** 65-69.

PHILIP, F., STEWART, S. & SOUTHARD, J. A. 2016. Very late stent thrombosis with second generation drug eluting stents compared to bare metal stents: Network meta-analysis of randomized primary percutaneous coronary intervention trials. *Catheter Cardiovasc Interv,* 88**,** 38-48.

PIERCY, K., L. & TROIANO, R., P. 2018. Physical Activity Guidelines for Americans From the US Department of Health and Human Services. *Circulation: Cardiovascular Quality and Outcomes,* 11**,** e005263.

PIPER, W. D., MALENKA, D. J., RYAN, T. J., SHUBROOKS, S. J., O'CONNOR, G. T., ROBB, J. F., FARRELL, K. L., CORLISS, M. S., HEARNE, M. J., KELLETT, M. A., WATKINS, M. W., BRADLEY, W. A., HETTLEMAN, B. D., SILVER, T. M., MCGRATH, P. D., O'MEARS, J. R. & WENNBERG, D. E. 2003. Predicting vascular complications in percutaneous coronary interventions. *American Heart Journal,* 145**,** 1022-1029.

PITTA, S. R., PRASAD, A., KUMAR, G., LENNON, R., RIHAL, C. S. & HOLMES, D. R. 2011. Location of femoral artery access and correlation with vascular complications. *Catheterization and Cardiovascular Interventions,* 78**,** 294-9.

POPOVIC, B., FREYSZ, L., CHOMETON, F., LEMOINE, J., ELFARRA, M., ANGIOI, M., SELTON-SUTY, C., DE CHILLOU, C. & ALIOT, E. 2010. Femoral pseudoaneurysms and current cardiac catheterization: Evaluation of risk factors and treatment. *International Journal of Cardiology,* 141**,** 75-80.

PRADA-DELGADO, O., ESTÉVEZ-LOUREIRO, R., CALVIÑO-SANTOS, R., BARGE-CABALLERO, E., SALGADO-FERNÁNDEZ, J., PIÑÓN-ESTEBAN, P., VÁZQUEZ-RODRÍGUEZ, J. M., ALDAMA-LÓPEZ, G., FLORES-RÍOS, X., SOLER-MARTÍN, M. R., VÁZQUEZ-GONZÁLEZ, N. & CASTRO-BEIRAS, A. 2012. Renal Insufficiency and Vascular Complications After Primary Angioplasty Via Femoral Route. Impact of Vascular Closure Devices Use. *Revista Española de Cardiología (English Edition),* 65**,** 258-264.

PRIDE, Y. B., PICCIRILLO, B. J. & GIBSON, C. M. 2012. Prevalence, Consequences, and Implications for Clinical Trials of Unrecognized Myocardial Infarction. *American Journal of Cardiology,* 111**,** 914-918.

PURSNANI, S., KORLEY, F., GOPAUL, R., KANADE, P., CHANDRA, N., SHAW RICHARD, E. & BANGALORE, S. 2012. Percutaneous Coronary Intervention Versus Optimal Medical Therapy in Stable Coronary Artery Disease. *Circulation: Cardiovascular Interventions,* 5**,** 476-490.

QASEEM, A., FIHN, S. D., WILLIAMS, S., DALLAS, P., OWENS, D. K., SHEKELLE, P. & PHYSICIANS*, F. T. C. G. C. O. T. A. C. O. 2012. Diagnosis of Stable Ischemic Heart Disease: Summary of a Clinical Practice Guideline From the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. *Annals of Internal Medicine,* 157**,** 729-734.

RAFTER, N., HICKEY, A., CONDELL, S., CONROY, R., O'CONNOR, P., VAUGHAN, D. & WILLIAMS, D. 2014. Adverse events in healthcare: learning from mistakes. *QJM: An International Journal of Medicine,* 108**,** 273-277.

RAO, S. V., O'GRADY, K., PIEPER, K. S., GRANGER, C. B., NEWBY, L. K., VAN DE WERF, F., MAHAFFEY, K. W., CALIFF, R. M. & HARRINGTON, R. A. 2005. Impact of Bleeding Severity on Clinical Outcomes Among Patients With Acute Coronary Syndromes. *The American Journal of Cardiology,* 96**,** 1200-1206.

RAPOSO, L., MADEIRA, S., TELES, R. C., SANTOS, M., GABRIEL, H. M., GONCALVES, P., BRITO, J., LEAL, S., ALMEIDA, M. & MENDES, M. 2015. Neurologic complications after transradial or transfemoral approach for diagnostic and interventional cardiac catheterization: A propensity score analysis of 16,710 cases from a single centre prospective registry. *Catheter Cardiovascular Interventions,* 86**,** 61-70.

RATIB, K., MAMAS, M. A., ROUTLEDGE, H. C., LUDMAN, P. F., FRASER, D. & NOLAN, J. 2013. Influence of access site choice on incidence of neurologic complications after percutaneous coronary intervention. *American Heart Journal,* 165**,** 317-324.

RAWSHANI, A., RAWSHANI, A., FRANZÉN, S., ELIASSON, B., SVENSSON, A.-M., MIFTARAJ, M., MCGUIRE, D. K., SATTAR, N., ROSENGREN, A. & GUDBJÖRNSDOTTIR, S. 2017. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes. *New England Journal of Medicine,* 376**,** 1407-1418.

REINER, Ž. 2018. The importance of smoking cessation in patients with coronary heart disease. *International Journal of Cardiology,* 258**,** 26-27.

RICCI, M. A., TREVISANI, G. T. & PILCHER, D. B. 1994. Vascular complications of cardiac catheterization. *The American Journal of Surgery,* 167**,** 375-378.

RICKHAM, P. P. 1964. Human Experimentation. Code of Ethics of the World Medical Association. Declaration of Helsinki. *Br Med J,* 2**,** 177.

ROFFI, M., PATRONO, C., COLLET, J.-P., MUELLER, C., VALGIMIGLI, M., ANDREOTTI, F., BAX, J. J., BORGER, M. A., BROTONS, C., CHEW, D. P., GENCER, B., HASENFUSS, G., KJELDSEN, K., LANCELLOTTI, P., LANDMESSER, U., MEHILLI, J., MUKHERJEE, D., STOREY, R. F. & WINDECKER, S. 2015. 2015 ESC Guidelines for the Management of Acute Coronary Syndromes in Patients Presenting Without Persistent ST-segment Elevation. *Revista Española de Cardiología (English Edition),* 68**,** 1125.

ROFFI, M., PATRONO, C., COLLET, J.-P., MUELLER, C., VALGIMIGLI, M., ANDREOTTI, F., BAX, J. J., BORGER, M. A., BROTONS, C., CHEW, D. P., GENCER, B., HASENFUSS, G., KJELDSEN, K., LANCELLOTTI, P., LANDMESSER, U., MEHILLI, J., MUKHERJEE, D., STOREY, R. F., WINDECKER, S., BAUMGARTNER, H., GAEMPERLI, O., ACHENBACH, S., AGEWALL, S., BADIMON, L., BAIGENT, C., BUENO, H., BUGIARDINI, R., CARERJ, S., CASSELMAN, F., CUISSET, T., EROL, Ç., FITZSIMONS, D., HALLE, M., HAMM, C., HILDICK-SMITH, D., HUBER, K., ILIODROMITIS, E., JAMES, S., LEWIS, B. S., LIP, G. Y. H., PIEPOLI, M. F., RICHTER, D., ROSEMANN, T., SECHTEM, U., STEG, P. G., VRINTS, C. & LUIS ZAMORANO, J. 2016. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevationTask Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *European Heart Journal,* 37**,** 267-315.

ROMAGNOLI, E., MANN, T., SCIAHBASI, A., PENDENZA, G., BIONDI-ZOCCAI, G. G. L. & SANGIORGI, G. M. 2011. Transradial approach in the catheterization laboratory: Pros/cons and suggestions for successful implementation. *International Journal of Cardiology*.

ROMAGUERA, R., WAKABAYASHI, K., LAYNEZ-CARNICERO, A., SARDI, G., MALUENDA, G., BEN-DOR, I., TORGUSON, R., KENT, K. M., SATLER, L. F., SUDDATH, W. O., LINDSAY, J., PICHARD, A. D. & WAKSMAN, R. 2012. Association Between Bleeding Severity and Long-Term Mortality in

Patients Experiencing Vascular Complications After Percutaneous Coronary Intervention. *The American Journal of Cardiology,* 109**,** 75-81.

SABATINE, M. S., GIUGLIANO, R. P., KEECH, A. C., HONARPOUR, N., WIVIOTT, S. D., MURPHY, S. A., KUDER, J. F., WANG, H., LIU, T., WASSERMAN, S. M., SEVER, P. S. & PEDERSEN, T. R. 2017. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. *New England Journal of Medicine,* 376**,** 1713-1722.

SAITO, S., IKEI, H., HOSOKAWA, G. & TANAKA, S. 1999. Influence of the ratio between radial artery inner diameter and sheath outer diameter on radial artery flow after transradial coronary intervention. *Catheterization and Cardiovascular Interventions,* 46**,** 173-178.

SAMPSON, M. & MCGRATH, A. 2015. Understanding the ECG. Part 1: Anatomy and physiology. *British Journal of Cardiac Nursing,* 10**,** 548-554.

SANTOS, M. A. D., DE BORBA, R. P., DE MORAES, C. V., VOLTOLINI, I., AZEVEDO, E. M., CARDOSO, C. R., DE SOUZA, E. N., MORAES, M. A. & DE OLIVEIRA CARDOSO, C. 2012. Evaluation of Radial Artery Patency after Transradial Catheterization. *Revista Brasileira de Cardiologia Invasiva (English Edition),* 20**,** 403-407.

SAVAGE, L., FLETCHER, P., STEWART, P., BASTIAN, B. & AGAHARI, I. PW305 A Clinical Assessment of the Glasgow ECG algorithm. *Global Heart,* 9**,** e319.

SAVAGE, M. L., POON, K. K. C., JOHNSTON, E. M., RAFFEL, O. C., INCANI, A., BRYANT, J., RASHFORD, S., PINCUS, M. & WALTERS, D. L. 2014. Pre-Hospital Ambulance Notification and Initiation of Treatment of ST Elevation Myocardial Infarction is Associated with Significant Reduction in Door-to-Balloon Time for Primary PCI. *Heart, Lung and Circulation,* 23**,** 435-443.

SCHNYDER, G., SAWHNEY, N., WHISENANT, B., TSIMIKAS, S. & TURI, Z. G. 2001. Common femoral artery anatomy is influenced by demographics and comorbidity: implications for cardiac and peripheral invasive studies. *Catheterization & Cardiovascular Interventions,* 53**,** 289-95.

SCHOLZE, J. 2010. Isolated systolic hypertension. An independent disease. *Herz,* 35**,** 568-74.

SCHULL, M. J., VERMEULEN, M. J. & STUKEL, T. A. 2006. The Risk of Missed Diagnosis of Acute Myocardial Infarction Associated With Emergency Department Volume. *Annals of Emergency Medicine,* 48**,** 647-655.

SCHULZ-SCHÜPKE, S., HELDE, S., GEWALT, S. & ET AL. 2014. Comparison of vascular closure devices vs manual compression after femoral artery puncture: The isar-closure randomized clinical trial. *JAMA,* 312**,** 1981-1987.

