School of Public Health

Development of a clinical quality registry for percutaneous coronary intervention among coronary heart disease patients in Northern Vietnam: A pilot registry study

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Author's Declaration

I declare that this thesis is my own account of my research and contains as its main content work which has not previously been submitted for a degree at any tertiary education institution.

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgement has been made. This thesis contains no material which has been accepted for the award of any other degree or diploma in any university. The published papers have co-authors who have identified and acknowledged my contribution, included in Appendix.

The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The proposed research study received human research ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number: **HRE2017-0378**

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Date: 10 February 2021

Abstract

Background

Cardiovascular diseases remain the leading cause of death worldwide, and coronary heart disease is known as the most common underlying cause of cardiovascular diseases deaths and morbidity. In Asia, the continent that is home to 60% of the world's population, the burden of coronary heart disease has grown significantly in recent decades. Considerable efforts have been put in place to manage the disease growth and improve quality of healthcare for patients. Percutaneous coronary intervention has become the optimal choice for cardiac based treatments for coronary heart disease patients. A variety of national and multicentre clinical quality registries have been established for monitoring, managing practice and improving outcomes for patients following percutaneous coronary intervention. Despite the success of these percutaneous coronary intervention registries, there remains wide variation between nations and requires the data from real practice, especially in low resources settings countries. This project describes the establishment of a pilot percutaneous coronary intervention registry in Vietnam and updates our understanding of percutaneous coronary intervention practices in Vietnam.

Objectives

The aim of this study was to develop a pilot clinical quality registry in order to understand the practice of percutaneous coronary intervention, profiles of patients undergoing percutaneous coronary intervention, and outcomes of these patients at 30 days and 12 months. The specific objectives were as follows: 1) to develop a framework/ model that could be utilised for a national registry in interventional cardiology in Vietnam; 2) to investigate the demographic and clinical characteristics

of patients undergoing percutaneous coronary intervention in Northern Vietnam; 3) to examine the percutaneous coronary intervention outcomes at one and 12 months in Northern Vietnam; 4) to investigate the predictors of percutaneous coronary intervention outcomes at 12 months in Northern Vietnam; and 5) to estimate in-hospital costs associated with percutaneous coronary intervention per coronary patients in Vietnam.

Methods

A hospital-based pilot registry study was conducted in the Vietnam National Heart Institute in Hanoi, Vietnam from September 2017 to May 2018. Participants were patients undergoing percutaneous coronary intervention during the study period. Data collection tools were adapted from those used in a well-known percutaneous coronary intervention registry in Australia with relevant modifications and printed into paper-based forms. Participants who agreed to participate in the study had data collected at baseline, and follow-ups at 30 days and 12 months. At baseline, information of patients' demographic, clinical history, presentations, treatments, percutaneous coronary intervention practices, blood tests, and in-hospital complications were collected via interviewing participants, reviewing medical records, and reading the secured disks in the catheterization laboratory. At the two follow-ups points, information on complications, rehospitalization, and quality of life were obtained via face to face or phone interviews. From the completed forms, data were coded and inputted twice into Epi-data, then transferred to SPSS for data analysis. The data were summarised by means or percentages as appropriate. Besides descriptive statistics and univariate analyses, multiple logistic and linear regressions were performed to

investigate the association between independent factors with outcomes and hospital cost.

Results

During the 9 months of data collection, 1,022 patients undergoing percutaneous coronary intervention were recruited from a total of 1,041 procedures conducted during that time frame. The estimated mean time to collect information from patients before discharge was 60 minutes. Of the collected data fields, 98% were successfully completed. The estimated cost for data collection was 4.4 USD and 1.1-2.2 USD per patient at baseline and follow-up. The viability of the first registry was confirmed by collecting the most representative sample size, high data quality, reasonable cost and time for data collection and strong support from patients, hospital staff and the leadership team at the institute where data were collected.

We identified patient profiles and investigated the clinical practices of percutaneous coronary intervention in Vietnam. The mean age was 68.3 years, two thirds were male, 54.4% of patients presented with acute coronary syndromes and 14.5% of them were ST-elevation myocardial infarction. The majority of lesions were classified as type B2 and C and the radial artery was the most common access location for percutaneous coronary intervention (79.2%). The use of drug-eluting stents was universal and the angiographic success rate was 99.4%. Cardiac complications following PCI were rare with the exception of major bleeding (2.0%). Information of sex differences was also investigated, in which female patients were older with relatively more comorbidities and a higher incidence of major bleeding than males ($p<0.05$).

Outcomes following procedures were obtained in hospital, at 30 days and 12 months. Poor outcomes were relatively low in those undergoing percutaneous coronary intervention in comparison with that of other registries in the region. Mortality rates were 0.9% at discharge, 1.9% at 30 days and 6.5% at 12 months. Predictors of poor outcomes 12 months post-percutaneous coronary intervention included being older than aged 75 years, being male, having acute myocardial infarction, left ventricular ejection fraction ≤ 40%, prior cerebral vascular disease and having an unsuccessful percutaneous coronary intervention.

Percutaneous coronary intervention remains a high cost procedure, which varied from 4,100 to 5,900 USD for each procedure depending on the entry location. Even though health insurance supported up to 60-70% of hospital fees, patients still need to contribute significantly (from 1,100 to 1,900 USD) for each time of hospital admission. Radial artery was the dominant access site for Vietnamese interventionists (80% of all patients). The transfemoral group reported more lesions of the left main artery and more previous procedures in comparison with the transradial group ($p<0.05$). The tranradial group was associated with a lower overall cost of admission (the adjusted difference was 1526.3 USD), shorter length of hospital-stay (2 days) and lower rates of major bleeding post-procedure. Procedural factors such as number of stents per lesion, PCI access sites having the most impact on the in-hospital cost of patients undergoing percutaneous coronary intervention.

Conclusions

By establishing the first percutaneous coronary intervention registry at a single centre in Vietnam, the study evaluated the sustainability of a clinical quality registry model in the area of percutaneous coronary intervention. Data obtained contribute to the understanding of percutaneous coronary intervention in Vietnam regarding patient's profiles, clinical practices, outcomes post procedures and cost related to percutaneous coronary intervention. Findings of the study provide the opportunity to expand the activity across other PCI centres in Vietnam to form a National PCI registry for Vietnam. This will allow for benchmarking the current practices, identifying the potential gaps, developing appropriate strategy for future healthcare improvement, which is essential for better management of percutaneous coronary intervention in Vietnam.

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Statement of Contribution

The School of Public Health at Curtin University provided the research environment that supported the PhD candidate to undertake this research. The PhD candidate was responsible for designing the methodology, undertaking recruitment, implementing data collection and analysis, and writing all publications presented as part of the thesis, with input from co-authors. Details are summarised as follows.

Supervisors:

1. Professor Christopher Reid
2. Associate Professor Richard Norman
3. Professor Rachel Huxley
4. Dr. Crystal Lee
5. Dr. Ngoc Minh Pham

Research collaborators and co-authors: The team in Vietnam National Heart Institute. Signed statements of the contribution of each co-author are provided in Appendix E.

Funding: Curtin International Postgraduate Research Scholarship/ Ministry of Education and Training Scholarship

Statement from Principal supervisor

I recommend that the thesis now is ready to submit for examination. The original work conducted as part of this thesis submission has led to four publications in peer-reviewed journals, three or which have been published or accepted and the 4th is currently under a second review following request for revisions from the Journal.

Professor Christopher Reid
Principal Supervisor

Table of Contents

List of Figures

List of Tables

List of Abbreviations

ACC/AHA	American College of Cardiology/ American Heart Association
ACS	Acute coronary syndrome
AMI	Acute myocardial infarction
APAC	Asia-Pacific
BARC	Bleeding Academic Research Consortium
BMS	Bare-metal stent
CVDs	Cardiovascular diseases
CQRs	Clinical quality registries
CABG	Coronary artery bypass grafting
CHD	Coronary heart disease
DAPT	Dual-anti platelet therapy
DES	Drug eluting stent
ECG	Electrocardiogram
GRACE	Global Registry of Acute Coronary Events
HI	Health insurance
LOS	Length of stay
L-MIC	Lower-middle-income country
LMICs	Low-and middle-income countries
MACCEs	Major adverse cardiac and cerebrovascular events
MACE	Major adverse cardiac event
MI	Myocardial infarction
NSTEMI	Non-ST-elevation myocardial infraction
OOP	Out of pocket

PCI	Percutaneous coronary intervention
PTCA	Percutaneous transluminal coronary angioplasty
QOL	Quality of life
STEMI	ST-elevation myocardial infraction
TFI	Trans-femoral intervention
TRI	Trans-radial intervention
UA	Unstable angina
VNHI	Vietnam National Heart Institute

Chapter 1 INTRODUCTION

1.1 Overview

Cardiovascular diseases (CVDs) are the leading causes of death and disability worldwide, and CVDs prevalence is increasing significantly across developing countries (Mortality and Causes of Death 2016, World Health Organization 2016, Thomas, Diamond et al. 2018). In 2017, an estimated 17.8 million people died from CVDs, accounting for 31% of total global deaths. More than three quarters of these deaths were located in low-and middle-income countries (LMICs) (G. B. D. Causes of Death Collaborators. 2018). Among CVDs, coronary heart disease (CHD) has been the most common underlying cause of disability and mortality. In 2016, it accounted for approximately 16.6% of total deaths worldwide (World Health Organization 2017, Thomas, Diamond et al. 2018) and places a large economic burden on individuals, families and healthcare systems (Zheng, Ehrlich et al. 2010, Gheorghe, Griffiths et al. 2018). Using effective treatments and improving quality of care for CHD patients have received great attention from stakeholders and clinical interventionists throughout the world.

Among the available treatment options, such as medications and revascularization for CHD patients, percutaneous coronary intervention (PCI) has been demonstrated to be an effective method in modern cardiac-based therapies (Gada, Kirtane et al. 2015). It has been used widely throughout the world since its inception in the late 1970s (Ui, Chino et al. 2005, Bangalore, Gupta et al. 2015). For example, approximately one million PCI procedures were performed in Asia in 2016, which was close to the volume in Europe or North America (Gao 2017). Notwithstanding the apparent

benefits of PCI, post-procedural cardiac complications including death, myocardial infarction (MI) are still concerning issues (Deb, Wijeysundera et al. 2013, Soo Hoo 2014, Hoebers, Claessen et al. 2015, Li, Wong et al. 2019, Chacko, J et al. 2020). Previous studies have been conducted to devise measures for prevention of post procedural cardiac complications and improvement in quality of life for patients following PCI. Clinical quality registries have been established to systematically provide intensive datasets from patients presenting with a specific procedure or diagnosis, and is considered an important platform for monitoring and benchmarking the performance of clinical care (McNeil, Evans et al. 2010, Gliklich, Dreyer et al. 2018). Especially, PCI registries have been widely established with the ultimate aim of ensuring and improving the quality of cardiology care and patient outcomes (Reid, Yan et al. 2014).

Asia accounts for nearly 60% of the world's population, and has witnessed a rapid rise in CHD burden, partly due to socio-economic and epidemiological transitions. While approximately 10% of total deaths in the region was attributed to CHD in 2000, the figure has increased to nearly 17.0% in 2016 (Gaziano, Bitton et al. 2010, World Health Organization 2016). To cope with this matter, various solutions and management strategies have been proposed and implemented. Beside the wide uptake of PCI procedures in Asian interventional cardiology centres, a variety of PCI registries has been established recently (Liew, Rosli et al. 2008, Park, Kim et al. 2014, Reid, Yan et al. 2014). Nonetheless, geographic variation and limited data available from less economically developed countries in the region require further PCI registries to be established for research, thereby helping inform policy with consideration of social, political and economic realities (Reid, Yan et al. 2014).