SECEMSKY, E. A., FERRO, E. G., RAO, S. V., KIRTANE, A., TAMEZ, H., ZAKROYSKY, P., WOJDYLA, D., BRADLEY, S. M., COHEN, D. J. & YEH, R. W. 2019. Association of Physician Variation in Use of Manual Aspiration Thrombectomy With Outcomes Following Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction: The National Cardiovascular Data Registry CathPCI Registry. *JAMA Cardiol*.

SETO, A. H., ABU-FADEL, M. S., SPARLING, J. M., ZACHARIAS, S. J., DALY, T. S., HARRISON, A. T., SUH, W. M., VERA, J. A., ASTON, C. E., WINTERS, R. J., PATEL, P. M., HENNEBRY, T. A. & KERN, M. J. 2010. Real-time ultrasound guidance facilitates femoral arterial access and reduces vascular complications: FAUST (Femoral Arterial Access With Ultrasound Trial). *JACC Cardiovascular Interventions,* 3**,** 751-8.

SINGER, A. J., THAN, M. P., SMITH, S., MCCULLOUGH, P., BARRETT, T. W., BIRKHAHN, R., REED, M., THODE, H. C., ARNOLD, W. D., DANIELS, L. B., DE FILIPPI, C., HEADDEN, G. & PEACOCK, W. F. 2017. Missed myocardial infarctions in ED patients prospectively categorized as low risk by established risk scores. *The American Journal of Emergency Medicine,* 35**,** 704-709.

SINNAEVE, P. R., ARMSTRONG, P. W., GERSHLICK, A. H., GOLDSTEIN, P., WILCOX, R., LAMBERT, Y., DANAYS, T., SOULAT, L., HALVORSEN, S., ORTIZ, F. R., VANDENBERGHE, K., REGELIN, A., BLUHMKI, E., BOGAERTS, K. & VAN DE WERF, F. 2014. ST-segment-elevation myocardial infarction patients randomized to a pharmaco-invasive strategy or primary percutaneous

coronary intervention: Strategic Reperfusion Early After Myocardial Infarction (STREAM) 1-year mortality follow-up. *Circulation,* 130**,** 1139-45.

SIRKER, A., KWOK, C. S., KOTRONIAS, R., BAGUR, R., BERTRAND, O., BUTLER, R., BERRY, C., NOLAN, J., OLDROYD, K. & MAMAS, M. A. 2016a. Influence of access site choice for cardiac catheterization on risk of adverse neurological events: A systematic review and meta-analysis. *American Heart Journal,* 181**,** 107-119.

SIRKER, A., KWOK, C. S., KOTRONIAS, R., BAGUR, R., BERTRAND, O., BUTLER, R., BERRY, C., NOLAN, J., OLDROYD, K. & MAMAS, M. A. 2016b. Influence of access site choice for cardiac catheterization on risk of adverse neurological events: A systematic review and meta-analysis. *American Heart Journal,* 181**,** 107-119.

SLICKER, K., LANE, W. G., OYETAYO, O. O., COPELAND, L. A., STOCK, E. M., MICHEL, J. B. & ERWIN, J. P. 2016. Daily cardiac catheterization procedural volume and complications at an academic medical center. *Cardiovascular diagnosis and therapy,* 6**,** 446-452.

SOLOMON, N. A., GLICK, H. A., RUSSO, C. J., LEE, J. & SCHULMAN, K. A. 1994. Patient preferences for stroke outcomes. *Stroke,* 25**,** 1721-5.

SPRUCE, K. & BUTLER, C. 2017. Enhancing Outcomes for Outpatient Percutaneous Coronary Interventions. *Clinical Nurse Specialist,* 31**,** 319-328.

STAESSEN, J. A., THIJS, L., GAÌ§SOWSKI, J., CELLS, H. & FAGARD, R. H. 1998. Treatment of isolated systolic hypertension in the elderly: further evidence from the Systolic Hypertension in Europe (Syst-Eur) trial. *The American Journal of Cardiology,* 82**,** 20-22.

STEG, P. G., JAMES, S. K., ATAR, D., BADANO, L. P., BLOMSTROM-LUNDQVIST, C., BORGER, M. A., DI MARIO, C., DICKSTEIN, K., DUCROCQ, G., FERNANDEZ-AVILES, F., GERSHLICK, A. H., GIANNUZZI, P., HALVORSEN, S., HUBER, K., JUNI, P., KASTRATI, A., KNUUTI, J., LENZEN, M. J., MAHAFFEY, K. W., VALGIMIGLI, M., VAN 'T HOF, A., WIDIMSKY, P. & ZAHGER, D. 2012. ESC

Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *European Heart Journal,* 33**,** 2569-619.

STEINWANDEL, U., GIBSON, N. P., RIPPEY, J. C., TOWELL, A. & ROSMAN, J. 2017. Use of ultrasound by registered nurses-a systematic literature review. *Journal of Renal Care,* 43**,** 132-142.

STONE, N. J., ROBINSON, J. G., LICHTENSTEIN, A. H., MERZ, C. N. B., BLUM, C. B., ECKEL, R. H., GOLDBERG, A. C., GORDON, D., LEVY, D., LLOYD-JONES, D. M., MCBRIDE, P., SCHWARTZ, J. S., SHERO, S. T., SMITH, S. C., WATSON, K. & WILSON, P. W. F. 2014. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults. *Circulation,* 129**,** S1-S45.

STOUT, K. K., DANIELS, C. J., ABOULHOSN, J. A., BOZKURT, B., BROBERG, C. S., COLMAN, J. M., CRUMB, S. R., DEARANI, J. A., FULLER, S., GURVITZ, M., KHAIRY, P., LANDZBERG, M. J., SAIDI, A., VALENTE, A. M. & HARE, G. F. V. 2018 AHA/ACC Guideline for the Management of Adults With Congenital Heart Disease. *Circulation,* 0**,** CIR.0000000000000603.

SUGGS, P., SHELIA, R., FAYE, C. & SONYA, H. 2013. Factors associated with groin complications post coronary intervention. *Clinical Nursing Studies,* 1**,** 26-34.

SVILAAS, T., VLAAR, P. J., VAN DER HORST, I. C., DIERCKS, G. F. H., DE SMET, B. J. G. L., VAN DEN HEUVEL, A. F. M., ANTHONIO, R. L., JESSURUN, G. A., TAN, E.-S., SUURMEIJER, A. J. H. & ZIJLSTRA, F. 2008. Thrombus Aspiration during Primary Percutaneous Coronary Intervention. *New England Journal of Medicine,* 358**,** 557-567.

TANG, L., WANG, F., LI, Y., ZHAO, L., XI, H., GUO, Z., LI, X., GAO, C., WANG, J. & ZHOU, L. 2014. Ultrasound Guidance for Radial Artery Catheterization: An Updated Meta-Analysis of Randomized Controlled Trials. *PLOS ONE,* 9**,** e111527.

TAYEH, O. & ETTORI, F. 2014. Door-to-balloon time in radial versus femoral approach for primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. *The Egyptian Heart Journal,* 66**,** 155-162.

THOMAS, M. P. & BATES, E. R. 2017. Update on primary PCI for patients with STEMI. *Trends in Cardiovascular Medicine,* 27**,** 95-102.

THYGESEN, K., ALPERT, J. S., JAFFE, A. S., CHAITMAN, B. R., BAX, J. J., MORROW, D. A., WHITE, H. D. & GROUP, E. S. C. S. D. 2018. Fourth universal definition of myocardial infarction (2018). *European Heart Journal***,** ehy462-ehy462.

THYGESEN, K., ALPERT, J. S., JAFFE, A. S., SIMOONS, M. L., CHAITMAN, B. R. & WHITE, H. D. 2012. Third Universal Definition of Myocardial Infarction. *Global Heart,* 7**,** 275-295.

THYGESEN, K., ALPERT, J. S., WHITE, H. D., JAFFE, A. S., APPLE, F. S., GALVANI, M., KATUS, H. A., NEWBY, L. K., RAVKILDE, J., CHAITMAN, B., CLEMMENSEN, P. M., DELLBORG, M., HOD, H., PORELA, P., UNDERWOOD, R., BAX, J. J., BELLER, G. A., BONOW, R., VAN DER WALL, E. E., BASSAND, J. P., WIJNS, W., FERGUSON, T. B., STEG, P. G., URETSKY, B. F., WILLIAMS, D. O., ARMSTRONG, P. W., ANTMAN, E. M., FOX, K. A., HAMM, C. W., OHMAN, E. M., SIMOONS, M. L., POOLE-WILSON, P. A., GURFINKEL, E. P., LOPEZ-SENDON, J. L., PAIS, P., MENDIS, S., ZHU, J. R., WALLENTIN, L. C., FERNANDEZ-AVILES, F., FOX, K. M., PARKHOMENKO, A. N., PRIORI, S. G., TENDERA, M., VOIPIO-PULKKI, L. M., VAHANIAN, A., CAMM, A. J., DE CATERINA, R., DEAN, V., DICKSTEIN, K., FILIPPATOS, G., FUNCK-BRENTANO, C., HELLEMANS, I., KRISTENSEN, S. D., MCGREGOR, K., SECHTEM, U., SILBER, S., TENDERA, M., WIDIMSKY, P., ZAMORANO, J. L., MORAIS, J., BRENER, S., HARRINGTON, R., MORROW, D., LIM, M., MARTINEZ-RIOS, M. A., STEINHUBL, S., LEVINE, G. N., GIBLER, W. B., GOFF, D., TUBARO, M., DUDEK, D. & AL-ATTAR, N. 2007. Universal definition of myocardial infarction. *Circulation,* 116**,** 2634-53.

TIDEMAN, P. A., TIRIMACCO, R., SENIOR, D. P., SETCHELL, J. J., HUYNH, L. T., TAVELLA, R., AYLWARD, P. E. & CHEW, D. P. 2014. Impact of a regionalised clinical cardiac support network on mortality among rural patients with myocardial infarction. *Medical Journal of Australia,* 200**,** 157-60.

TIROCH, K. A., ARORA, N., MATHENY, M. E., LIU, C., LEE, T. C. & RESNIC, F. S. 2008. Risk Predictors of Retroperitoneal Hemorrhage Following Percutaneous Coronary Intervention. *The American Journal of Cardiology,* 102**,** 1473-1476.

TISI, P. V. & CALLAM, M. J. 2013. Treatment for femoral pseudoaneurysms. *Cochrane Database Syst Rev***,** Cd004981.

TOGGWEILER, S., LEIPSIC, J., BINDER, R. K., FREEMAN, M., BARBANTI, M., HEIJMEN, R. H., WOOD, D. A. & WEBB, J. G. 2013. Management of Vascular Access in Transcatheter Aortic Valve Replacement: Part 2: Vascular Complications. *JACC: Cardiovascular Interventions,* 6**,** 767-776.

TOLLESON, T. R., O'SHEA, J. C., BITTL, J. A., HILLEGASS, W. B., WILLIAMS, K. A., LEVINE, G., HARRINGTON, R. A. & TCHENG, J. E. 2003. Relationship between heparin anticoagulation and clinical outcomes in coronary stent intervention: observations from the ESPRIT trial. *Journal of the American College of Cardiology,* 41**,** 386-393.