Vietnam, a lower-middle-income country in Southeast Asia, has experienced a significant increase in the burden of non-communicable diseases (Institute for Health Metrics and Evaluation 2010), partly due to the rapid transition of economy and epidemiology with CHD being the leading cause of death. In 2018, CHD caused about 67,500 deaths, which was 13.2% of total deaths, a 69% increase from the figure in 2014 (World Health Rankings 2017). Nonetheless, there has been no PCI registry established in Vietnam despite the widespread use of PCI among the available cardiac treatment therapies for CHD patients.

1.2 Background of Vietnam

Vietnam is located in Southeast Asia and it has borders with China in the North, Laos and Cambodia in the West, and the Eastern Sea in the East. The geography of the country is quite diverse with one side facing the sea and three-quarters of the area consisting of mountains and hills. There are two main deltas: the Red River Delta in the North and the Mekong River Delta in the South (Ministry of Foreign and Affair 2017). Six administrative zones are divided within the area of 331 000 km^2, including the Red River Delta, the Northern midlands and mountain areas, the North Central and Central coastal areas, the Central Highlands, the South East, and the Mekong River Delta.

The nation contains 63 provinces and 713 smaller areas such as districts, cities or towns. There are 11,162 wards, town districts, or communes under these districts in the administrative system. Currently, 35.7% of the population lives in urban areas, while the rest remains in rural areas (General Statistics Office 2019). The 2020 Human Development Report shows that the Human Development Indicators of Vietnam is

0.693 and ranked 118th in the world (United Nations Development Programme 2020). The population of Vietnam was approximately 94.7 million in 2018. The ratio between males and females was estimated as 0.977 (General Statistics Office 2019).

The country has a diverse culture with 54 ethnic groups of people, with the Kinh being the most populous, with over 86% of the population. They mainly occupy lowland areas and deltas, while other ethnic groups are located in midlands or mountainous areas. Regarding religion, approximately 70% of the population follows a specific religion, namely Buddhism, Taoism and Confucianism (Ministry of Foreign and Affairs 2017). In 2018, the literacy rate of Vietnamese people aged 15 years and older was 95% with higher proportion in males relative to females (96.5% versus 93.6%) (The World Bank 2018). The average life expectancy at birth was 73.5 years for whole country in 2018, and females are estimated to live until 76.2 years, longer than males by almost 5 years (70.9 years) (General Statistics Office 2019).

Despite facing challenges in the progress of development, Vietnam has achieved most targets in the Millennium Development Goals (MDGs) (Socialist Republic of Viet Nam 2015). For MDG1, Vietnam had great achievement in eradicating extreme poverty and hunger. The expenditure-based poverty rate dropped from 58.1% in 1993 to 14.5% in 2008 and 9.8% in 2013, preventing millions of people from experiencing poverty and increasing significantly their living standards. The country has also succeeded in attaining MDG2, universalising primary education with an enrolment rate of 99.0% in 2014. In MDG3, the country has achieved the target on gender equality and female empowerment. For instance, the literacy rate and education attainment were relatively equal between males and females across all educational

levels by 2014. Women currently account for 48.7% of the labour workforce in the country. With MDG4, the current achievement showed that Vietnam is on track to achieve a reduction in child mortality, which aimed to reduce two-thirds of deaths in children between 1990 and 2014. For instance, the infant mortality rate and under five mortality rate reduced by 2 and 2.5 times, respectively during the period from 1990 to 2014. Besides that, the country has reached the goal regarding maternal health (MDG 5) by reducing maternal mortality and improving women's reproductive health. Furthermore, malaria and tuberculosis have been well controlled and the spread of HIV/AIDS has been managed successfully (Socialist Republic of Viet Nam 2015).

1.3 Study design

A hospital-based registry study was conducted in Vietnam National Heart Institute (VNHI), Hanoi, Vietnam between September 2017 and May 2019. At baseline, data were collected through a number of activities, including interviewing patients, abstracting the medical records and reading and coding the PCI data into paper forms by interventional cardiologists. Follow-ups data were collected through direct or phone interviews depending on the physical presence of patients at VNHI. The questionnaires used in the study were adapted from the current version of standardised data abstraction forms developed for the Victorian Cardiac Outcomes Registry (VCOR), Australia (Victorian Cardiac Outcomes Registry 2013), including the standard case report form (CRF) and dataset definitions for all fields. To ensure the appropriateness to the Vietnamese setting, the data collection forms were translated into Vietnamese and tailored by two Vietnamese clinical cardiologists.

1.4 Aims and objectives

1.4.1 Aims of the study

The aim of this study was to develop a model of a clinical quality registry in order to understand the practice of PCI, profiles of patients undergoing PCI, and outcomes of these patients at 30 days and 12 months, with the potential for it to be expanded to a national model.

1.4.2 Objectives of the study

The specific objectives of this study were:

- To establish a framework/ model of PCI registry in Vietnam.
- To investigate the demographic and clinical characteristics of patients undergoing PCI in Vietnam.
- To examine the PCI outcomes at one and 12 months in Vietnam.
- To investigate the predictors of PCI outcomes at 12 months in Vietnam.
- To estimate in-hospital costs associated with PCI for coronary patients in Vietnam.

1.5 Significance of the study

Data regarding the patient characteristics, practices, success and outcomes of patients undergoing PCI in Vietnam remain limited despite the increasing use of PCI s in Vietnam. This study is the first to develop a PCI registry in Hanoi, Vietnam, in which the methodology for developing a registry model for interventional cardiology in Vietnam was assessed. It envisages to provide evidence for evaluating the clinical and patient outcomes associated with the procedure, which is crucial for the steady improvement in the quality of cardiac intervention in Vietnam. The profile of

Vietnamese patients and associated cost of PCI in hospital is also documented. Ultimately, the cost information obtained enables the assessment of hospital cost of PCI patients, which provides the first cost evaluation and potential benefits for clinical interventionists in Vietnam.

1.6 Outline of the thesis

There are eight chapters in this thesis as follows:

Chapter one gives the general background on PCI and Vietnam as the study location. The aims and objectives of the study are described in this chapter together with the significance of the study.

Chapter two is the summary of the literature review. It describes the current use of PCI at the global, continental and national levels. It also describes previous findings on clinical outcomes post PCI across different time horizons, information concerning hospital costs of patients undergoing PCI, and other associated factors.

Chapter three is the methodology used in this registry study. The description of the study design, study settings, participants and sample size calculations, the procedures and instruments of data collection, statistical analysis, and ethical considerations are provided.

Chapter four to seven provide results and discussion of the objectives of the study. These chapters are a mixture of descriptive findings and published papers, which have been referenced in each chapter, and provided in the thesis appendix.

Chapter eight provides a summary of the main findings of the thesis and gives some recommendations, both specific to the use of PCI in Vietnam, and to those seeking to conduct such studies in similar settings in future.

Ethics approval confirmation, information sheet, questionnaires, and other relevant documents are presented in the Appendices.

Chapter 2 LITERATURE REVIEW

2.1 Overview

This chapter describes a critical review of the literature on issues related to PCI for CHD. The review begins with the epidemiology, the pathophysiology, clinical classification of atherosclerotic CHD and management options. The following section focuses on PCI revascularization and gives details regarding the definitions, history and current status of PCI worldwide and in Vietnam. Current understanding of post procedural clinical outcomes and in-hospital cost of patients undergoing PCI is also presented in this section. Next, information related to the health care system and the health insurance in Vietnam will be presented. Finally, the clinical quality registries with a focus on PCI registries will be discussed.

2.2 Coronary heart disease

2.2.1 The epidemiology of coronary heart diseases

Cardiovascular diseases (CVDs) have remained the top cause of morbidity and mortality worldwide across the globe for many years (Roth, Johnson et al. 2017, Thomas, Diamond et al. 2018). Among cardiovascular illness, coronary heart disease (CHD) has remained the single largest cause of death globally. Also referred to as ischemic heart disease or atherosclerotic cardiovascular disease, CHD manifests as myocardial infarction or ischemic cardiomyopathy (Khan, Hashim et al. 2020). Indeed, CHD has been identified as a significant threat for robust economic development in the 21st century as it caused approximately 9 million deaths in 2016 in countries across all income groups (Nowbar, Gitto et al. 2019). In addition to mortality, the number of individuals with non-fatal CHD is increasing globally with chronic disabilities and impaired quality of life. The global burden of disease study reported that in 2017 CHD affected around 126.5 million people globally (1,655 per 100,000), increasing 74.9% compared to the figure from 1990. Around 10.6 million new cases occurred and there were 5.3 million years lived with disability and 165.0 million years of life lost (Dai, Much et al. 2020, Khan, Hashim et al. 2020). Together with burden of disease, CHD has placed a large economic burden for populations due to the cost required for hospitalizations, treatments, revascularizations, clinic and emergency visits and prescribed medicines. The World Heart Federation reported that the global cost of CVD in 2010 was approximately US $863 billion, and it is expected to rise to over US $1 trillion by 2030 (Khan, Hashim et al. 2020). In the United States, CHD cost is approximately 1-1.5% of gross domestic product.

From the year 1998, the direct medical cost for CHD events were estimated to be $17,532 for fatal AMI, $15,540 for nonfatal AMI, $2,569 for stable angina, $12,058 for unstable angina, and $713 for sudden CHD death (Russell, Huse et al. 1998, Thom, Haase et al. 2006). The last decade has seen a considerable decrease in CHD mortality in Western countries thanks to a major focus on primary prevention and advances in diagnosis and treatment therapies. However, CHD has placed new challenges for the health care system in lower and middle-income countries (LMIC) due to increasing rates of cardiovascular risk factors (Gaziano, Bitton et al. 2010, Nowbar, Gitto et al. 2019). Notably, the cost for CHD in low-and middle-income countries (LMICs) was also comparable to high economically developed countries according to the findings of a systematic review in 2015. Data from 83 studies from 16 electronic databases estimated that the cost per CHD episode was up to $5000, with an "episode" referring to the cost associated with any finite interaction with a healthcare provider due to CHD. For chronic treatment, the average monthly fees ranged from $300 to $1000 for each patient (Gheorghe, Griffiths et al. 2018)

2.2.2 Pathophysiology and clinical classification of atherosclerotic coronary heart disease

CHD which is also known as coronary artery disease or ischemic heart disease is a complex chronic disease which involves the remodelling and narrowing of the coronary arteries providing myocardial oxygen to the heart (Sayols-Baixeras, Lluis-Ganella et al. 2014). The underlying pathophysiological mechanism of CHD is known as atherosclerosis, which starts and develops for decades prior to an acute event (Ambrose and Singh 2015). Briefly, atherosclerosis is a silent progressive process

characterized by accumulation of lipids, fibrous elements, and inflammatory molecules in the inner walls of the coronary arteries that is accelerated by well-known risk factors such as high blood pressure, high cholesterol, smoking, diabetes, and genetics (Sayols-Baixeras, Lluis-Ganella et al. 2014, Ambrose and Singh 2015). Consequently, the inner layer of the coronary arteries is gradually thickened, which may over time lead the lumen of the artery to be narrow in various degrees. Atherosclerotic plaque growth and changes are shown in Figure 2.1.

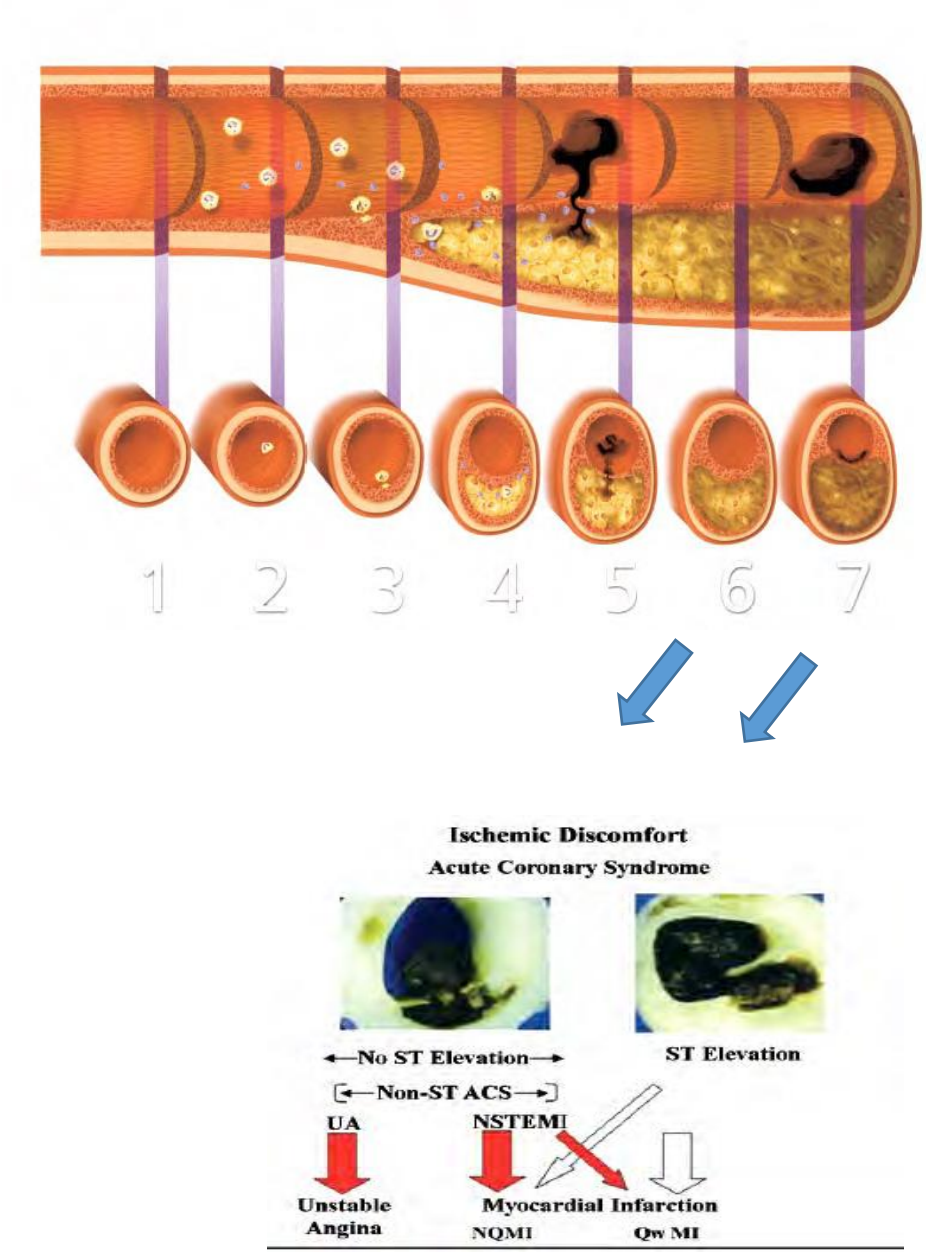

Figure 2-1 Formation stages of coronary atherosclerotic plaque and the consequences

The top of the diagram represents longitudinal and cross-sectional images of the coronary artery, in which stages of the atherosclerotic plaque and the effects were shown.

Labels are as following: (1) Cross section of normal artery; (2) Start of extracellular lipid accumulation in the inner layer (intima) of coronary artery; (3) The stage of fibrofatty; (4) The progression of lesions when the fibrous cap was weakened; (5) The

rupture of the fibrous cap and stimulation of thrombogenesis; (6) The response with thrombus resorption, accumulation of collagen and growth of smooth muscle cell; (7) The erosion of endothelial layer, may cause acute myocardial infarction.

The blue arrows show the chance to develop ST elevation in clinical presentation of patients.

(Reproduced from Libby, P; et al.(Libby 2001) and Davies, M.J.(Davies 2000))

At the first stage, low-density lipoprotein (LDL) cholesterol starts to efflux to the subendothelial space, and then be modified and oxidized by various agents. Oxidized/modified LDL cholesterol particles are potent chemotactic molecules including expression of vascular cell adhesion molecule and intercellular adhesion molecule at the endothelial surface, and contribute to monocyte adhesion and the movement to the subendothelial space. Monocytes differentiate to macrophages in the intima (Ghattas, Griffiths et al. 2013, Sayols-Baixeras, Lluis-Ganella et al. 2014). Foam cells enhance macrophages binding to oxidized LDL cholesterol via scavenger receptors (Glass and Witztum 2001), resulting in pro-inflammatory actions, including the release of cytokines. This process ends with the formation of the first typical atherosclerotic lesion, i.e., the fatty streak (Sayols-Baixeras, Lluis-Ganella et al. 2014).

In the sub-endothelial space, the accumulation of other types of leukocytes occurs, including lymphocytes and mast cells (Libby, Ridker et al. 2011). The mix between monocytes, macrophages, foam cells, and T-cells results in cellular, immune responses, and a chronic inflammatory state (Sayols-Baixeras, Lluis-Ganella et al. 2014). Migration of smooth muscle cells from the medial layer of the artery into the intima follows, resulting in the development from a fatty streak to a more complex

lesion (Glass and Witztum 2001). In the intima, smooth muscle cells produce extracellular matrix molecules and creates a fibrous cap covering the original fatty streak. The death of foam cells inside the fibrous cap releases lipids, which accumulates in the extracellular space and forms a lipid-rich pool, namely the necrotic core. This process results in the second atherosclerotic lesion, the fibrous plaque.

The thickness of the fibrous cap is very important for the integrity of the atherosclerotic plaque (Sakakura, Nakano et al. 2013), and depending on that thickness, two types of plaque can be classified, i.e., stable and unstable or vulnerable. Stable plaques are normally made with an intact, thick fibrous cap formulated by smooth muscle cells in a matrix rich in type I and III collagen (Finn, Nakano et al. 2010). This kind of plaque often causes flow-limiting stenosis, leading to tissue ischemia and potentially stable angina. In contrast, vulnerable plaques have a thin fibrous cap composed mostly of type I collagen and few or no smooth muscle cells, but abundant macrophages and pro-inflammatory and pro-thrombotic molecules (Sakakura, Nakano et al. 2013). These plaques can be subject to erosion or rupture, releasing the core of the plaque to circulating coagulation proteins, causing thrombosis, sudden occlusion of the artery lumen, and usually an acute coronary syndrome (ACS) (Tanaka, Nakamura et al. 2004, Libby, Ridker et al. 2011, Ghattas, Griffiths et al. 2013).

The position, amount and changes in size over time of the atherosclerotic plaques can lead to various degrees of coronary artery lumen obstruction. When the myocardial oxygen consumption is increased due to an increase in heart rate and myocardial contractility, depending on the time and volume of the coronary artery lumen obstruction, this may result in the imbalance between myocardial oxygen supply and

oxygen consumption. Patients may have some ischemic chest symptoms as a result of this imbalance especially when the coronary lumen diameter reduces to over 50% of the normal size (Shugman 2012).

One or more coronary arteries may narrow through the development of atherosclerotic plaques. During a period of increased demand for myocardial oxygen, such as following exercise, the symptoms of ischemia can be triggered and the spectrum of CHD may present. Clinically, the spectrum of clinical presentations of CHD has been classified into chronic or stable CHD, ACS and sudden cardiac death (Sayols-Baixeras, Lluis-Ganella et al. 2014). Chronic CHD comprises silent ischemia and stable angina while the spectrum of ACS is characterised by acute symptoms and includes unstable angina, non-ST-segment elevation myocardial infarctions (NSTEMI) and ST-segment elevation myocardial infarctions (STEMI) (Figure 2.1). These classifications are determined by the electrocardiogram (ECG) and cardiac biomarker levels which includes creatine kinase (CK), creatine kinase MB (CKMB) and/or the more specific and sensitive cardiac biomarkers, Troponins (Troponin T [TnT] or Troponin I [TnI]) (Thygesen, Alpert et al. 2007). Among the range of ACS, STEMI is the most severe form that often results in mechanical instability, cardiac rhythm disturbance and/or sudden cardiac death.

2.2.3 Acute coronary syndromes

Acute coronary syndromes (ACS) are clinical syndromes that include unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI). The symptoms include chest discomfort with or without radiation to the arms, back, jaw, or neck; or breathlessness; weakness;

diaphoresis; nausea and/or light headedness. Compared to stable angina, these symptoms are more severe, prolonged and usually occur at rest. Myocardial infarction is often accompanied with more prolonged myocardial ischemic symptoms (> 30 minutes) and the necrosis of myocardial cells (Amsterdam, Wenger et al. 2014, Nunez-Gil, Riha et al. 2019).

At admission to the health care system, clinical assessment and evaluation for patients is important as their types of ACS (UA, NSTEMI or STEMI) decide the medical management at hospitals (Amsterdam, Wenger et al. 2014, Nunez-Gil, Riha et al. 2019). Beside full medical history and clinical examination, patients should get a 12 lead ECG recording and blood test for myonecrosis markers including troponins (TnT or TnI), CKMB and/or CK. In these clinical settings, UA is classified if patients presenting with normal levels of myonecrosis markers with or without ECG changes (ST-segment depression, or prominent T-wave inversion) (Rousan and Thadani 2019). NSTEMI is characterized by changing T-wave in ECG (ST-segment depression or prominent T- wave inversion) and positive /elevated levels of myonecrosis markers but no persistent ST-segment elevation (Amsterdam, Wenger et al. 2014). STEMI is characterized by persistent ST-segment elevation or new left bundle branch block in ECG and positive/ elevated levels of markers of myonecrosis (Nunez-Gil, Riha et al. 2019).

2.2.4 Management options

2.2.4.1 Pharmacotherapies

The purpose of medical management is to improve prognosis, reduce severe symptoms, and reduce morbidity and cardiac death for CHD patients. Depending on the status of patients, the medical approach may be different. Patients with stable-CHD should receive treatment for controlling risk factors and plaque growth and preventing thrombosis if the endothelial lining is dysfunctional or plaques are unstable. Medical management of risk factors includes controlling hypertension, diabetes, and hyperlipidaemia; maintaining healthy lifestyles and diets; quitting smoking; being physical active; and avoiding bad psychosocial factors such as distress (Knuuti, Wijns et al. 2020). Some anti-hypertensive agents such as calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, and thiazide diuretics are used as first-line options for hypertension patients (Unger, Borghi et al. 2020). At presentation, pre-existing type 2 diabetes patients can keep taking current prescribed medicines while new diagnosed patients should receive oral antidiabetic agents such as metformin (Marin-Penalver, Martin-Timon et al. 2016). Pharmacological therapy for hyperlipidaemia patients includes statins, ezetimibe and fibrates (Cicero, Landolfo et al. 2019).

The management and control of plaque growth is attempted through aggressive cholesterol lowering treatment such as statins. Thrombosis prevention is accompanied with the use of antiplatelet agents. The current evidence supports the use of low doses of aspirin (75-100 mg /day) in ischaemic prevention in CHD patients (Knuuti, Wijns et al. 2020).