TORPY, J. M., LYNM, C. & GLASS, R. M. 2004. Percutaneous Coronary Intervention. *JAMA,* 291**,** 778-778.

TOUSOULIS, D., OIKONOMOU, E., ECONOMOU, E. K., CREA, F. & KASKI, J. C. 2016. Inflammatory cytokines in atherosclerosis: current therapeutic approaches. *European Heart Journal,* 37**,** 1723-32.

TRICOMI, A. J., MAGID, D. J., RUMSFELD, J. S., VINSON, D. R., LYONS, E. E., CROUNSE, L., HO, P. M., PETERSON, P. N. & MASOUDI, F. A. 2008. Missed opportunities for reperfusion therapy for ST-segment elevation myocardial infarction: results of the Emergency Department Quality in Myocardial Infarction (EDQMI) study. *Am Heart J,* 155**,** 471-7.

TRIMARCHI, S., SMITH, D. E., SHARE, D., JANI, S. M., O'DONNELL, M., MCNAMARA, R., RIBA, A., KLINE-ROGERS, E., GURM, H. S. & MOSCUCCI, M. 2010. Retroperitoneal Hematoma After Percutaneous Coronary Intervention: Prevalence, Risk Factors, Management, Outcomes, and

Predictors of Mortality. *A Report From the BMC2 (Blue Cross Blue Shield of Michigan Cardiovascular Consortium) Registry,* 3**,** 845-850.

TU, H. T., CAMPBELL, B. C., CHRISTENSEN, S., COLLINS, M., DE SILVA, D. A., BUTCHER, K. S., PARSONS, M. W., DESMOND, P. M., BARBER, P. A., LEVI, C. R., BLADIN, C. F., DONNAN, G. A., DAVIS, S. M. & ECHOPLANAR IMAGING THROMBOLYTIC EVALUATION TRIAL, I. 2010. Pathophysiological determinants of worse stroke outcome in atrial fibrillation. *Cerebrovascular Disease,* 30**,** 389-95.

UHLEMANN, M., MÖBIUS-WINKLER, S., MENDE, M., EITEL, I., FUERNAU, G., SANDRI, M., ADAMS, V., THIELE, H., LINKE, A., SCHULER, G. & GIELEN, S. 2012. The Leipzig Prospective Vascular Ultrasound Registry in Radial Artery Catheterization: Impact of Sheath Size on Vascular Complications. *JACC: Cardiovascular Interventions,* 5**,** 36-43.

VALGIMIGLI, M., FRIGOLI, E., LEONARDI, S., ROTHENBÜHLER, M., GAGNOR, A., CALABRÒ, P., GARDUCCI, S., RUBARTELLI, P., BRIGUORI, C., ANDÒ, G., REPETTO, A., LIMBRUNO, U., GARBO, R., SGANZERLA, P., RUSSO, F., LUPI, A., CORTESE, B., AUSIELLO, A., IERNA, S., ESPOSITO, G., PRESBITERO, P., SANTARELLI, A., SARDELLA, G., VARBELLA, F., TRESOLDI, S., DE CESARE, N., RIGATTIERI, S., ZINGARELLI, A., TOSI, P., VAN 'T HOF, A., BOCCUZZI, G., OMEROVIC, E., SABATÉ, M., HEG, D., JÜNI, P. & VRANCKX, P. 2015. Bivalirudin or Unfractionated Heparin in Acute Coronary Syndromes. *New England Journal of Medicine,* 373**,** 997-1009.

VAN DER ENDE, M. Y., HARTMAN, M. H. T., SCHURER, R. A. J., VAN DER WERF, H. W., LIPSIC, E., SNIEDER, H. & VAN DER HARST, P. 2017. Prevalence of electrocardiographic unrecognized myocardial infarction and its association with mortality. *International Journal of Cardiology,* 243**,** 34-39.

VAN MIEGHEM, C., SABBE, M. & KNOCKAERT, D. 2004. The clinical value of the ECG in noncardiac conditions. *Chest,* 125**,** 1561-76.

VIDI, V. D., MATHENY, M. E., GOVINDARAJULU, U. S., NORMAND, S.-L. T., ROBBINS, S. L., AGARWAL, V. V., BANGALORE, S. & RESNIC, F. S. 2012. Vascular Closure Device Failure in Contemporary Practice. *JACC: Cardiovascular Interventions,* 5**,** 837.

WELSH, R. C., DECKERT-SOOKRAM, J., SOOKRAM, S., VALAIRE, S. & BRASS, N. 2016. Evaluating clinical reason and rationale for not delivering reperfusion therapy in ST elevation myocardial infarction patients: Insights from a comprehensive cohort. *International Journal of Cardiology,* 216**,** 99-103.

WHELTON, P. K., CAREY, R. M., ARONOW, W. S., CASEY, D. E., COLLINS, K. J., DENNISON HIMMELFARB, C., DEPALMA, S. M., GIDDING, S., JAMERSON, K. A., JONES, D. W., MACLAUGHLIN, E. J., MUNTNER, P., OVBIAGELE, B., SMITH, S. C., SPENCER, C. C., STAFFORD, R. S., TALER, S. J., THOMAS, R. J., WILLIAMS, K. A., WILLIAMSON, J. D. & WRIGHT, J. T. 2018. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. *A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines,* 71**,** e127-e248.

WHITE, K., MACFARLANE, H., HOFFMANN, B., SIRVAS-BROWN, H., HINES, K., ROLLEY, J. X. & GRAHAM, S. 2018. Consensus Statement of Standards for Interventional Cardiovascular Nursing Practice. *Heart, Lung and Circulation,* 27**,** 535-551.

WHO. 2011. *The World Health Organisation* [Online]. Available: http://www.who.int/topics/cardiovascular_diseases/en/ [Accessed May 2011 2011].

WIJESINGHE, N., NUNN, C. M., SEBASTIAN, C., HEALD, S., MCALISTER, H. F. & DEVLIN, G. P. 2008. COMPLICATIONS OF PRIMARY ANGIOPLASTY IN MYOCARDIAL INFARCTION (PAMI) IN A REAL-WORLD CARDIAC CATHETERISATION LABORATORY: EIGHT-YEAR EXPERIENCE. *Heart, Lung and Circulation,* 17, Supplement 2**,** S31.

WILLIAMS, B., MANCIA, G., SPIERING, W., AGABITI ROSEI, E., AZIZI, M., BURNIER, M., CLEMENT, D. L., COCA, A., DE SIMONE, G., DOMINICZAK, A., KAHAN, T., MAHFOUD, F., REDON, J., RUILOPE, L., ZANCHETTI, A., KERINS, M., KJELDSEN, S. E., KREUTZ, R., LAURENT, S., LIP, G. Y. H., MCMANUS, R., NARKIEWICZ, K., RUSCHITZKA, F., SCHMIEDER, R. E., SHLYAKHTO, E., TSIOUFIS, C., ABOYANS, V. & DESORMAIS, I. 2018. 2018 ESC/ESH Guidelines for the management of arterial hypertension. *Eur Heart J,* 39**,** 3021-3104.

WILLIAMS, P. T. 2009. Reductions in incident coronary heart disease risk above guideline physical activity levels in men. *Atherosclerosis,* 209**,** 524-527.

WILLIAMS, T., INDER, K., SAVAGE, L. & COLLINS, N. 2016. *Risk Factor Profile of Patients Sustaining Femoral Vascular Complications in a Tertiary Referral Cardiac Catheterisation Laboratory*.

WILSON, S. J., MITCHELL, A., GRAY, T. J. M., LOH, H. J. & CRUDEN, N. L. 2017. Patent haemostasis prevents radial artery occlusion in patients with an acute coronary syndrome. *International Journal of Cardiology,* 240**,** 78-81.

YAN, B. P., AJANI, A. E., CLARK, D. J., DUFFY, S. J., ANDRIANOPOULOS, N., BRENNAN, A. L., LOANE, P. & REID, C. M. 2011. Recent trends in Australian percutaneous coronary intervention practice: insights from the Melbourne Interventional Group registry. *Medical Journal of Australia,* 195**,** 122-7.

YANCY, C. W., JESSUP, M., BOZKURT, B., BUTLER, J., CASEY, D. E., COLVIN, M. M., DRAZNER, M. H., FILIPPATOS, G. S., FONAROW, G. C., GIVERTZ, M. M., HOLLENBERG, S. M., LINDENFELD, J., MASOUDI, F. A., MCBRIDE, P. E., PETERSON, P. N., STEVENSON, L. W. & WESTLAKE, C. 2017. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. *A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America***,** 23682.

YATSKAR, L., SELZER, F., FEIT, F., COHEN, H. A., JACOBS, A. K., WILLIAMS, D. O. & SLATER, J. 2007. Access site hematoma requiring blood transfusion predicts mortality in patients undergoing

percutaneous coronary intervention: data from the National Heart, Lung, and Blood Institute Dynamic Registry. *Catheterization & Cardiovascular Interventions,* 69**,** 961-6.

YIADOM, M. Y., A. B., BAUGH, C., W., MCWADE, C., M., LIU, X., SONG KYOUNG, J., PATTERSON, B., W., JENKINS, C., A., TANSKI, M., MILLS, A., M., SALAZAR, G., WANG, T., J., DITTUS, R., S., LIU, D. & STORROW, A., B. 2017. Performance of Emergency Department Screening Criteria for an Early ECG to Identify ST-Segment Elevation Myocardial Infarction. *Journal of the American Heart Association,* 6**,** e003528.

ZEYMER, U., RAO, S. V. & MONTALESCOT, G. 2016. Anticoagulation in coronary intervention. *European Heart Journal,* 37**,** 3376-3385.

IJC Heart & Vasculature 22 (2019) 177–180

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vasculature

Missed Acute Myocardial Infarction (MAMI) in a rural and regional setting

Trent Williams [a,b,*,1], Lindsay Savage [a,2], Nicholas Whitehead [a,3], Helen Orvad [a,4], Claire Cummins [a,5], Steven Faddy [c,6], Peter Fletcher [a,d,e,7], Andrew J. Boyle [a,d,e,8], Kerry Jill Inder [b,e,9]

[a] John Hunter Hospital, Hunter New England Local Health District, Newcastle, Australia
[b] School of Nursing and Midwifery, University of Newcastle, Australia
[c] NSW Ambulance, Australia
[d] School of Medicine, University of Newcastle, Australia
[e] Hunter Medical Research Institute, Newcastle, Australia

ARTICLE INFO

Article history:
Received 14 October 2018
Received in revised form 2 February 2019
Accepted 25 February 2019
Available online xxxx

Keywords:
ST segment myocardial infarction
Reperfusion therapy
Diagnosis
Electrocardiography

ABSTRACT

Background: Delay in treatment and/or failure to provide reperfusion in ST-segment elevation myocardial infarction (STEMI) impacts on morbidity and mortality. This occurs more often outside metropolitan areas yet the reasons for this are unclear. This study aimed to describe factors associated with missed diagnosis of acute myocardial infarction (MAMI) in a rural and regional setting.