Patients suspected of having ACS should receive urgent medical attention with several therapies. To restrict the excessive activation and aggregation of platelet, dual antiplatelet therapy (DAPT), including acetylsalicylic acid (ASA) and one of the second type of antiplatelet agent (P2Y12 inhibitor), is considered as a standard of medical care for ACS patients (Chew, Scott et al. 2016, Ibanez, James et al. 2018, Valgimigli, Bueno et al. 2018). At the first medical administration, a loading dose of 150-300 mg of ASA or aspirin tablets (oral and rapidly absorbed is preferred) is used unless there are contraindications, or ASA can be administered intravenously with dose of 75-150mg when oral intake is impossible (Kubica, Adamski et al. 2018). The most common oral platelet P2Y12 are clopidogrel, prasugrel, and ticagrelor. The current guidelines recommended the newer inhibitors (prasugrel and ticagrelor) and the loading dose 180mg of ticagrelor, followed by 90mg twice a day or prasugrel 60mg, followed by 10mg daily is advisable (Chew, Scott et al. 2016, Kubica, Adamski et al. 2018, Valgimigli, Bueno et al. 2018). Anticoagulation, beta-blockers, angiotensin receptor blocker, and additional treatments such as morphine, nitro-glycerine, and oxygen may all be provided according to ACS presentation (Switaj, Christensen et al. 2017).

The use of optimal medical therapy has been recognised as vital for all coronary patients regardless of clinical presentation and revascularization strategy (Iqbal and Serruys 2017). Optimal medical therapy has been proven to improve outcomes of both stable coronary or ACS patients. The Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) trial, which was a multicentre, randomized, clinical trial of 1800 patients with complex diseases, also confirmed that the lack of optimal therapy was associated with adverse clinical

outcomes in patients treated with PCI or CABG (Iqbal, Zhang et al. 2015). In patients with stable coronary artery disease, a systematic review and meta-analysis including 12 randomized clinical trials reported that PCI did not reduce the risk of mortality and adverse events after the procedure in comparison with optimal medical therapy (Pursnani, Korley et al. 2012). Despite the positive clinical impact on outcomes, there remained the need to improve the adherence to medical therapy in these coronary patients (Iqbal, Zhang et al. 2015, Iqbal and Serruys 2017).

Figure 2.2 shows steps of evaluation and management of patients suspected of having CHD.

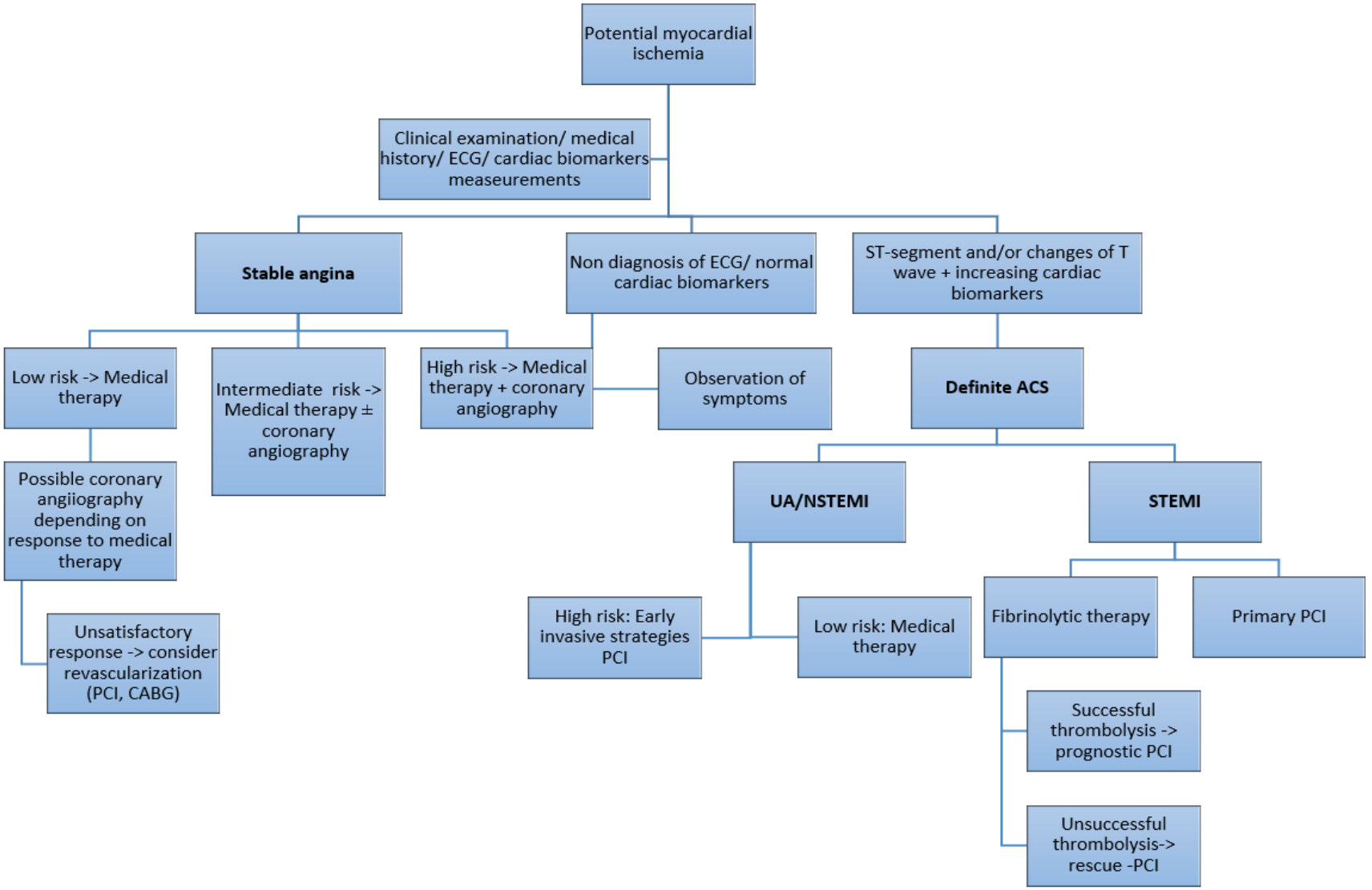
Potential myocardial ischemia
Clinical examination/ medical history/ ECG/ cardiac biomarkers measeurements
Stable angina
Non diagnosis of ECG/ normal cardiac biomarkers
ST-segment and/or changes of T wave + increasing cardiac biomarkers
Low risk -> Medical therapy
Intermediate risk -> Medical therapy ± coronary angiography
High risk -> Medical therapy + coronary angiography
Observation of symptoms
Definite ACS
Possible coronary angiiography depending on response to medical therapy
UA/NSTEMI
STEMI
Unsatisfactory response -> consider revascularization (PCI, CABG)
High risk: Early invasive strategies PCI
Low risk: Medical therapy
Fibrinolytic therapy
Primary PCI
Successful thrombolysis -> prognostic PCI
Unsuccessful thrombolysis-> rescue -PCI

Figure 2-2 Steps of evaluation and management of patients suspected of having coronary heart disease

ACS= acute coronary syndromes; CABG= coronary artery bypass grafting; ECG= electrocardiogram; NSTEMI= non-ST segment elevation myocardial infarction; PCI= percutaneous coronary intervention; STEMI= ST-segment elevation myocardial infarction; UA= unstable angina.

Modified from Anderson, J.L, et al. and Fox, K, et al.(Fox, Garcia et al. 2006, Anderson, Adams et al. 2007)

2.2.4.2 Risk factor management

Risk factors which may contribute to CHD can be classified into: a) modifiable risk factors which include hypercholesterolemia, smoking, diabetes, hypertension, a sedentary lifestyle and obesity; and b) non-modifiable risk factors which include age over 65 years, male gender and family history of ischemic heart disease. The current guidelines continue to emphasize the necessity of reducing the CHD risk factors as the best mode of primary prevention, mostly focusing on the modifiable risk factors (Knuuti, Wijns et al. 2020). These actions include controlling of chronic diseases such as diabetes, hypertension and hypercholesterolemia, and suggesting changing behavioural risk factors into healthy lifestyle such as quitting smoking, reducing alcohol consumption and tobacco use, and maintaining diet quality and physical activity (Yusuf, Joseph et al. 2020).

2.2.4.3 Revascularization

The two available strategies for coronary revascularization are coronary artery bypass grafting (CABG) surgery and PCI. A variety of studies have demonstrated the advantageous effects of these revascularization methods in offering survival benefits and reducing the risk of death over medical therapy alone (Keeley, Boura et al. 2003, Windecker, Stortecky et al. 2014). These details are discussed in the next sections.

2.2.5 Revascularization strategies for coronary heart disease

The two most common coronary revascularization procedures, CABG and PCI, are conducted with the aim to improve the prognosis or symptoms and quality of life in patients with CHD. The revascularization process comprises two steps: 1) indication and selection type of the revascularization procedures, and 2) performance of the

selected procedure. The role of the clinical cardiologist in doing the first step is fundamental. The decisions on the type of revascularization technique are made based on the patient's clinical characteristics, functional and anatomical features of coronary arteries (Alonso Martin, Curcio Ruigomez et al. 2005). In general, patients with three vessel disease or left main CHD are recommended for CABG whereas the majority of patients with one or two vessel disease are considered for PCI as the optimal treatment (Daemen and Serruys 2006, Melly, Torregrossa et al. 2018).

2.2.5.1 Coronary artery bypass graft surgery

CABG is defined as "open heart surgery in which a section of a blood vessel is grafted from the aorta to the coronary artery to bypass the blocked section of the coronary artery and improve the blood supply to the heart" (Diodato and Chedrawy 2014). The first CABG surgery using Rosenak (tantalum) rings was performed successfully by Goetz in 1960. After that, with much attention and efforts in improving technique and safety, the invasive evolution of CABG had been seen in many parts of the world (Melly, Torregrossa et al. 2018). In modern cardiac-based therapies, CABG is still recognized as the most commonly performed cardiac surgery worldwide with approximately 200,000 single cases performed annually in the US alone (Melly, Torregrossa et al. 2018, Squiers and Mack 2018) .

CABG has been studied extensively and compared with medical therapy in many clinical trials, which have typically shown advantage of CABG in improving patient prognosis and preventing fatal events. When PCI was performed successfully and introduced widely in humans, the use of CABG had lost its previous priority in cardiac-based therapies (Diodato and Chedrawy 2014). There have been continuous debates in

choosing the optimal procedure between PCI, with or without stenting, with CABG (Spadaccio and Benedetto 2018). In 2012, the ASCERT trial studied 190,000 patients 65 years or older with two- or three-vessel disease to investigate the effectiveness between the two cardiac revascularization procedures. There were 86,244 patients who underwent CABG and 103,549 patients who received PCI treatment. The median follow-up period was 2.67 years. The finding revealed that there was no significant difference in mortality between the groups (6.24% CABG versus 6.55% PCI; risk ratio, 0.95; 95% confidence interval, 0.90 to 1.00) at 1 year. However, at 4 years follow-up, the rate of mortality in patients with CABG was lower than those with PCI (16.4% versus 20.8%; risk ratio, 0.79; 95% confidence interval, 0.76 to 0.82) (Weintraub, Grau-Sepulveda et al. 2012). In one systematic review in 2013, including 13 randomized clinical trials and 5 meta-analyses, CABG surgery was recommended for patients with complex coronary lesions such as unprotected left main disease, multi-vessel CAD and left main disease; or patients with severe morbidities such as diabetes. Patients with less complicated coronary disease or having high surgical risk were recommended to receive PCI (Deb, Wijeysundera et al. 2013). Similar findings were also found in recent reviews and meta-analyses (Palmerini, Serruys et al. 2017, Spadaccio and Benedetto 2018).

In summary, CABG is an effective cardiac revascularization procedure. It is comparable with PCI in term of patient's outcomes and more preferable in complex coronary disease patients.