Methods: Using a retrospective cohort design, patients who presented with STEMI and failed to receive reperfusion therapy within four hours were identified as MAMI. Univariate analyses were undertaken to identify differences in clinical characteristics between the treated STEMI group and the MAMI group. Mortality, 30-day readmission rates and length of hospital stay are reported.

Results: Of 100 patients identified as MAMI (70 male, 30 female), 24 died in hospital. Demographics and time from symptom onset were similar in the treated STEMI and MAMI groups. Of the MAMI patients who died, rural hospitals recorded the highest inpatient mortality (69.6% $p = 0.008$). MAMI patients compared to treated STEMI patients had higher 30 day readmission (31.6% vs 3.3%, $p = 0.001$) and longer length of stay (5.5 vs 4.3 days $p = 0.029$). Inaccurate identification of STEMI on electrocardiogram (72%) and diagnostic uncertainty (65%) were associated with MAMI. The Glasgow algorithm to identify STEMI was utilised on 57% of occasions, with 93% accuracy.

Conclusion: Mortality following MAMI is high particularly in smaller rural hospitals. MAMI results in increased length of stay and readmission rate. Electrocardiogram interpretation and diagnostic accuracy require improvement to determine if this improves patient outcomes.

* Corresponding author at: Department of Cardiology, John Hunter Hospital, Lookout Road, New Lambton Heights 2305, Australia.
E-mail addresses: Trent.williams@hnehealth.nsw.gov.au (T. Williams), Lindsay.Savage@hnehealth.nsw.gov.au (L. Savage), nick@imagineant.com (N. Whitehead), Helen.orvad@hnehealth.nsw.gov.au (H. Orvad), ClaireMarie.Cummins@hnehealth.nsw.gov.au (C. Cummins), Steven.Faddy@health.nsw.gov.au (S. Faddy), peter.fletcher@hnehealth.nsw.gov.au (P. Fletcher), Andrew.boyle@hnehealth.nsw.gov.au (A.J. Boyle), Kerry.inder@newcastle.edu.au (K.J. Inder).
[1] PhD (Nursing) candidate: School of Nursing and Midwifery University of Newcastle, Australia. Clinical Nurse Specialist: Department of Cardiovascular Medicine John Hunter Hospital, Hunter New England Health Local Health District, Newcastle, Australia.
[2] Cardiac Liaison Manager: Hunter New England Local Health District, Newcastle, Australia.
[3] Advance Trainee Cardiology: Department of Cardiovascular Medicine, John Hunter Hospital, Hunter New England Health, Newcastle, Australia.
[4] Clinical Nurse Consultant: Department of Cardiovascular Medicine. Tamworth Rural Referral Hospital, Hunter New England Health Local Health District, Tamworth, Australia.
[5] Registered Nurse Department of Cardiovascular Medicine John Hunter Hospital, Hunter New England Health Local Health District, Newcastle, Australia.
[6] Manager: Clinical Project Evaluation, NSW Ambulance.
[7] Conjoint Professor of Medicine: Hunter New England Health/School of Medicine and Public - University of Newcastle.
[8] Professor of Cardiovascular Medicine Hunter New England Health. Director of Priority Clinical Centre for Cardiovascular Health - University of Newcastle.
[9] Associate Professor of Nursing: School of Nursing and Midwifery, Faculty of Health and Medicine, University of Newcastle.

https://doi.org/10.1016/j.ijcha.2019.02.013

1. Introduction

The burden of heart disease is 20% greater in rural compared to metropolitan populations, with a higher rate of mortality and multiple hospital transfers often required to access specialised care [1]. Appropriate and timely clinical care of patients presenting with acute coronary syndromes (ACS), including acute myocardial infarction (AMI), is the subject of comprehensive guidelines nationally and internationally [2,3]. Timely access to evidence-based management of ST segment elevation myocardial infarction (STEMI) is imperative for optimal clinical outcomes [4].

For patients presenting with STEMI in non-metropolitan hospitals, reperfusion treatment is predominantly thrombolysis. If thrombolysis is delivered in a timely fashion, followed by transfer to a percutaneous coronary intervention (PCI) capable hospital, this provides outcomes similar to primary PCI, which is recommended where facilities are available [5]. The impact of delay in treatment and failure to provide reperfusion doubles mortality, and impacts on morbidity outcomes [6]. Differing clinical presentations and organisational factors can make the diagnosis of ACS challenging for clinicians, resulting in some patients not receiving appropriate care [7]. Internationally, the experience of failure to treat STEMI has been documented [8,9]. Australian data indicates more than one third of people presenting with STEMI and eligible for treatment did not receive recommended reperfusion therapy [10]. This rate is higher outside the metropolitan environment; reasons for this are unclear [6]. The purpose of this study was to outline the consequences of MAMI across a large health district. In addition, we sought to assess the demographic, clinical, ECG and organisational factors associated with patients presenting with STEMI and eligible for reperfusion therapy who did not receive timely treatment in a regional area.

2. Materials and methods

A retrospective medical record review of patients presenting to hospital with STEMI to identify those with a missed diagnosis of acute myocardial infarction (MAMI) was conducted from 2011 to 2016.

2.1. Setting

The health district services an area of 131,785 km^2, covering major cities, inner regional, outer regional and remote populations [11]. The district comprises 37 hospitals, including general practitioner run hospitals (n = 27), general physician on site/Fellow Australasian College of Emergency Medicine (FACEM) hospitals (n = 7), nurse only hospitals (n = 2), and a tertiary referral centre (n = 1).

The health district's reperfusion strategy for patients with ACS, implemented in 2010, utilises the computerised Glasgow algorithm for identification of STEMI on electrocardiograph (ECG). This algorithm has acceptable diagnostic accuracy in interpretation of STEMI [4,12]. Integrated within this system is the ability to electronically transmit ECGs for review by a cardiologist when STEMI is detected using the algorithm. Under this reperfusion strategy >500 acute STEMI patients are identified and treated per annum across the district.

2.2. Sample

Medical records of patients who presented with STEMI to any hospital in the district and failed to receive timely reperfusion therapy, when not contraindicated, were reviewed from 2011 to 2016. For this analysis STEMI diagnosis was based directly on European Society of Cardiology guidelines, and includes patients who exhibited a clinical presentation, ECG changes, and pathology consistent with STEMI [12]. Patients were required to meet criteria for standard reperfusion therapy [2]. Patients who presented with a STEMI and who were not identified, had treatment commenced, or it was clear on review that STEMI was not considered within a four-hour period were defined as MAMI. All clinical case histories, medical records, ECG, and pathology were reviewed independently by two senior cardiologists to confirm MAMI, in the absence of any clinical contraindications to either reperfusion therapy. To take account for time and resource challenges a four hour arrival to treatment time was set, this took into consideration guideline directives to commence reperfusion therapy within 120 min of arrival in combination with the above parameters [12]. Five patients were excluded from the analysis due to end-stage disease processes, including cancer and dementia.

2.3. Data sources

A database of patients identified as MAMI was developed and populated using information from medical records and online clinical databases. Ethical approval was obtained from the institutional human research ethics committee (AU201711-02). This study was conducted in accordance with the declaration of Helsinki. Patients were identified as MAMI through retrospective examination of clinical databases (ECG, ACS and STEMI) and audit of transfer to other hospitals reports.

2.4. Factors of interest

- Patient factors; including age, gender, aboriginality and cardiovascular disease risk factors
- Hospitalisation-related factors; including inpatient mortality, length of hospital stay and 30-day-readmission, type of myocardial infarction and time of presentation to hospital,
- ECG factors and STEMI characteristics; Timing of ECG, usage of Glasgow ECG interpretation algorithm, appropriate recognition of STEMI using the algorithm, delays in diagnosis and accuracy of interpretation of ECG. Inaccurate ECG interpretation was defined as failure to make a STEMI diagnosis despite ECG criteria indicating STEMI, regardless of whether the Glasgow algorithm was used. Diagnostic uncertainty was defined as delay in access to expert clinical support and confusion around the correct treatment and referral processes. Treatment indecision is defined as where STEMI was diagnosed yet reperfusion therapy was not given despite an absence of contraindication.
- Organisational factors; Hospitals were classified as tertiary (bed capacity >500), metropolitan (>200 and ≤ 500 beds), rural referral (>100 and ≤200 beds) and small rural (≤100 beds).

2.5. Statistical methods

Data analysis was conducted using IBM SPSS Statistics (version 22, Chicago, IL, USA). Descriptive statistics are presented by counts and percentages for categorical variables and means and standard deviation (SD) for continuous variables. Patient demographic data from the MAMI group were contrasted against data for treated STEMI at the local referral hospital. The two groups are heterogeneous and should be viewed for presentation demographics only. Univariate analyses to identify differences in clinical characteristics were performed on data comparing two groups. The sample size was insufficient to undertake multivariate analysis. Categorical variables were analysed using a chi-square test, while continuous variables such as age were analysed via analysis of variance (ANOVA). Comparisons were performed using Bonferroni corrections and statistical significance level was set to $p < 0.05$.

3. Results

Over the five-year period approximately 1392 patients presented with a STEMI to the hospitals in the region. Of these, 100 patients were identified as missed acute myocardial infarctions (MAMI); 24 of these MAMI patients died in hospital.

Table 1
Characteristics of MAMI patients compared to treated STEMI from 2011 to 2016.

Variable	Treated STEMI (n = 1292)	MAMI Patients (n = 100)	*P* value
Male gender n (%)	950 (73.5)	70 (70)	0.465
Age (years) m (SD)	63.9 (12.9)	66.3 (12.4)	0.302
Indigenous n (%)	47 (3.6)	4 (4)	0.776
Hypertension n (%)	796 (61.6)	42 (42)	0.076
Dyslipidaemia n (%)	496 (38.4)	38 (38)	1.000
Diabetes n (%)	314 (24.3)	33(34)	0.081
Prior smoking n (%)	693 (53.6)	42(42)	0.039
Prior myocardial infarction n (%)	231 (17.9)	26 (26)	0.072
Prior CABG n (%)	37 (2.9)	9 (9)	**0.008**
Prior PCI n (%)	130 (10.1)	14 (14)	0.291
Presentation to hospital m (SD)			
7 am–3 pm	707 (54.7)	62 (62)	0.190
3 pm–11 pm	377 (29.2)	21(21)	0.115
11 pm–7 am	204 (15.8)	17 (17)	0.767
Symptom onset to presentation (minutes) m (SD)	150.5 (144.4)	155.6 (131.4)	0.903
Anterior infarction n (%)	528 (41)	67 (67)	**0.000**
Length of stay; m (SD)	4.3 (3.7)	5.5 (4.5)	**0.029**
30-day readmission n (%)	43 (3.3)	24 (24)	**0.001**

CABG: Coronary Artery Bypass Graft; **M**: Mean; **PCI** Percutaneous Coronary Intervention; **SD**: standard deviation; **STEMI**: ST segment Myocardial Infarction.

Characteristics of the treated STEMI and MAMI groups are presented in Table 1. Compared with the treated STEMI group, demographics of the MAMI group were similar in terms of age, comorbidities and time from symptom onset to presentation. MAMI patients were more likely to have previous CABG (9% vs 2.9%; $p = 0.008$) and present with anterior infarction (67% vs 41%; $p < 0.001$).

Patients who survived MAMI had a significantly higher thirty-day readmission rate compared with treated STEMI (24% vs 3.3%, $p = 0.001$). The MAMI cohort showed a longer length of stay when compared with the treated STEMI group (5.5 days versus 4.3 days, $p = 0.029$). The MAMI patients who died in hospital (n = 24) had a higher proportion of women compared with the MAMI group that survived to discharge (46% versus 25%).

MAMI patients most commonly presented to small rural hospitals (Fig. 1). Of the patients with MAMI who died, smaller rural hospitals recorded the highest inpatient mortality (69.6% $p = 0.008$) compared to no mortality for MAMI in the large tertiary referral hospital (Fig. 1).

The most common factors associated with MAMI were failure to identify STEMI on ECG (72%) and diagnostic uncertainty (65%) respectively. Of the MAMI patients, 57% had an ECG performed on a machine equipped with the Glasgow algorithm. Where the Glasgow algorithm was utilised, it correctly identified STEMI in 93% of occasions. Despite correct machine identification of STEMI in these cases, reperfusion therapy was not given in a timely manner.

4. Discussion

This paper describes the patient characteristics and clinical factors associated with the missed diagnosis of acute myocardial infarction in a rural and regional setting. Patients who had MAMI had a three-fold higher mortality when compared to the region's published mortality rate [5]. There was a 20% increased LOS, and eight times the readmission rate for MAMI patients compared to treated STEMI patients. Alarmingly anterior infarction was the most represented infarct type among patients with MAMI. Understanding the problem more specifically will assist in informing clinicians and policy makers.

The high proportion of STEMI patients not receiving reperfusion therapy is widely described in the literature and has been examined over a long period of time [13–15]. Previous reasons for not receiving reperfusion when indicated included late presentation, atypical symptomatology, gender and co-morbidity factors, plus clinician performance and system issues [9,15–17]. The preponderance of MAMI in rural compared to metropolitan hospitals reflects the difficultly of practice away from a tertiary centre in the treatment of STEMI [18]. Previous contributing reasons reported for this include the complex clinical presentation of ACS [7]. Difficulties maintaining a viable clinical roster with scarce resources and potentially long distances remain a challenge in the rural and regional setting [18]. Interpretation of complex ECGs when this is not the core clinician's role or expertise remains challenging, although the availability of effective ECG algorithms should minimise this [4]. The impact that a centralised ECG reading service to assist with accurate ECG interpretation and to help reduce diagnostic uncertainty would have on rural and regional health districts would be important to investigate and needs to be tested in a prospective research trial.

5. Strengths and limitations

This retrospective analysis allows the evaluation of health outcomes in a real-world rural setting, however there are several important limitations. Data were collected from various sources where the denominator of missed MI cannot be accurately ascertained and direct causation of MAMI cannot be determined due to the limitations of current data systems. We compared the differences of two relatively small groups and the sample size limited statistical comparisons. In particular,

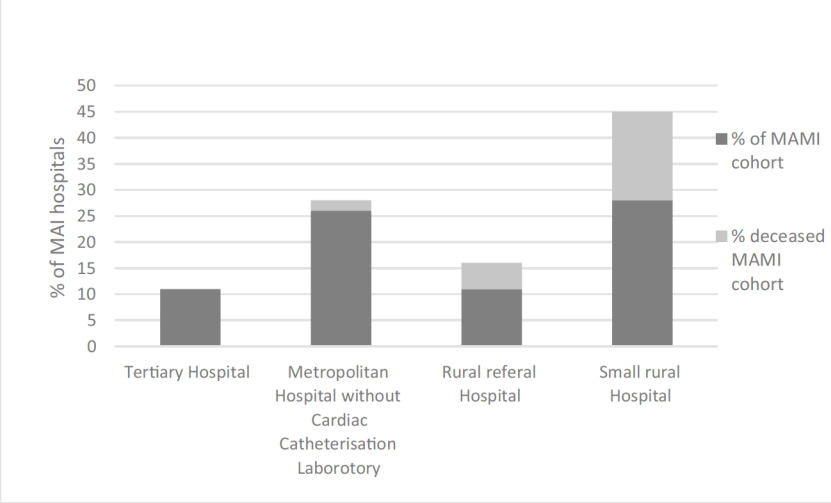


Fig. 1. Initial presentation hospital and outcomes for patients presenting with MAMI The majority of patients presented to rural hospitals, with no particular hospital overrepresented. Higher mortality was seen with MAMI in these locations. MAMI: missed acute myocardial infarction.

important determinants of MAMI may have been missed due to a type II error. A variety of data sources were utilised to minimise missing relevant patients. Medical record review data is reliant on the accuracy and interpretation of documentation of care. Two cardiologists confirming MAMI enabled reliability of diagnosis and admission parameters based on the application of an evidence based guideline definition of STEMI. This paper identifies the consequences of missed diagnosis of myocardial infarction, identifies modifiable factors associated with the development of MAMI, and may inform potential barriers to the successful treatment of STEMI.

6. Conclusion

MAMI occurs more often in smaller rural hospitals, results in increased mortality, longer LOS, and higher rate of hospital readmission. Common factors associated with MAMI are failure to correctly interpret the ECG and diagnostic difficulty. Better identification of MI may reduce MAMI and should be the focus of future research to improve patient outcomes in rural settings.

Declarations

A grant was obtained from Boehringer to the health service to fund staffing; they had no input into the study, data analysis, or writing of the manuscript. AB has received research support from Abbott Vascular and Cellmid; and consulting fees and/or honoraria from Astra Zeneca, Boehringer, Ingelheim and Pharmaxis. There are no other conflicts of interest to declare.

References

[1] D.B. Brieger, J. Redfern, Contemporary themes in acute coronary syndrome management: from acute illness to secondary prevention, Med. J. Aust. 199 (3) (2013) 174–178.
[2] D.P. Chew, I.A. Scott, L. Cullen, J.K. French, T.G. Briffa, P.A. Tideman, et al., National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016, Heart Lung Circ. 25 (9) (2016) 895–951.
[3] Roffi M, Patrono C, Collet J-P, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevationTask Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). European Heart Journal. 2016;37(3):267–315.
[4] Savage L, Fletcher P, Stewart P, Bastian B, Agahari I. PW305 a clinical assessment of the Glasgow ECG algorithm. Glob. Heart9(1):e319.
[5] A.A. Khan, T. Williams, L. Savage, P. Stewart, A. Ashraf, A.J. Davies, et al., Pre-hospital thrombolysis in ST-segment elevation myocardial infarction: a regional Australian experience, Med. J. Aust. 205 (3) (2016) 121–125.
[6] Farshid A, Brieger D, Hyun K, Hammett C, Ellis C, Rankin J, et al. Characteristics and clinical course of STEMI patients who received no reperfusion in the Australia and New Zealand SNAPSHOT ACS registry. Heart Lung Circ.25(2):132–9.
[7] Pride YB, Piccirillo BJ, Gibson CM. Prevalence, consequences, and implications for clinical trials of unrecognized myocardial infarction. Am. J. Cardiol.111(6):914–8.
[8] A.J. Tricomi, D.J. Magid, J.S. Rumsfeld, D.R. Vinson, E.E. Lyons, L. Crounse, et al., Missed opportunities for reperfusion therapy for ST-segment elevation myocardial infarction: results of the emergency department quality in myocardial infarction (EDQMI) study, Am. Heart J. 155 (3) (2008) 471–477.
[9] M.J. Schull, M.J. Vermeulen, T.A. Stukel, The risk of missed diagnosis of acute myocardial infarction associated with emergency department volume, Ann. Emerg. Med. 48 (6) (2006) 647–655.
[10] D.P. Chew, J. French, T.G. Briffa, C.J. Hammett, C.J. Ellis, I. Ranasinghe, et al., Acute coronary syndrome care across Australia and New Zealand: the SNAPSHOT ACS study, Med. J. Aust. 199 (3) (2013) 185–191.
[11] Statistics ABo. Australian Statistical Geography Standard (ASGS): Australian Bureau of Statistics; 2018 [cited 2018 01/03/2018]. Available from: http://www.abs.gov.au/websitedbs/D3310114.nsf/home/Australian+Statistical+Geography+Standard+(ASGS).
[12] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevationThe Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal. 2018;39(2):119–77.
[13] Kannel WB, Abbott RD. Incidence and Prognosis of unrecognized myocardial infarction: Based on 26 years follow-up in the Framingham study. In: Rutishauser W, Roskamm H, editors. Silent Myocardial Ischemia. Berlin, Heidelberg: Springer Berlin Heidelberg; 1984. p. 131–7.
[14] Masoudi FA, Magid DJ, Vinson DR, Tricomi AJ, Lyons EE, Crounse L, et al. Implications of the failure to identify high-risk electrocardiogram findings for the quality of Care of Patients with Acute Myocardial Infarction. Results of the Emergency Department Quality in Myocardial Infarction (EDQMI) Study. 2006;114(15):1565–71.
[15] R.C. Welsh, J. Deckert-Sookram, S. Sookram, S. Valaire, N. Brass, Evaluating clinical reason and rationale for not delivering reperfusion therapy in ST elevation myocardial infarction patients: insights from a comprehensive cohort, Int. J. Cardiol. 216 (2016) 99–103 Supplement C.
[16] M.Y. van der Ende, M.H.T. Hartman, R.A.J. Schurer, H.W. van der Werf, E. Lipsic, H. Snieder, et al., Prevalence of electrocardiographic unrecognized myocardial infarction and its association with mortality, Int. J. Cardiol. 243 (2017) 34–39 Supplement C.
[17] A.J. Singer, M.P. Than, S. Smith, P. McCullough, T.W. Barrett, R. Birkhahn, et al., Missed myocardial infarctions in ED patients prospectively categorized as low risk by established risk scores, Am. J. Emerg. Med. 35 (5) (2017) 704–709.
[18] J.M. Katzenellenbogen, F.M. Sanfilippo, M.S.T. Hobbs, T.G. Briffa, M.W. Knuiman, L. Dimer, et al., Complex impact of remoteness on the incidence of myocardial infarction in aboriginal and non-aboriginal people in Western Australia, Aust. J. Rural Health 20 (6) (2012) 305–311.