2.3 Percutaneous coronary intervention

2.3.1 Definitions/ principles of the procedure

PCI, also called percutaneous transluminal coronary angioplasty (PTCA), is defined as a minimally invasive procedure to open blocked or stenosed coronary arteries allowing the normal flow of blood to the myocardium. Percutaneous means through the skin, coronary refers to the vessel name targeted, and intervention or angioplasty refers to the intervention technique used to widen the narrowed coronary arteries (Figure 2.3) (Landau, Lange et al. 1994, Malik and Tivakaran 2020). The indications of PCI depend on the level of occlusion of the coronary artery. If there is 100% occlusion of the coronary artery (STEMI), patients will be given emergency PTCA immediately to prevent further damage of myocardial muscle. If the presentations are categorized as non-STEMI or unstable angina, patients will undergo PCI within 24 to 48 hours. PCI is also beneficial for those with stable angina who are unresponsive to optimal medical therapy with the aim of relieving the persistent angina symptoms (Malik and Tivakaran 2020).

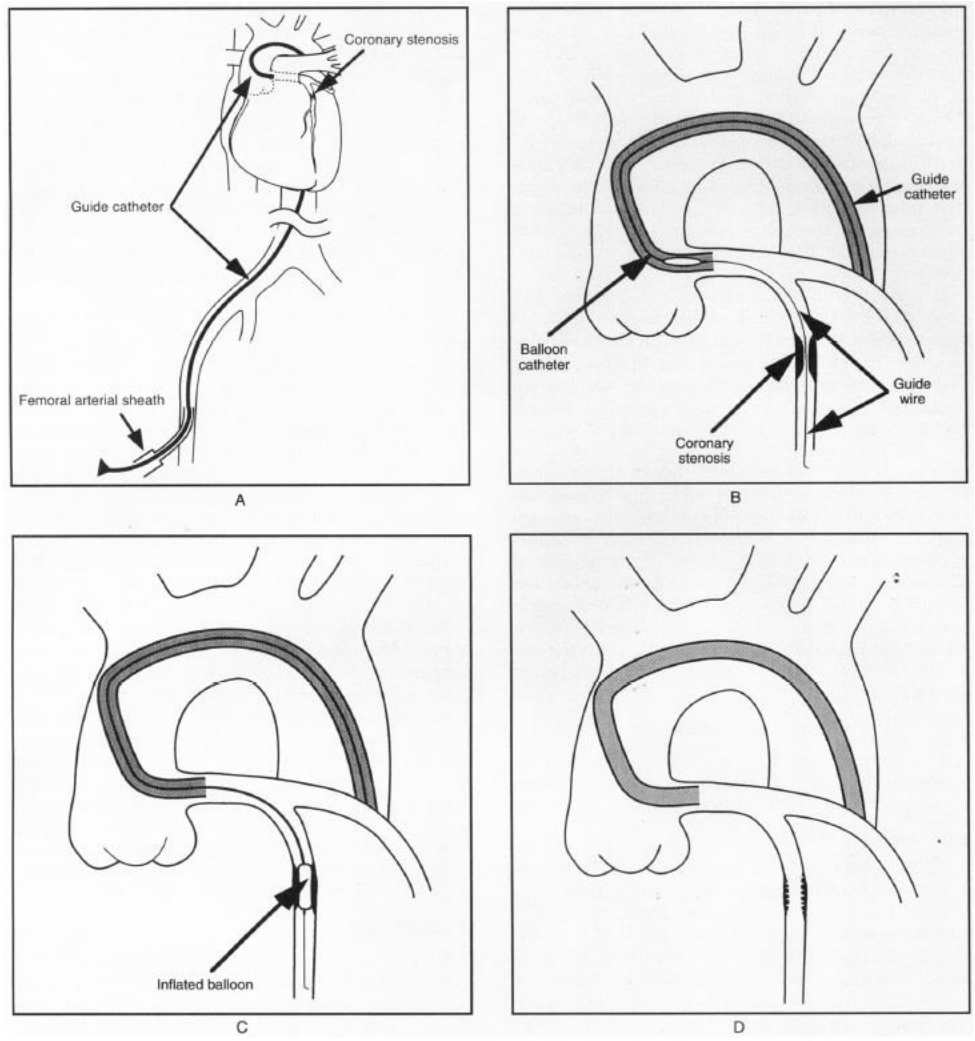

Figure 2-2 Percutaneous coronary intervention

A: Introduction of the guide catheter through a femoral arterial sheath forward the diseased coronary artery

B: The guide wire is advanced into the diseased artery and the stenosis

C: The balloon is inflated at the position adjacent to the stenosis

D: Final angiogram after the guide wire and balloon remove

Produced by Landau, C., et al. (Landau, Lange et al. 1994)

The performance of PCI procedure should be undertaken by a skilled team including an interventional cardiologist, a radiology technologist performing PTCA and a nurse.

Sufficient equipment is essential for ensuring the success of these procedures, which normally are large-lumen guide catheter, a flexible guide wire, and a balloon catheter (Landau, Lange et al. 1994).

When the patient is anesthetized under local anaesthesia, a needle is inserted into the vascular access point, following by the insertion of a guide wire. While removing the needle, a sheath with an introducer is placed over the guide wire and into the artery. After that, the guide wire and introducer are removed while the sheath remains in the vessel lumen. The most common approach is via femoral artery (in the groin) which has been considered as the traditional vascular access point. The radial artery (in the wrist) and the brachial artery (in the elbow) have recently been added as alternative access routes for PCI procedures. From these vascular access points, the guiding catheter is advanced to the ostium of the targeted coronary artery (right or left coronary artery).

Then, a long narrow tube, known as the "diagnostic catheter" containing a manifold with a syringe follows the guide wire and is passed retrograde through the femoral artery, iliac artery, descending aorta, over the aortic arch to the proximal ascending aorta. A contrast material (dye) is injected through the manifold, allowing the checking of inter-arterial pressure and administering medications. In the meantime, an x-ray machine allows the operators to visualize the spread of the contrast material through the coronary arteries system via a screen monitor. Angiography of the diseased artery is performed to determine the location of the diseased segment. If there are severe stenosis existing inside the coronary arteries, PTCA can then be conducted. The diagnostic catheter is removed in this step, and a similar guide catheter is used instead.

When the guide catheter is placed in the diseased artery, a PTCA guide wire is advanced via the catheter and across the stenosis in the artery. Once the PTCA guide wire is passed across the stenosis, it is left there while a balloon wire can be advanced over the PTCA guide wire until the balloon is directly over the stenosis. Under controlled pressure, the balloon is inflated and deflated repeatedly to open the culprit coronary lesion. For most PCI, a stent is then put in place to exchange for the balloon wire. A stent acts as a metal scaffold to prevent the reduction in coronary artery diameter. While the balloon is deflated and moved out, the stent remains inside the diseased segment. The injection of contrast media can be used to visualise and confirm the patency of the coronary artery. The whole procedure can last from 30 minutes to 3 hours depending on the particular cases (Landau, Lange et al. 1994, Meier, Bachmann et al. 2003, Malik and Tivakaran 2020).

2.3.2 History of percutaneous coronary intervention

The first fundamental step in the evolution of PCI was coronary angiography performed by Mason Sones in 1957. Andreas Gruentzig and Myler performed the first percutaneous balloon coronary intervention during a CABG procedure in May 1977 (Gruntzig 1978, Mueller and Sanborn 1995, Iqbal, Gunn et al. 2013). Four months later, Andreas Gruentzig successfully completed the first coronary angioplasty as an alternative for CABG in an awake patient in Switzerland, marking a significant revolutionary step in the development of PCI (Newsome, Kutcher et al. 2008, Iqbal, Gunn et al. 2013). In the description of the first five patients with severe stenotic coronary artery lesions, percutaneous coronary angioplasties were recorded as a non-surgical method for revascularization of coronary arteries. Among the first 50 patients, balloon PCI was implemented in 32 patients and 29 patients showed improvement in

cardiovascular function at medical follow-ups. Five patients required an emergency CABG, and 3 patients showed evidence of MI based on the electrocardiogram (Gruntzig, Senning et al. 1979).

After this initial achievement, early studies reported that the new technique of balloon angioplasty could decrease the severity of ischemic symptoms and improve the ischemic manifestation in CHD patients (Bentivoglio 1985, Hoffmeister, Gruntzig et al. 1986, Zijlstra, den Boer et al. 1988). The first report from a PCI registry of the National Heart, Lung and Blood Institute collected data from 34 centres performing coronary angioplasty in the United States and Europe since September 1977. Among 631 patients (mean age was 51 years, range from 23 to 76 years), 80% had single vessel coronary disease and 17% had two or three vessel disease. PTCA was well performed (over 20% of coronary stenosis reduction) in 59% of the diseased coronary arteries (the mean reduction in stenosis was from 83% to 31%), and in 6%, emergency coronary bypass surgery was required. 4% of patients had MI. Among 65 patients treated with, 83% were reported to have improved ischemic symptoms compared to before the procedure (Kent, Bentivoglio et al. 1982). The success rate of PTCA increased over decades, and was reported to be up to approximately 90% from early of 21th century (Bentivoglio 1985, Newsome, Kutcher et al. 2008).

Despite the positive results, two major drawbacks were identified following PTCA, namely acute vessel closure and restenosis (Grech 2003, Newsome, Kutcher et al. 2008, Iqbal, Gunn et al. 2013). Acute vessel closure can happen very soon after the procedure, and 6-8% of cases were found to have this complication within the first 24 hours due to dissection or elastic recoil. Immediate elastic recoil (minutes-hours) often

leads to a rebound artery occlusion, triggering other severe complications such as AMI and may require emergency CABG. Restenosis often occurs within the first six months among 30% of cases due to the development of neo-intimal proliferation in the artery and this process can involve many mechanical, biochemical and histological factors following PCI with a balloon (Holmes, Holubkov et al. 1988, Narins, Holmes et al. 1998, Newsome, Kutcher et al. 2008, Iqbal, Gunn et al. 2013).

In summary, the introduction of balloon angioplasty performed by Andreas Gruentzig in 1977 marked an important milestone in the development of cardiac-based treatments. While the initial success of balloon angioplasty was well acknowledged, the incidence of artery occlusion and occurrence of re-stenosis after procedures remained the main challenges for researchers, clinicians and scientists. Other efforts were put to find alternative ways to maintain the initial achievement and reduce procedural complications.

2.3.3 The evolution of percutaneous coronary intervention

In an effort to combat the shortcomings of balloon angioplasty, the use of synthetic devices was considered to maintain the lumen patency of the diseased artery. Pioneering work to implant the first coronary stent in a human was performed by Sigwart et al in 1986 (Sigwart, Puel et al. 1987). This stent was described as the first self-expanding bare-mental stent (BMS) following balloon angioplasty, and it was approved in the United States for coronary patients who had high risk of acute vessel closure after failed PTCA (Ruygrok and Serruys 1996, Sousa, Serruys et al. 2003). The advances of this new technology in reducing early elastic recoil and could be considered as an alternative way to avoid emergency CABG after failed PTCA were

confirmed in subsequent studies (Newsome, Kutcher et al. 2008). In two landmark trials conducted in 1993, the STRESS and the BENESTENT trials indicated that BMS implantations were superior to balloon angioplasty alone. Restenosis rates reduced from 42% to 32% ($p = 0.04$) in the STRESS trial, and from 32% to 22% ($p = 0.02$) in the BENESTENT trial. The prevalence of target vessel revascularization went down from 25% -35% in the balloon angioplasty alone group to 10-15% with stenting group in the STRESS trial (Fischman, Leon et al. 1994, Serruys, de Jaegere et al. 1994). These results promoted BMS implantation to be the accepted standard of care and by 1999, approximately 85% of all PTCA involved stent implantation (Newsome, Kutcher et al. 2008).