Femoral vascular complications following cardiac catheterisation

Trent Williams (Corresponding Author), PhD (Nursing) candidate, School of Nursing and Midwifery, University of Newcastle, and Clinical Nurse Specialist, Department of Cardiovascular Medicine, John Hunter Hospital, Hunter New England Local Health District; **Arshad Khan,** Advance Trainee Cardiology, Department of Cardiovascular Medicine, John Hunter Hospital, Hunter New England Health; **Lindsay Savage,** Cardiac Stream Lead, Hunter New England Local Health District; **Jeremy Condon,** PhD (Nursing) candidate: School of Nursing and Midwifery, University of Newcastle, and Department of Cardiovascular Medicine John Hunter Hospital, Hunter New England Local Health District; **Andrew J Boyle,** Professor of Cardiovascular Medicine, Hunter New England Local Health District, and Director of Priority Clinical Centre for Cardiovascular Health, University of Newcastle; **Nicholas Collins,** Cardiologist, Director of Cardiac Catheterisation Laboratory, Department of Cardiovascular Medicine, John Hunter Hospital, Hunter New England Local Health District; **Kerry J Inder,** Associate Professor of Nursing: School of Nursing and Midwifery, Faculty of Health and Medicine, University of Newcastle; all at Newcastle, Australia. **Email:** trent.williams@hnehealth.nsw.gov.au **Twitter:** @HNEHealth

ABSTRACT

Aim: This study examines the factors associated with femoral vascular complications (FVCs) following cardiac catheterisation. **Methods:** In a study using a case control design, patients with an FVC (pseudoaneurysm or retroperitoneal bleed) were examined over 5 years. Multivariable logistic regression was used to determine associations with FVCs. Results are reported as adjusted odds ratios (AOR) and 95% confidence intervals (CIs). **Results:** Seventy-eight (0.65%) patients experienced FVCs (mean age: 65 years, sex: 50% female). Factors that increased the likelihood of experiencing FVC were being female (AOR 2.9, 95% CI 1.3–6.1), smoking (AOR 7.4, 95% CI 3.5–16), having diabetes mellitus (AOR 7.5, 95% CI 3.4–16), having hypertension (AOR 2.9, 95% CI 1.2–6.9), taking anticoagulant medication (AOR 16, 95% CI 5.5–45) having an elevated body mass index (AOR 1.1, 95% CI 1.0–1.2) and the use of vascular closure devices (AOR 3.4, 95% CI 0.61–19). Use of a compression device reduced the likelihood of FVCs developing (AOR 0.6, 95% CI 0.3–1.0). **Conclusion:** Sex, cardiovascular disease risk factors, and procedural factors remain important in developing FVCs.

KEY WORDS

◆ Percutaneous coronary intervention ◆ Femoral access ◆ Retroperitoneal bleed ◆ Coronary angiography ◆ Vascular closure device ◆ Vascular complication

Submitted for peer review: 8 October 2017. Accepted for publication: 1 November 2018. Conflict of interest: None.

Femoral vascular complications (FVCs) are an infrequent yet serious complication of cardiac catheterisation with significant morbidity, mortality and cost implications (Yatskar et al, 2007; Cox, 2008; Dencker et al, 2016). Each year, approximately 7 million cardiac catheterisation procedures are performed internationally with a reported access site complication rate of up to 6% (Patel et al, 2010). FVCs range from the more minor complications including haematomas, through to the more clinically significant pseudoaneurysm and retroperitoneal bleed, which may have the greatest impact on bleeding and subsequent adverse events (Applegate et al, 2008).

Background

Risk factors for FVC are well established and include female sex, older age, obesity and higher femoral artery puncture (Farouque et al, 2005). With the emergence of complex procedures in structural heart disease such as transcatheter aortic valve replacement (TAVR), addressing issues pertinent to femoral vascular access and associated complications is timely and important.

The increasing use of the transradial vascular access approach in particular, in addition to the use of fluoroscopic landmarks and vascular ultrasound, may reduce the incidence of FVC (Levine et al, 2011). However, some studies have shown the high uptake of transradial access has resulted in a higher proportion of femoral access complications in the patients who do have femoral access reported (Azzalini et al, 2015). Knowledge of risk factors for these potentially significant clinical problems remains important for the contemporary nursing workforce.

Aims

The aims of this paper are to:

- Examine the risk factor profile of consecutive patients who sustain an FVC, defined as a pseudoaneurysm or retroperitoneal bleed, following cardiac catheterisation or percutaneous coronary intervention (PCI) at a large tertiary referral hospital
- Describe the specific risk factors for femoral pseudoaneurysm and retroperitoneal bleeding groups. This will help to identify patients at increased risk of FVCs and identify strategies that may help to prevent FVCs.

Methods and methodology

Research design

The study was performed using a case control design.

Study setting

The tertiary referral centre used in this study is based in a region of New South Wales in Australia with a population of 910 436 people. The cardiac catheterisation laboratory is staffed by 20 specialist nurses, as well as senior interventional cardiologists, fellows and training resident staff trainee doctors, undertaking approximately 2000 cardiac catheterisation procedures and 850 PCIs annually.

Ethical approval

The need for formal ethical approval was waived after review by the institutional human research ethics committee as it was a retrospective examination of registry data.

Selection of cases

Patients who sustain an FVC have clinical, demographic and procedural data recorded prospectively in a separate procedural complication registry. The authors reviewed all medical records of patients who underwent cardiac catheterisation or PCI using femoral artery access who had been diagnosed with an FVC over a 5-year period. All adults in the procedural complication register who experienced a retroperitoneal bleed or a pseudoaneurysm were used in this study as cases. The two databases were linked using three identifiers: sex; date of birth; and unique medical record number. This sample included all diagnostic cardiac catheterisation procedures and PCIs performed over the study time frame including emergent cases.

Selection of controls

Details of consecutive patients who undergo cardiac catheterisation or PCI are prospectively recorded in a central database, including demographic, clinical and procedural data. The control group was randomly selected from the central database at a ratio of four controls to one case to increase statistical confidence. Controls were adults who had undergone coronary angiography or PCI using femoral artery access and did not develop an FVC.

For the purposes of this study, FVC is defined as any patient who was diagnosed with a pseudoaneurysm or retroperitoneal haemorrhage using Doppler ultrasound or computerised tomography after undergoing invasive assessment and treatment.

Statistical methods

Descriptive statistics are presented in counts and percentages for categorical variables, and means and standard deviation (SD) for continuous variables. Comparison of categorical variables was performed using the χ^2 test; and continuous variables using t-tests or Mann-Whitney U tests, depending on distribution.

Associations between demographic, disease-specific, procedural and medical management characteristics and FVCs were examined using binary logistic regression. Collinearity of variables in the model was checked using variance inflation factors, and linearity assumption for continuous variables and the log (outcome) were examined. Age and body mass index (BMI) were analysed as continuous variables; all other variables were analysed as categorical variables. Variables included in the model were selected based on clinical relevance, and model selection was performed to create the final model.

Where necessary, because of the low number of patients who experienced an FVC, variables were removed if non-significant in adjusted modelling. The degree of association of each variable in the model was taken into account with the outcome and it was ensured that the inclusion or removal of each variable did not grossly affect either the fit of the model (measured by likelihood ratio test and Akaike information criterion) or the estimates for remaining variables. For outcomes with very low numbers, multivariate modelling was not performed. Crude and adjusted odds ratios (ORs), 95% CIs and Wald *P*-values are presented for the logistic regression modelling.

The variables examined in the model included age, sex, BMI, diabetes, hypertension, smoking status, peripheral vascular disease (PVD), previous coronary artery bypass graft (CABG), cardiogenic shock, anticoagulant/antiplatelet medication, renal failure, vascular closure device and the use of a femoral compression device based on clinical significance. For this analysis, the authors adjusted for age and sex. Multivariate analyses were not performed to examine the association of variables with retroperitoneal bleed/haematoma because the number of patients was small. All analyses were programmed using SAS v9.4 (SAS Institute, Cary, North Carolina, US).

Results

All femoral vascular complications

Within a total of 12 005 procedures performed over a 5-year period, 78 patients sustained an FVC (0.65%). Characteristics of the sample who did and did not sustain an FVC are shown in *Table 1*. Fifty-five patients sustained a pseudoaneurysm, while 23 experienced a retroperitoneal bleed/haematoma. Of this group of 78 patients, 50% were male and the mean age was 65 years. Thirteen patients (16.7%) required surgery to manage their FVC. These cases were matched with 250 controls who had undergone a procedure using femoral vascular access and did not sustain a FVC. The mean age (SD) of the controls was 62 (±13) years; 61% were male.

The authors compared the baseline characteristics of the non-complication group to those who sustained an FVC (*Table 1*). BMI was higher in the FVC complications group than in the group without FVC complications (29.2 [SD ±5.9] vs 27.2 [SD ±3.9]; $P<0.001$). Those who sustained an FVC were more likely to have diabetes (14.8% vs 53.8%, $P<0.0001$), have hypertension (63.6% vs 82%, $P= 0.002$) and smoke (31.6% vs 70.5% $P<0.001$). Patients who sustained an FVC had a higher mean blood pressure at the time of puncture than the non-FVC group (151 mmHg vs 133 mmHg $p<0.0001$). Those who had been administered

Table 1. Characteristics of patients who sustained FVC versus those who did not; n=328

Femoral vascular complications Characteristic	No (n=250)	Yes (n=78)	Total (n=328)	p-value
Demographics				
Age in years (Mean, SD)	62 (13)	65 (14)	63 (13)	0.121
Gender (Female)	90 (36%)	39 (50%)	129 (39%)	0.027
CVD risk factors				
BMI (Mean, SD)	27.2 (3.9)	29.2 (5.9)	27.7 (4.5)	0.001
Diabetes (Yes)	37 (14.8%)	42 (53.8%)	79 (24%)	<0.0001
Hypertension (Yes)	159 (63.6%)	64 (82%)	223 (68%)	0.002
Smoker (Yes)	79 (31.6%)	55 (70.5%)	134 (41%)	<0.001
PVD (Yes)	26 (10.4%)	18 (23.1%)	44 (13%)	0.004
Procedural factors				
Systolic BP on puncture (Mean, SD)	133 (26)	151 (18)	137 (25)	<0.0001
Creatinine - pre procedure (Mean, SD)	90 (21)	101 (57)	92 (34)	0.007
Creatinine group (Normal <=104)	212 (79%)	55 (21%)	267 (81%)	0.005
Inpatient angiogram	136 (54.4%)	47 (60.4%)	183 (56%)	0.363
Rescue PCI	3 (1.2%)	5 (6.4%)	8 (2.4%)	0.009
Primary PCI	17 (6.8%)	3 (3.8%)	20 (6.1%)	0.341
Previous CABG	14 (5.6%)	4 (5.1%)	18 (5.5%)	0.873
Cardiogenic shock	10 (91%)	1 (9.1%)	11 (3.4%)	0.784
Medical management pre procedure				
Acetylsalicylic acid (ASA)	73 (29.2%)	68 (87.2%)	141 (43%)	<0.001
Clopidogrel	77 (30.8%)	37 (47.4%)	114 (35%)	0.007
Pre procedure Enoxaparin within 12 hours of procedure (No)	2 (0.8%)	12 (15.4%)	14 (4.3%)	<0.0001
Warfarin within 24 hours	0	6 (100%)	6 (1.8%)	<0.001
Haemostasis method				
Closure device used	7 (2.8%)	8 (10.4%)	15 (4.6%)	0.006
Digital pressure removal	126 (50.4)	44 (56.3%)	170 (52%)	0.504
Femoral compression device	117 (46.8%)	26 (33.3%)	143 (44%)	0.036

clexane within 12 hours of an arterial puncture were more likely to have an FVC than those who did not have a FVC (15.4% vs 0.8%, *P*<0.0001).

The procedural indications within the overall patient sample were diversely distributed with no statistical significance (outpatient diagnostic cardiac catheterisation, 26%; inpatient cardiac catheterisation, 56%; rescue PCI 2.4%; and primary PCI 6.1%). A 6 Fr arterial sheath was used in 98% of cases, while intra-aortic balloon pumps were used in 1.5% of patients. During the procedure, 26 patients (7.9%) received abciximab and one (0.3%) received bivalirudin. Eighteen patients (5.5%) had a CABG procedure with no statistical difference between groups. A higher rate of vascular closure device use was found in the FVC group than in the non-FVC group (10.4% vs 2.8%, *P*=0.006).