Despite these advances and encouraging success, follow-up studies found that the BMS insertion only reduced but did not eliminate in-stent restenosis. Re-stenosis was still persistent at the rate of 20-30% in medium and long-term follow-up studies (Newsome, Kutcher et al. 2008, Canfield and Totary-Jain 2018). The reason was attributed to the combination of proliferation and migration of vascular smooth muscle cells inside the stents. The other challenge in the early application of BMS was the early occurrence of stent thrombosis, which might lead to dangerous complications such as STEMI in 90% and mortality in 20% of cases. Clinical trials of BMS reported the prevalence of stent thrombosis varied from 16-24% in the first 30-days after stent implantation (Newsome, Kutcher et al. 2008).

In attempts to enhance the safety of BMS stenting, the techniques of stent deployment were much improved and the use of anticoagulation was replaced with dual-antiplatelet therapy in optimal medical therapy following PCI. Initially,

anticoagulation was used together with aspirin as the main therapeutic modality for the reduction of early thrombotic events. Further studies confirmed the superior combination of aspirin with a thienopyridine in comparison with uses of anticoagulation and aspirin, which promoted a new cornerstone of antithrombotic prophylaxis (Newsome, Kutcher et al. 2008). Among current thienopyridine, clopidogrel showed advances in safety profiles including lower incidences of skin rash, neutropenia, and thrombotic thrombocytopenic purpura. Then the dual antiplatelet therapy including aspirin and clopidogrel become the medical standard therapy to reduce the incidence of early thrombotic events. Advances in stenting deployment techniques and dual antiplatelet therapies have reduced the incidence of stent thrombosis to the rate of 1.2% (Wenaweser, Rey et al. 2005).

Another revolution in interventional cardiology was the development of drug-eluting stent (DES) in an attempt to inhibit the restenosis process. DES had been developed by coating the surface of BMS with a layer of polymer containing anti-proliferative material which has the advantage to eliminate the neo-intimal proliferation, which reduced the restenosis incidence and the requirement for reintervention (Newsome, Kutcher et al. 2008). This manufactured structure of DES allows the release of drug directly at the diseased lesions, which maximizes the effect of drug in preventing local intimal proliferation after the procedure. Initially, the first generation of DES was coated with either sirolimus or paclitaxel, two agents were found to effectively inhibit the migration of vascular smooth cell and proliferation by various mechanisms. The superior advances in reducing restenosis of new DES compared with BMS at 6-12 months were confirmed by several randomized controlled trials with careful patient recruitment (Moses, Leon et al. 2003, Stone, Ellis et al. 2004). At initial follow-ups,

both types of DES were shown to continually ensure the clinical safety and efficacy in preventing restenosis at 74% reduction after initial deployment (Sousa, Costa et al. 2003, Grube and Buellesfeld 2004). These advanced findings led to the approval of public use of DES in Europe in 2002. In the United States, the Food and Drug Administration gave the approval for sirolimus-eluting stents use in 2003 while paclitaxel-eluting stents were approved in 2004. In 2005, approximately 85% of implanted stents in the United States and Europe were DES (Newsome, Kutcher et al. 2008). However, later clinical registries reported the increasing risk of MI and mortality due to late thrombosis in patients implanted with DES, mostly with those who discontinued dual anti-platelet therapy (Stone, Moses et al. 2007).

To enhance the safety of the first DES generation with regard to incidence of thrombosis, second-generation DES with durable polymers were invented. The platform was improved with material of cobalt-chromium or platinum-chromium, making it thinner than the predecessors. The newer derivatives of sirolimus, namely everolimus and zotarolimus, were used with the aim of improving lipophilicity and cellular uptake (Canfield and Totary-Jain 2018). The advances of second-generation DES were reducing thrombosis and target lesion revascularization rates, confirmed in large randomized controlled trials with thousands of participants (Toyota, Shiomi et al. 2015, Jensen, Thayssen et al. 2016).

The third-generation DES with biodegradable polymers was designed to ensure the proper time of drug release and avoid the hypersensitivity reaction to the durable polymer as well as improve the stent integrity and healing of the arteries. Similar safety and efficacy outcomes were shown in reliable studies for these biodegradable polymer-

based DES and they received the food and drug administration approval for use in 2015 (Canfield and Totary-Jain 2018).

2.3.4 Current status of percutaneous coronary intervention worldwide

PCI is well known as a major cardiac procedure with increasing volume annually worldwide. In the United States, it was estimated approximately 520,000 procedures were performed and the PCIs rate per 10,000 population was 16.4 in 2013 (Stuntz and Palak 2016). In the United Kingdom, the national British Cardiovascular Intervention Society registry reported, for the period from 2007 to 2013, 427,500 PCIs were performed in 93 hospitals in England and Wales. The centre annual volume increased from a mean of 889 to 917 in that period (O'Neill, Nicholas et al. 2017). In Australia, the number of patients undergoing PCI has also been increasing over time, especially since the 1980s. It was estimated that annual rate was increased around 21% between 1995 and 1996 in the whole country. After that, the growth of PCI had slowed in 1999-2000 (annual rate was 12% increase). In 2000, there were 21,784 PCI procedures performed in Australia (Australian Institute of Health & Welfare 2003). Data from the Melbourne Interventional Group registry reported that the total procedures in one multi-centre registry was 2083 in 2005, it reached a total of 2263 procedures in 2013 (Yeoh, Yudi et al. 2017). Similar patterns were seen in Asia, the continent containing around 60% of the world's population. According to the China Patient-Centered Evaluative Assessment of Cardiac Events–Retrospective Study of Coronary Catheterization and Percutaneous Coronary Intervention (China PEACE-Retrospective Cath PCI Study) which included 55 urban hospitals performing PCI, the use of PCI increased 21-fold from 2001 to 2011. Particularly, there were approximately 209,000 procedures reported in 2011 (Zheng, Curtis et al. 2016). In

South Korea, data from the National Health Insurance revealed that PCI became more prevalent over time. There was 8% increase in total PCIs performed from 2011 to 2015 (Han, Park et al. 2018). Among LMICs, published reports revealed that the prevalence of PCI procedures in routine cardiovascular practices is increasing over time. For instance, the number of patients undergoing PCI in the period of 2015-2016 according to Malaysian national PCI registry was 19,494, an increase of over 5,000 patients compared with the period of 2013-2014 (National Cardiovascular Disease Database 2016). Similarly, reports from the Indian National Interventional Council revealed that the increasing of PCI practice is steady over time. In 2013, there were approximately 22,000 PCIs performed, while the corresponding number reached nearly 40,000 in 2017 in the nation (Arramraju, Koganti et al. 2019).

The implantation of stents in PCI is designed to maximise the normal diameter of coronary arteries after the procedure. Despite the popularity of PCI worldwide, the stent selection strategy between BMS and DES varies significantly across regions and countries, probably due to the variation in international and regional guidelines (Amin, Spertus et al. 2012, Iqbal, Gunn et al. 2013). For example, some cardiovascular interventionists agree that all patients should receive DES in PCI procedures, others accept the idea that shorter lesion (≤15mm) in relatively big vessels (≥3mm diameter) in patients with no diabetes can receive BMS implantation. Diabetic patients having diseased lesions longer than 15 mm and in less than 3mm diameter vessels should be treated with DES (Messori and Trippoli 2009). Due to the need of DAPT following the procedure with DES, BMS would be recommended for patients who are contraindicated with DAPT (Pfisterer, Brunner-La Rocca et al. 2009). While DES is currently preferred in numerous Asian countries such as China, South Korea and India,

the mixed picture of the relative use of DES and BMS have been seen in many other parts of the world as Australia, the United States and the United Kingdom (Amin, House et al. 2013, Zheng, Curtis et al. 2016, O'Neill, Nicholas et al. 2017, Yeoh, Yudi et al. 2017, Han, Park et al. 2018, Arramraju, Koganti et al. 2019).

Medical therapy support after PCI procedures is important to prevent the risk of stent thrombosis, especially with the intake of DAPT. However, there remains controversy in the duration and choice of anti-platelet agents in current practice. Normally, the cardiovascular interventionist will decide the use of anti-platelet based on the clinical presentation of patients, the choice of stent and local/regional policies (Iqbal, Gunn et al. 2013). It is recommended that PCI patients with ACS and those implanting with DES should receive longer duration of DAPT. The current European Society of Cardiology (ESC) recommends 6-12 months of DAPT for DES use. However, based on data suggesting low risk of stent thrombosis with some types of DES such as Xience-V and Xience-Prime, 3 months intake of DAPT was approved in Europe (Palmerini, Biondi-Zoccai et al. 2012). Among anti-platelet agents, clopidogrel remains the most commonly used as a pro-drug, but number of patients were reported to have poor responses and clopidogrel resistance. The newer agents, namely prasugrel and ticagrelor have been developed recently to overcome the drawback of the former (Storey 2011). It was shown that prasugrel had significantly reduced ischemic event rates such as stent thrombosis, especially in ACS patients treated with scheduled PCI. However, people are still concerned about the risk of bleeding and effects of prasugrel with mortality (Wiviott, Braunwald et al. 2007). Ticagrelor, an active drug, can rapidly reach the sufficient levels of platelet inhibition after intestinal absorption and has been proved to reduce the mortality risk of ACS patients compared with clopidogrel

(Wallentin, Becker et al. 2009). In the APAC region, the figures of anti-platelet use are diverse. While Korean cardiac interventionists mostly prefer clopidogrel than other agents (Han, Park et al. 2018), their colleagues in Malaysia have increased the use of ticagrelor to 20% in recent years (National Cardiovascular Disease Database 2016). Australian interventionists probably are the ones who prefer mixing both these traditional and new agents with approximately 60% of patients received clopidogrel and 30% treated with ticagrelor (Yeoh, Yudi et al. 2017)

2.3.5 The burden of coronary heart disease, increase of risk factors and current status of percutaneous coronary intervention in Vietnam

As a nation undergoing rapid economic and epidemiological transition, Vietnam has experienced an increasing burden of CHD over the years. While CHD was attributed to 36,533 deaths, equivalent to 7.8% of all-causes mortality in 2014, this disease brought about 67,500 deaths, accounting for 13.2% of Vietnamese total deaths in 2018 (World Health Rankings 2017). There are a number of possible explanations for this dramatic increase in CHD rate, including an increase in rates of cardiovascular risk factors, higher life expectancy and the aging population in Vietnam.

The well-known risk factors for CVDs include hypertension, diabetes, hypercholesterolemia, cigarette smoking, and overweight and obesity (Lim, Vos et al. 2012). In recent years, the prevalence of these factors was shown to be significantly increased in the Vietnamese general population. According to nationally representative data in the National Adult Overweight Survey, the prevalence of hypertension in Vietnam was 20.7% in 2005 (Do, Geleijnse et al. 2015). It was

estimated that the prevalence of hypertension increased by around 0.9% per year in the period of 2001 to 2009 (Nguyen, Pham et al. 2012). A recent systematic review revealed the pooled prevalence of measured hypertension was 21.1% in 2019 based on 10 studies in the country (Meiqari, Essink et al. 2019). The same pattern was seen for diabetes. In 2012, it was reported that 5.4% of Vietnamese adult were diagnosed with diabetes, this figure was increased to 6.0% in a literature review in 2017 (Khue 2015, Ngoc, Lin et al. 2020). Vietnam has a high prevalence of cigarette smoking in men for many years. In 2014, a study recruited more than 14,500 participants reported that 74.9% men and 2.6% women were ever-smokers in Vietnam (Bui, Blizzard et al. 2015), while the Global Adult Tobacco Survey 2015 showed 45.3% men and 1.1% women were current smokers. The reduction in tobacco smoking in Vietnam during the period 2010-2015 was not as high as expected, especially in rural areas (Van Minh, Giang et al. 2017). In addition, due to the change of diet intake, the rates of overweight and obesity in Vietnamese adults aged 25–74 years were reported as 28.6% and 2.1%, respectively (using the Asian-specific body mass index cut-offs i.e. ≥23 kg/m^2 and ≥25 kg/m^2) in 2015. It was estimated that the body mass index rate increased 1.9 times during the period from 2000 to 2015 (Ngoc, Lin et al. 2020). While data regarding hypercholesterolemia have been limited in Vietnam, one study on cardiovascular disease risk factors including 2,306 participants in 2009 revealed that the prevalence of dyslipidaemia was relatively high in all age groups. For instance, 33.4% of women and 54.8% of men aged 25-34-years in this study were confirmed with dyslipidaemia and the rates were worse in the older age group, with 66.5% women and 63.9% men aged ≥75 years (Nguyen, Pham et al. 2012).