Using logistic regression analysis, the unadjusted results for the development of an FVC showed that being female (OR 1.8, 95% CI 1.1–3.0), having diabetes mellitus (OR 6.7, 95% CI 3.8–12), having hypertension (OR 2.6, 95% CI 1.4–4.9), being a current smoker (OR 5.2, 95% CI 3.0–9.0), having PVD (OR 2.6, 95% CI 1.3–5.0), having an elevated creatinine level (OR 2.3, 95% CI 1.3–4.2) and taking antiplatelet or anticoagulant medication (OR 8.6, 95% CI 3.8–20) significantly increased the odds of an FVC. A one-point increase in BMI was associated with a 10% increase in the odds of experiencing an FVC (OR 1.1, 95% CI 1.0–1.2). The use of a vascular closure device (OR 4.0, 95% CI 1.4–11) increases the likelihood of FVC but the use of a femoral compression device (OR 0.6, 95%CI 0.3–1.0) reduced the odds of an FVC. Age (OR 1.0, 95% CI 1.0–1.03) and previous CABG (OR 0.9, 95%, CI 0.3–2.9) were not associated with FVC in this sample (*Table 2*).

After adjusting for age and sex (*Table 2*), results showed that women were three times more likely to develop an FVC than men (AOR 2.9, 95% CI 1.3-6.1), and that elevated BMI (AOR 1.1, 95% CI 1.0–1.2), diabetes mellitus (AOR 7.5, 95% CI 3.4–16), hypertension (AOR 2.9, 95% CI 1.2–6.9), smoking (AOR 7.5, 95% CI 3.5-16) and taking anticoagulant or antiplatelet medications (AOR 16, 95% CI 5.5–45) increased the odds of FVC. The presence of an elevated creatinine level >104 mmol/litre (AOR 2.5, 95% CI 1.1–5.7) was also significantly associated with the development of vascular complications. The use of a vascular compression device during sheath removal reduced the odds of an FVC by 60% (AOR 0.4, 95% CI 0.2–0.9). Age, cardiogenic shock and the use of a vascular closure device were not independently associated with FVC in this

Table 2. Crude and adjusted odds ratios for development of femoral vascular access complication (retroperitoneal bleed or pseudoanuerysm)

Characteristic	Unadjusted			Adjusted		
	Odds Ratio	95%CI Lower	95%CI Upper	Odds Ratio	95%CI Lower	95%CI Upper
Age (in years)	1.0	0.99	1.0	1.0	0.98	1.0
Gender (Female vs Male)	1.8	1.1	3.0	2.9	1.3	6.1
Body mass index	1.1	1.0	1.2	1.1	1.0	1.2
Diabetes (Yes vs No)	6.7	3.8	12	7.5	3.4	16
Hypertension (Yes vs No)	2.6	1.4	4.9	2.9	1.2	6.9
Smoker (Yes vs No)	5.2	3.0	9.0	7.4	3.5	16
Peripheral vascular disease (Yes vs No)	2.6	1.3	5.0	.	.	.
Previous CABG (Yes vs No)	0.9	0.3	2.9	.	.	.
Cardiogenic shock (Yes vs No)	4.1	1.2	14	4.3	0.8	24
Anticoagulant/Antiplatelet medication (Yes vs No)	8.6	3.8	20	16	5.5	45
Creatinine group (>104 vs Normal <=104)	2.3	1.3	4.2	2.5	1.1	5.7
Closure device used (Yes vs No)	4.0	1.4	11	3.4	0.61	19
Femoral compression device (Yes vs No)	0.57	0.33	1.0	0.40	0.2	0.9

adjusted analysis. Because numbers were low, it was not possible to adjust for PVD and previous CABG in the analysis.

Factors associated with the development of pseudoaneurysm

Further analysis was undertaken to determine the risk profile of patients sustaining pseudoaneurysm and retroperitoneal bleed, adjusted for age and sex. The adjusted odds for pseudoaneurysm development (n=55) compared with patients who did not sustain a pseudoaneurysm were reported. For every one point increase in BMI, there was a 10% increased odds of a pseudoaneurysm (AOR 1.1, 95% CI 1.0–1.2). Having diabetes mellitus (AOR 4.1, 95% CI 2.0–8.5), smoking (AOR 4.1 95%, CI 2.0–8.5) or having peripheral vascular disease (AOR 3.3, 95% CI 1.3–7.9) and taking anticoagulant and antiplatelet medication (AOR 7.5, 95%, CI 2.8–20) were shown to increase the likelihood of pseudoaneurysm development. The use of a femoral compression device was shown to reduce the odds of vascular complications (AOR 0.4 95%, CI 0.2–0.9).

Factors associated with the development of retroperitoneal bleed

Demographics, disease-specific characteristics for patients who had a retroperitoneal bleed (n=23) compared with those who did not were examined.

A logistic regression model was used to predict the likelihood of retroperitoneal bleed developing in this small group. The model considered sex, age, BMI, diabetes, smoking status, hypertension, PVD, previous CABG, cardiogenic shock, closure device used, femoral compression device removal, renal impairment, heparin dose, and anticoagulation and antiplatelet use.

While the number of patients affected was small (n=23), in this model, sex and smoking significantly predicted the development of retroperitoneal bleed (P<0.05). Results indicated that male sex conferred a reduced risk of developing retroperitoneal bleed (AOR 0.28, P=0.17, 95% CI 0.10–0.80), while smoking (AOR 4.7, P=0.005, 95% CI 1.56–13) was associated with the development of a retroperitoneal haemorrhage.

Discussion

This study, conducted at a large regional tertiary referral centre, examined factors associated with the development of FVCs, specifically pseudoaneurysm and retroperitoneal haemorrhage following cardiac catheterisation and PCI. Female sex, elevated BMI, diabetes mellitus, the use of a vascular closure device, hypertension, smoking and renal impairment were associated with an increased likelihood of any FVC. For pseudoaneurysm development, high BMI, diabetes mellitus, smoking, peripheral vascular disease and anticoagulant use were shown to be contributors. For retroperitoneal bleed, female sex and smoking were risk factors in a small group of patients.

The use of vascular closure devices was associated with an increased likelihood of FVC in this sample, while the application of a femoral compression device was shown to reduce the odds of FVC. A meta-analysis of randomised control trials, which included 4000 patients, showed closure devices may increase the risk of FVCs, with a caveat of poor methodological structure of some included studies (Koreny et al, 2004). A meta-analysis comparing vascular closure devices with manual compression involving 7528 patients reported increases in FVCs with vascular closure devices in a low-risk group of people having cardiac catheterisation only (Biancari et al, 2010). Conversely, vascular closure devices have been shown to reduce the risk of vascular and bleeding complications, when used in combination with intraprocedure medication use such as bivalirudin (Marso et al, 2010). In a large, registry-based study of 1 522 935 patients undergoing PCI, vascular closure device use and bivalirudin were associated with a significantly lower incidence of bleeding, particularly in a group with a high risk of bleeding complications.

A further benefit of the use of vascular closure devices was shown in the reduction of bleeding including haematocrit loss (a marker for bleeding) in the PCI group. (Romaguera et al, 2012). Overall, 7718 patients who had undergone PCI through femoral access were evaluated for FVCs and the consequent effect of the degree of blood loss on long-term mortality. Femoral closure devices were shown to be an independent predictor in a reduction in bleeding and FVCs. Definitive conclusions regarding the overall safety of vascular closure devices may be difficult to make without randomised control data comparing the variety of arterial closure methods in a large sample (Schulz-Schüpke et al, 2014). Given that experience with these devices in the management of vascular closure in structural heart disease procedures is increasing, continued improved results in their use could be anticipated in patients undergoing coronary interventions (Toggweiler et al, 2013).

The risk factors for FVCs are well established and our results demonstrate that, despite advances in vascular access techniques, the profile of patients, especially women, at risk of such complications remains unchanged (Levine et al, 2011). As operators increasingly use transradial artery access for coronary procedures, resulting in less procedural experience in femoral artery access, and with the emergence of structural interventions requiring a large calibre sheath (using femoral access), femoral vascular complications remain clinically relevant. Recognition that patients with particular characteristics remain at a higher risk, despite presumed awareness, should reinforce the need to direct approaches to minimise the likelihood of vascular complications.

The data in this study are consistent with those in previous studies, confirming female sex is a strong independent risk factor in the development of FVCs (Piper et al, 2003; Farouque et al, 2005; Tiroch et al, 2008). Potential contributors to the increased risk noted in women (Schnyder et al, 2001; Farouque et al, 2005) includes a smaller diameter femoral artery, the underappreciated effects of oestrogen on arterial structures (Celermajer et al, 1994) and the effect of smaller body size compared with males, which may impair recognition of standard landmarks that may make arterial puncture more problematic (Farouque et al, 2005). In addition, female sex in combination with smoking and its reduction in the thickness of the arterial walls, is thought to be implicated in the development of FVC (Suggs et al, 2013).

This sample suggests that a higher BMI is associated with the development of FVC. Previously published literature has demonstrated that obesity and a high body surface area or BMI are significant risk factors in the development of an FVC (Ates et al, 2006; Kassem et al, 2013). Compared to a transradial approach, the femoral approach has a significantly higher incidence of procedural-related morbidity, related to bleeding and vascular complications in the high BMI group for cardiac catheterisation and PCI (Hibbert et al, 2012). The present study supports the need for continued vigilance among nursing staff, even in the transradial era, in identifying patients who undergo cardiac catheterisation with a high BMI as a high-risk group.

Hypertension is an important patient-related risk factor for the development of an FVC. This may relate to the presence of hypertension at the time of arterial puncture as well as a documented history of hypertension (Ricci et al, 1994; Cox et al, 2004; Tiroch et al, 2008; Popovic et al, 2010). Measures to prevent hypertension at the time of vascular access, such as pharmacological approaches to sedation and blood pressure management, are important. Renal insufficiency—even when mild—has been shown to be a risk factor in the development of vascular complications (Applegate et al, 2008; Tiroch et al, 2008). The association of renal impairment with vascular complications may be attributed to several clinical factors, including the likely platelet and arterial walls changes that patients with uraemia exhibit; or renal impairment may be associated with comorbidities associated with bleeding complications (Prada-Delgado et al, 2012). This dataset supports previously described research findings (Osten et al, 2008).

This study shows a significant association between the use of combination anticoagulant including the use of heparin, oral anticoagulants, GP IIb/IIIa inhibitors and the incidence of FVCs. The use of GP IIb/IIIa inhibitors has previously been shown to be an independent risk factor in the development of both bleeding and FVCs in several studies (Horwitz et al, 2003; Tiroch et al, 2008). This study population was varied in terms of acute and outpatient populations and the subsequent use of GP IIb/IIIa inhibitors can be considered low.

Furthermore, in patients considered to be at high risk, vascular access procedures may be carried out by a more experienced operator, thereby reducing the risk associated with aggressive antithrombotic therapy (Ammann et al, 2003). More experienced operators have been shown to have lower complication rates, and a higher procedural volume may be a protective factor in the development of complications (Levine et al, 2011); this could well be used to generate further hypotheses for future study, particularly in the realm of structural heart disease.