Furthermore, the Vietnamese population has witnessed an increase in life expectancy in recent decades largely due to achievements in economic and health care system developments. It was estimated that in 2008, the life expectancy at birth was 69.7 and 77.7 years in males and females, respectively (Harper 2011). In 2018, the predicted years of life for Vietnamese people were 71.7 and 80.9 years for males and females, respectively (World Health Rankings 2018). Paralleling with increasing life expectancy in the country, Vietnam has also experienced with the aging population. According to the Ministry of Health, the proportion of people aged 60 years and older grew from 8% to 10% in the period of 1999 to 2012 (Vietnam Ministry of Health and Health Partnership Group 2015). At present, 12.3% of the total population is aged 60 years and over in Vietnam (HelpAge network in Asia Pacific 2020). The prevalence of elderly people in society often results in greater demand for specific health services, including the special care for chronic diseases such as CHDs.

PCI was adopted for the first time in Vietnam in 1995 in 108 Military Central Hospital and has been introduced widely to approximately 70 cardiac centres nationwide at present. The use of PCI in Vietnam has become more popular and is increasing. It was reported that over 2,250 patients received this technique in 2013 in a single national centre alone and there is a 15% increase annually (Vietnam National Heart Institue 2017). Despite the popular use of PCI in Vietnam, understanding the patient profiles, clinical practices and post procedural outcomes remains limited. To date, there is no PCI registry in the country and information of these procedures is not collected by a systematic database in clinical quality registries as is the case in other LMICs.

2.4 The health care system and the health insurance in Vietnam

2.4.1 Health care system

The health care system (HCS) was originally established in the Northern part of Vietnam after the independent declaration in 1945 and subsequently extended to the South when the country reunited in 1975. At first, the HCS was fully organized and funded by the government, in which all heath care services were free from central to grassroot levels despite the low gross national product per capita and limited resources of the country. The economic reform occurring from the late 1980s has impacted significantly on all aspects of society, including the HCS from a fully supplied by government into a mixed public-private provider system since 1989. This reform resulted in the introduction of health service fees and the legalization of private health sector as well as drug markets (Ladinsky, Nguyen et al. 2000, Le 2010). Additionally, health insurance was developed in 1992 and provided financial protection in access to health care services as well as financial resource for HCS (Tran 2011).

The current HCS in Vietnam is structurally divided into four administrative levels: central, provincial, district and commune (Figure 2.4) (Vietnam Ministry of Health and Health Partnership Group 2008, Le 2010, Tran 2011). At each level, Vietnamese people are provided with four services, namely curative care, primary health care, family planning and preventive medicine (Ministry of Health and Health Partnership Group 2010, Harper 2011). Although health services are provided by the combination of public and private systems, the public sector plays a substantial part in providing the available medical services and the private system is mostly active in the curative area with a focus on outpatient care (Harper 2011). Under government sectors, up to 2018, there were 295,800 patient beds in the nation and the number of patient beds per

10,000 inhabitants (excluding beds in health centre in communes, wards, offices, and enterprises) was 28. The number of doctors nationwide was 84,800 in 2018, increasing by 14% in comparison with that of 2017 (General Statistics Office 2019). It was estimated that 8.6 doctors are available per 10,000 inhabitants. In 2017, there were around 1,100 public hospitals in Vietnam, in which 47 are at the central level, 419 at the provincial level and 684 at the district level. Besides that, the private sector also provides 182 private hospitals located mostly in urban areas (World Health Organization 2020). At the commune level, 99% of more than 1,000 communes have a Commune Health Station and 66% of these have a general physician (Harper 2011).

Despite the high number of patient beds per inhabitant in the country, the Vietnam's HCS still faces the problem of exceeding the recommended threshold occupation rate of the World Health Organization (Gaskill and Nguyen 2015). Almost all public hospitals in Vietnam currently suffer from very high occupancy rates, especially in national level hospitals in big cities. The reason for this is the out-dated equipment and the limited quality of medical staff at lower level hospitals, resulting in the willingness of Vietnamese patients to travel long distance (over 50km) and face overcrowding at national level hospitals (Nguyen, Yamamoto et al. 2018). Some reputable national hospitals reported extremely high occupancy rates, such as K Hospital with 250%; Cho Ray Hospital with 139%; and Bach Mai Hospital with 168% (Gaskill and Nguyen 2015). This over workload in high level hospitals results in unexpected low quality of treatment provided for patients in these hospitals (Nguyen, Yamamoto et al. 2018). Furthermore, it has taken more time to provide full treatment for Vietnamese patients than that in other countries in the Asian region. For instance, the average number of hospital stay was 7.0 days in Vietnam in 2009 compared to 6.5 days and 4.7 days,

respectively, in Thailand and Singapore during the same period. The outdated medical equipment and limited access to the newest drug agents are raised as the main constraint in improving quality of care in Vietnam (Gaskill and Nguyen 2015).

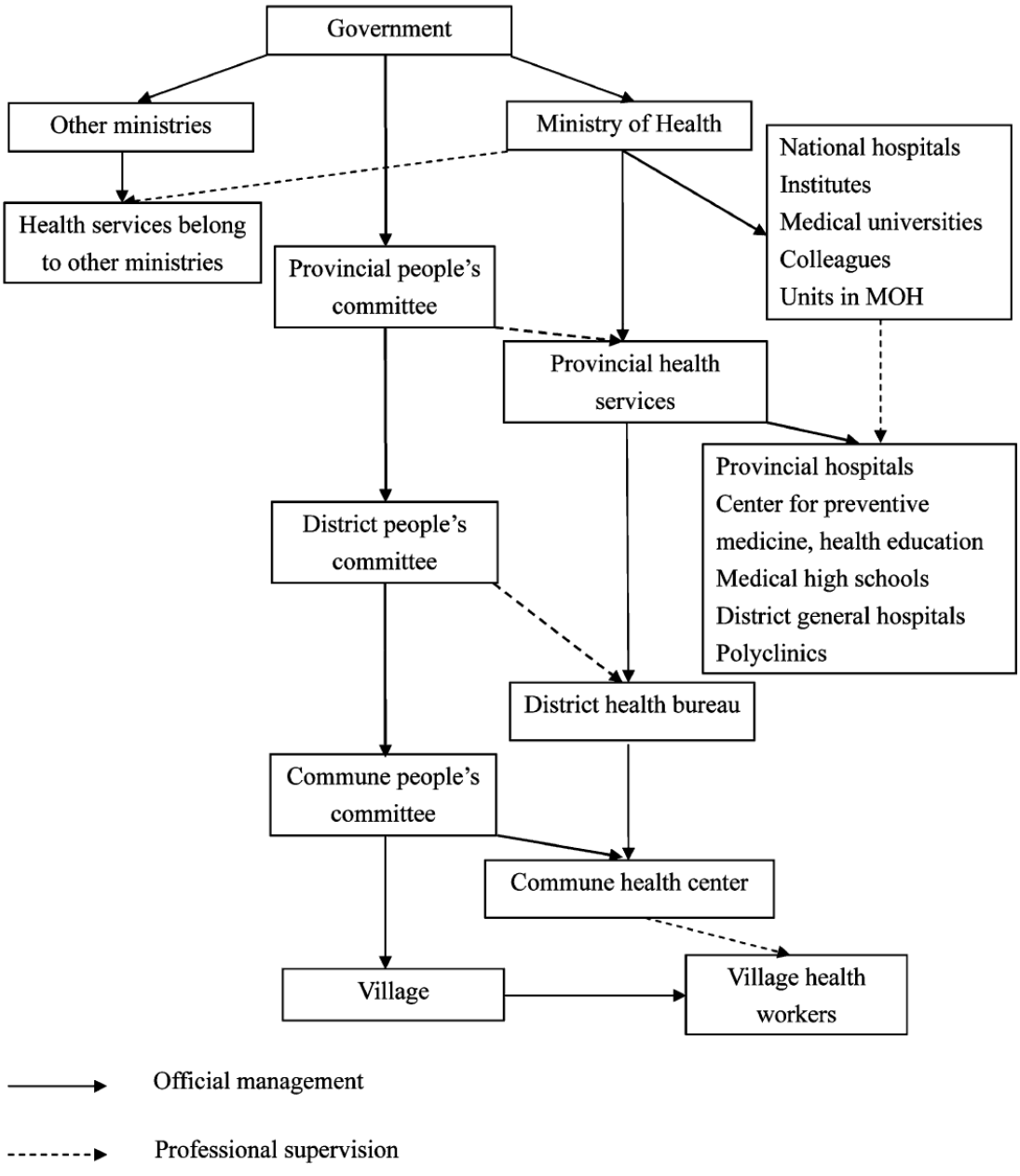

Figure 2-3 Vietnam public health system

(adopted from Le, D.C., (Le 2010))

2.4.2 Health insurance

In order to improve quality of health, universal health coverage defined as ensuring that all people have access to effective health care services with an affordable cost has been the major goal for health reform in many countries in the world. While health financing system was established in many countries with the aim to move towards universal coverage, it is still a challenge for LMICs due to the lack of funding for health care services (Tran 2011, Thi Thuy Nga, FitzGerald et al. 2018). As a L-MIC, Vietnam spent 5.5 % of GDP on health and health spending per capita was 129.6 USD in 2017. The Vietnamese government is clearly committed to universal coverage of health by implementing a variety of policies, including the introduction of social health insurance (HI) in 1992. (Statista 2018).

A number of attempts to amend policies and legislation have been put in place to revise the HI law. Over the past 25 years, Vietnam has made significant progress in achieving the goal of HI universal coverage by expanding HI coverage to about 80% of the population in 2016 with an average increase of 4.3% each year (Thi Thuy Nga, FitzGerald et al. 2018). Furthermore, HI has made an increasing contribution to public financing in recent years with the increasing contribution rising from 27% to 35% in the total health financing source in Vietnam in the period from 2010 to 2015 (Vietnam Ministry of Health & Health Partnership Group 2016). The current HI schemes divide issued members into 25 different membership categories and benefit packages. Depending on the categorized groups, the premium for insured members varies from 0 to 4.5% of the minimum salary which is equivalent to 720,000 VND (32.7 USD) per person per year in 2016 (Vietnam Government 2008, Tran 2011). Most insured members are required to contribute the out-of-pocket (OOP) expenses for accessed

medical services with the exception of some particular groups such as high-ranking police officers; meritorious people (persons awarded for revolutionary merit); the poor and minority ethnic groups; and children under six years of age. Other groups have to contribute the co-payment varying from 5% to 20% of total medical expenses if they are referred patients. If these insured members bypass lower referral facilities, higher co-payment rates are required, which is 30% at district hospitals, 50% at provincial levels and 70% at central and tertiary hospitals (Tran 2011, Vietnam Government 2014). Recent data revealed that OOP payments for health remained high at 48.8% in total of health financing resource in 2012 and appeared to be increasing in the nation (Vietnam Ministry of Health & Health Partnership Group 2016).