The centre in this study relies on predominantly a 6 Fr arterial access system for cardiac catheterisation. While the sample of patients who received a larger size sheath is small, a larger sheath size has been shown to increase the likelihood of an FVC (Uhlemann et al, 2012).

Strengths and limitations

The main strength of this study is that the dataset consists of consecutive, prospectively obtained clinical data and allows vascular complications to be assessed in a diverse patient sample, including in people undergoing rescue PCI and treatment for cardiogenic shock.

This study was a case control design so traditional limitations of unintentional bias and the difficulties of matching may be apparent in this sample (Mann, 2003). However, given that the outcome of FVC is relatively uncommon, this was the only feasible and efficient approach and may be helpful in generating hypotheses that can be tested

Key Points

- Femoral vascular complications (FVCs) are an infrequent yet serious complication of cardiac catheterisation and percutaneous coronary intervention because they have significant morbidity, mortality and cost implications
- Female sex, high body mass index, diabetes mellitus, hypertension, smoking, age, anticoagulant use and renal impairment were associated with an increased likelihood of FVC following these procedures
- Despite the adoption of transradial access internationally, FVCs remain an important issue for cardiology nurses because of their morbidity and mortality consequences
- Although transradial access for coronary procedures is becoming more prevalent, the emergence of structural interventions requiring a large calibre sheath means FVCs still remain highly clinically relevant for nurses
- An important aspect of nursing care is to be able to identify modifiable and non-modifiable risk factors for FVCs

using stronger designs. The data are from a single centre and the authors were not able to report the experience level of the operator undertaking vascular access as this was not routinely recorded. High experience level and procedural volume has been associated with a reduction in FVCs in previous studies (Levine et al, 2011).

Conclusion

Several modifiable and non-modifiable risk factors are associated with the development of FVC, including being female, smoking and having a high BMI, diabetes mellitus or hypertension, as well as clinical issues such as anticoagulant use and renal impairment.

While these risk factors are well established, the persisting increased risk experienced by these patients reflects the continued need for improvements in approaches to femoral vascular access. Continued vigilance around modifiable procedural aspects, including anticoagulation and haemostasis method, remain an important aspect of nursing care. BJCN

Acknowledgements: The authors gratefully acknowledge the assistance of CRεDITSS (Clinical Research Design, IT and Statistical Support) and Dr Neva Bull.

References

Ammann P, Brunner-La Rocca HP, Angehrn W, Roelli H, Sagmeister M, Rickli H. Procedural complications following diagnostic coronary angiography are related to the operator's experience and the catheter size. Catheter Cardiovasc Interv. 2003; 59(1):13–8. https://doi.org/10.1002/ccd.10489

Applegate R, Sacrinty MT, Kutcher MA et al. Trends in vascular complications after diagnostic cardiac catheterization and percutaneous coronary intervention via the femoral artery, 1998 to 2007. JACC Cardiovasc Interv. 2008; 1(3):317–26. https://doi.org/10.1016/j.jcin.2008.03.013

Ates M1, Sahin S, Konuralp C et al. Evaluation of risk factors associated with femoral pseudoaneurysms after cardiac catheterization. J Vasc Surg. 2006 Mar;43(3):520–4. https://doi.org/10.1016/j.jvs.2005.11.009

Azzalini L, Tosin K, Chabot-Blanchet M et al. The benefits conferred by radial access for cardiac catheterization are offset by a paradoxical increase in the rate of vascular access site complications with femoral access: the Campeau Radial Paradox. JACC Cardiovasc Interv. 2015; 8(14):1854–64. https://doi.org/10.1016/j.jcin.2015.07.029

Biancari F, D'Andrea V, Di Marco C, Savino G, Tiozzo V, Catania A. Meta-analysis of randomized trials on the efficacy of vascular closure devices after diagnostic angiography and angioplasty. Am Heart J. 2010; 159(4):518–31. https://doi.org/10.1016/j.ahj.2009.12.027

Celermajer DS, Sorensen KE, Spiegelhalter DJ, Georgakopoulos D, Robinson J, Deanfield JE. Aging is associated with endothelial dysfunction in healthy men years before the age-related decline in women. J Am Coll Cardiol. 1994 Aug;24(2):471–6. https://doi.org/10.1016/0735-1097(94)90305-0

Cox N, Resnic FS, Popma JJ, Simon DI, Eisenhauer AC, Rogers C. Comparison of the risk of vascular complications associated with femoral and radial access coronary catheterization procedures in obese versus nonobese patients. Am J Cardiol. 2004; 94(9):1174–7. https://doi.org/10.1016/j.amjcard.2004.07.088

Cox G. New interventions in asthma including bronchial thermoplasty. Curr Opin Pulm Med. 2008; 14(1):77–81. https://doi.org/10.1097/MCP.0b013e3282f333c8

Dencker D, Pedersen F, Engstrøm T et al. Major femoral vascular access complications after coronary diagnostic and interventional procedures: a Danish register study. Int J Cardiol. 2016; 202:604–8. https://doi.org/10.1016/j.ijcard.2015.09.018

Farouque HM, Tremmel JA, Raissi Shabari F et al. Risk factors for the development of retroperitoneal hematoma after percutaneous coronary intervention in the era of glycoprotein IIb/IIIa inhibitors and vascular closure devices. J Am Coll Cardiol. 2005; 45(3):363–8. https://doi.org/10.1016/j.jacc.2004.10.042

Hibbert B, Simard T, Wilson KR et al. Transradial versus transfemoral artery approach for coronary angiography and percutaneous coronary intervention in the extremely obese. JACC Cardiovasc Interv. 2012; 5(8):819–26. https://doi.org/10.1016/j.jcin.2012.04.009

Horwitz PA, Berlin JA, Sauer WH, Laskey WK, Krone RJ, Kimmel SE; Registry Committee of the Society for Cardiac Angiography Interventions. Bleeding risk of platelet glycoprotein IIb/IIIa receptor antagonists in broad-based practice (results from the Society for Cardiac Angiography and Interventions Registry). Am J Cardiol. 2003; 91(7):803–6. https://doi.org/10.1016/S0002-9149(03)00012-2

Kassem HH, Elmahdy MF. Essam BE, Mahdy SG. Incidence and predictors of post-catheterization femoral artery pseudoaneurysms. Egypt Heart J. 2013; 65(3):213–21. https://doi.org/10.1016/j.ehj.2012.07.003

Koreny M, Riedmüller E, Nikfardjam M, Siostrzonek P, Müllner M. 2004. Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. ACC Curr J Rev. 13(4):44–4. https://doi.org/10.1016/j.accreview.2004.03.054

Levine GN, Bates ER, Blankenship JC et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol. 2011; 58(24):e44–122. https://doi.org/10.1016/j.jacc.2011.08.007

Mann CJ. Observational research methods. Research design II: cohort, cross sectional, and case-control studies. Emerg Med J. 2003; 20(1):54–60. https://doi.org/10.1136/emj.20.1.54

Marso SP, Amin AP, House JA et al. Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. JAMA. 2010; 303(21):2156–64. https://doi.org/10.1001/jama.2010.708

Patel MR, Jneid H, Derdeyn CP et al. Arteriotomy closure devices for cardiovascular procedures: a scientific statement from the American Heart Association. Circulation. 2010; 122(18):1882–93. https://doi.org/10.1161/CIR.0b013e3181f9b345

Piper WD, Malenka DJ, Ryan TJ Jr et al. Predicting vascular complications in percutaneous coronary interventions. Am Heart J. 2003; 145(6):1022–9. https://doi.org/10.1016/S0002-8703(03)00079-6

Popovic B1, Freysz L, Chometon F et al. Femoral pseudoaneurysms and current cardiac catheterization: evaluation of risk factors and treatment. Int J Cardiol. 2010; 141(1):75–80. https://doi.org/10.1016/j.ijcard.2008.11.111

Prada-Delgado O, Estévez-Loureiro R, Calviño-Santos R et al. Renal insufficiency and vascular complications after primary angioplasty

via femoral route. Impact of vascular closure devices use. Rev Esp Cardiol (Engl Ed). 2012 Mar;65(3):258–64. https://doi.org/10.1016/j.recesp.2011.10.020
Osten MD, Ivanov J, Eichhofer J et al. Impact of renal insufficiency on angiographic, procedural, and in-hospital outcomes following percutaneous coronary intervention. Am J Cardiol. 2008; 101(6):780–5. https://doi.org/10.1016/j.amjcard.2007.11.009
Ricci MA, Trevisani GT, Pilcher DB. Vascular complications of cardiac catheterization. Am J Surg. 1994; 167(4):375–8. https://doi.org/10.1016/0002-9610(94)90119-8
Romaguera R, Wakabayashi K, Laynez-Carnicero A et al. Association between bleeding severity and long-term mortality in patients experiencing vascular complications after percutaneous coronary intervention. Am J Cardiol. 2012; 109(1):75–81. https://doi.org/10.1016/j.amjcard.2011.08.007
Schnyder G, Sawhney N, Whisenant B, Tsimikas S, Turi ZG. Common femoral artery anatomy is influenced by demographics and comorbidity: implications for cardiac and peripheral invasive studies. Catheter Cardiovasc Interv. 2001; 53(3):289–95. https://doi.org/10.1002/ccd.1169
Schulz-Schüpke S, Helde S, Gewalt S et al. Comparison of vascular closure devices vs manual compression after femoral artery puncture: the ISAR-CLOSURE randomized clinical trial. JAMA. 2014; 312(19):1981–7. https://doi.org/10.1001/jama.2014.15305
Suggs P, Shelia R, Faye C, Sonya H. Factors associated with groin complications post coronary intervention. Clin Nurs Stud. 2013; 1(1): 26–34. https://doi.org/10.5430/cns.v1n1p26
Tiroch KA, Arora N, Matheny ME, Liu C, Lee TC, Resnic FS. Risk predictors of retroperitoneal hemorrhage following percutaneous coronary intervention. Am J Cardiol. 2008; 102(11):1473–6. https://doi.org/0.1016/j.amjcard.2008.07.039
Toggweiler S, Leipsic J, Binder RK et al. Management of vascular access in transcatheter aortic valve replacement: part 2: Vascular complications. JACC Cardiovasc Interv. 2013; 6(8):767–76. https://doi.org/10.1016/j.jcin.2013.05.004
Uhlemann M, Möbius-Winkler S, Mende M et al. The Leipzig prospective vascular ultrasound registry in radial artery catheterization: impact of sheath size on vascular complications. JACC Cardiovasc Interv. 2012 Jan;5(1):36–43. https://doi.org/10.1016/j.jcin.2011.08.011
Yatskar L, Selzer F, Feit F et al. Access site hematoma requiring blood transfusion predicts mortality in patients undergoing percutaneous coronary intervention: data from the National Heart, Lung, and Blood Institute Dynamic Registry. Catheter Cardiovasc Interv. 2007; 69(7):961–6. https://doi.org/10.1002/ccd.21087

CPD Reflection Questions

- What practice changes or assessment skills can nurses bring to a ward to decrease the chances of an FVC?
- What other procedural complications should cardiology nurses be focused on to improve patient outcomes?
- Should the combination of high-risk features in our patients ensure they be assessed for consideration of transradial access?