With the regulation of current HI, OOP expenditure still leaves patients with financial risk, especially with high medical-care costs. While there is no limitation for co-payment, the maximum benefit supporting the use of costly and high technological services is up to 40 months of the minimum monthly salary per treatment visit, which is equivalent to 48.4 million VND (2.200 USD) per hospital admission (Tran 2011, Vietnam Government 2014). Furthermore, due to the frequent shortages of some essential drugs in hospitals, patients have to buy drugs in private pharmacies. This expenditure is not reimbursed regardless of whether or not patients are insured (Tran 2011). The average monthly wage in Vietnam is 5,080 VND Thousand (230.9 USD) in 2017 (Trading Economics 2017). This situation can drive the poor with serious illnesses to experience financial destitution and expand the gap between different social groups in receiving medical resources in favour of the rich. As spending on medical care can account for a very high proportion of family income, specifically in families with severely ill members, there is a significant probability of quitting

treatment or using traditional medicines with unknown success among poor patients (Vuong, Flessa et al. 2014, Vuong 2015).

2.5 Clinical outcomes of patients post percutaneous coronary intervention

Clinical outcomes of patients are typically a key focus of interventionists and cardiologists after the completion of PCIs. Many well-known PCI registries suggested positive outcomes post procedures of PCI patients at different time frames, including discharge, 30 days and longer follow-ups. In a recent report which included 8,687,338 PCIs in the United States from 2003 to 2016, data revealed that although there were significant increase in the proportions of risk factors and the percentage of PCI for MI group (22.8% to 53.1%), risk-adjusted mortality rates just increased slightly after PCI procedures (in STEMI group: 4.9 to 5.3%, $p<0.001$; in UA or stable angina: 0.8 to 1.0%, $p<0.001$, but not in NSTEMI group: 1.6 to 1.6%, $p=0.18$) (Alkhouli, Alqahtani et al. 2020). Data retrieved from the multi-centre Melbourne Interventional Group registry, which included 19,858 procedures in the period of 2005-2013 in Australia, reported relatively low rates of poor cardiac outcomes at discharge, 30 days and 12 months respectively (mortality: 2.3%; 2.4%; 4.4%; MI: 1.1%; 1.9%; 4.5%; major adverse cardiovascular event: 2.2% at 30 days and 13.3% at 12 months). The average length of hospital stay increased from 3.5 days to 4.2 days in the period (Yeoh, Yudi et al. 2017). Similar patterns were seen in the report of the Malaysian National Cardiovascular Database for Percutaneous Coronary Intervention Registry year 2015-2016. Overall mortality was 2.0%; 2.8% and 6.8% at discharge, 30 days and 1 year respectively. The mean length of hospital stay was 4.3 days and 5.4 days in groups of

patients with heart rate at presentation <90 and >90 beats/minute (National Cardiovascular Disease Database 2016).

Importantly, outcomes post procedures differ significantly according to demographic factors or modifiable risk factors of the PCI patients. To date, demographic factors such as age and sex of coronary patients were reported to be associated with post PCI outcomes. Studies regarding the sex differences in outcomes following PCIs have revealed that male patients have better prognosis after procedures than their female counterparts. For instance, male patients had significantly lower rates of mortality than those of females at discharge (OR 0.58, 95% CI 0.52–0.63, $p<.001$), 30-day (OR 0.64, 95% CI 0.61–0.66, $p=.04$), 1-year (OR 0.67, 95% CI 0.60–0.75, $p<.001$), and at least 2-years follow-ups (OR 0.71, 95% CI 0.63–0.79, $p=.005$) (Guo, Yin et al. 2018). The major adverse cardiac event (MACE) rate was significantly lower in male patients after initial PCI compared with females in <1-year or at least 1-year (OR 0.67, 95% CI 0.56–0.80, $P<.001$ and OR 0.84, 95% CI 0.76–0.93, $P<.001$) (Guo, Yin et al. 2018). Furthermore, older patients experience worse coronary artery- related outcomes compared to their younger counterparts, which was confirmed in a variety of studies (Topaz, Finkelstein et al. 2017, Numasawa, Inohara et al. 2019). Modifiable cardiovascular risk factors are well-known in accelerating CHD events, while their impact on mortality post PCIs of CHD patients have been confirmed in recent studies. A total of 100 studies consisting of 884,190 patients included in one meta-analysis, revealing that certain risk subgroups such as diabetes, hypertensive and metabolic syndrome were associated with higher mortality rates following PCIs. For instance, diabetes was associated with significantly higher short and long-term mortality of patients post PCI (Relative risk, RR 2.11; 95% CI: (1.91–2.33) and 1.85; 95% CI:

(1.66–2.06), respectively); groups of hypertensive and metabolic syndrome patients were also reported with significantly higher long-term mortality RR 1.45; 95% CI: (1.24–1.69) and RR 1.29; 95% CI: (1.11–1.51), respectively (Bundhun, Wu et al. 2015).

Additionally, factors regarding clinical presentation, procedural practices and decision of interventionists and operators in PCI centres have shown considerable impact on outcomes post procedures. The acute MI population, especially the STEMI sub-group, was reported to have worse outcomes than any other groups. These findings were confirmed in a variety of registries across the regions (National Cardiovascular Disease Database 2016, Biswas, Duffy et al. 2018, Han, Park et al. 2018, Alkhouli, Alqahtani et al. 2020). For instance, the overall in-hospital mortality rates reported by the Melbourne Interventional Group in 2005-2016 were 5.8% and 2.3% for STEMI group only and for the whole cohort, respectively. Other worse cardiac outcomes such as MI, major bleeding, stroke, and unplanned CABG surgery were revealed to be higher in STEMI group (Yeoh, Yudi et al. 2017, Biswas, Duffy et al. 2018). Outcomes post PCIs might also be varied due to the type of stents used. A number of systematic reviews and meta-analyses have suggested the advantage of DES in comparison with BMS (Neupane, Khawaja et al. 2019, Piccolo, Bonaa et al. 2019). A study including data of 26,616 patients from 20 randomised trials with a mean of 3.2 years follow-up, DES was proved to reduce the risk of primary outcomes relative to the BMS group (HR 0.84, 95% CI 0.78- 0.90, $p<0.001$) and this lower risk was found to last up to 1 year. Risks of definite stent thrombosis and target-vessel revascularisation were also reported to be lower in DES group. This finding suggested BMS should no longer be considered the gold standard and supported the use of DES in modern PCI practices in

order to ensure the safety outcomes for PCI patients (Piccolo, Bonaa et al. 2019). Further, access sites in PCIs have been documented to be associated with procedure-related outcomes for many years. Among these available data, transradial artery access has been proved to be associated with lower bleeding and vascular complications, especially with ACS patients (Mamas, Ratib et al. 2012, Mason, Shah et al. 2018). A recent meta-analysis including 5,055 patients with STEMI reported favourable outcomes of radial approach in comparison with femoral approach. Radial access was associated with risk reduction of mortality (2.7% vs. 4.7%; OR 0.55. 95% CI 0.40-0.76, $p<0.001$) and major bleeding (1.4% vs. 2.9%, OR 0.51, 95% CI 0.31-0.85, $p=0.01$) in these patients (Karrowni, Vyas et al. 2013).

In patients with chronic coronary diseases, PCI has been well recognized in reducing angina symptoms, which provides better quality of life in these patients (Chacko, J et al. 2020). In comparison with optimal medical therapy, the freedom from angina was significantly improved after PCI (RR, 1.20; 95% CI, 1.06-1.37) (Pursnani, Korley et al. 2012). In patients with ACS presentation, PCI has been proved to significantly prevent MACE in these patients (Chen, Barywani et al. 2018, Chacko, J et al. 2020). In a meta-analysis of 46 randomized controlled trials including 37,757 patients, results reported that in the three unstable scenarios of coronary syndromes, PCI was associated with a significant mortality reduction (RR, 0.84 [95% CI, 0.75-0.93])(Chacko, J et al. 2020).

In comparison with optimal medical therapy, outcomes post PCI were comparable with stable coronary artery disease (Pursnani, Korley et al. 2012, Khan, Singh et al. 2019), but superior in more complex coronary artery such as chronic total occlusions (Li,

Wong et al. 2019). In one systematic review and meta-analysis including 11,493 participants with chronic total occlusions, medical therapy was significantly associated with higher risk of all-cause mortality (risk ratio (RR) 1.99, 95% CI 1.38–2.86), cardiac mortality (RR 2.36 (1.97–2.84)), and MACE (RR 1.25 (1.03–1.51)) (Li, Wong et al. 2019). In the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, adding PCI together with optimal medical therapy provided greater ischemia reduction in comparison with patients received optimal medical therapy alone (Shaw, Berman et al. 2008).

To summary, outcomes following PCI of CHD patients are positive with relatively low rates of fatal events and these outcomes are associated with a variety of factors. Understanding the outcomes post PCIs and factors associated with these outcomes is essential for interventionists and operators in enhancing safety and quality of life for CHD patients.

2.6 In-hospital cost of patients undergoing percutaneous coronary intervention

PCI is well-known for its high-cost among cardiovascular based treatments for CHD patients, mainly due to the cost of revascularization procedures and hospital stay. The total PCI cost varies significantly worldwide. In a recent systematic review and meta-analysis, which included 12 randomized controlled trials and 2962 patients revealed that total PCI cost ranged from 3,391 to 10,102 EUR per patient with ordinary discharge, while early discharge (discharge on the same day with the intervention, or 48-72 hours post intervention) consumed from 2,856 to 8,227 Euros for total cost at hospitals (Abdelnoor, Andersen et al. 2017). PCI cost appeared to be most expensive

in the US. According to a retrospective cohort of patients undergoing PCI at 5 hospitals, the adjusted in-hospital cost of patients was 14,954 USD and 15,784 USD based on sub-groups using the radial and femoral access site, respectively (Amin, House et al. 2013). In the context of this current study, it is important to consider the in-hospital costs of PCI patients in Asia, where there is a large population with low income. In a study which recruited 5306 PCI patients in China, the total hospital costs were 9,190 USD and 10,701 USD for radial and femoral approach, respectively in 2013 (Jin, Li et al. 2016). A relatively contrasting picture was seen in LMICs, where the cost of PCI procedures was much lower than that of other regions (but not as a proportion of average income). For instance, the average cost for elective PCI in five cardiac centres in Malaysia ranged from 3,186 to 4,018 USD in 2016 (Lee, Ong et al. 2017).

There are some factors associated with consumables cost for PCI procedures such as access site, length of stay (LOS), and stent used. A variety of previous studies have estimated there to be a cost saving of radial approach in comparison with femoral access site, even though femoral PCI was the traditional approach (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016, Mamas, Tosh et al. 2017). Data from over 320,000 patients undergoing PCI obtained from the British Cardiovascular Intervention Society database in 2010-2014 revealed that radial PCI contributed to the cost-saving of 96.32 GBP per procedure (25% reduction) versus femoral PCI. The underlying reason for this cost-saving came from the reduction of LOS (190.43 GBP) rather than from cost of complications (23.94 GBP) (Mamas, Tosh et al. 2017). Similarly, a US study also found that the cost-saving of radial PCI was related significantly with shorter hospital stay rather than with bleeding (Amin, House et al.

2013). Besides this, a consecutive cohort with over 5,300 participants in China revealed that lower cost in radial approach was mainly driven by lower PCI-related costs, especially in the exclusive use of vascular closure devices in femoral PCI (Jin, Li et al. 2016). The type of stent used was also reported to be associated with PCI cost. A patient level meta-analysis of 5 randomized trials revealed that the second-generation of DES reduced cost of PCI in comparison with the first generation of DES or BMS, partly due to the price of clopidogrel (Ferko, Ferrante et al. 2017). Furthermore, length of hospital stay has been recognized as one of the associating factors of PCI cost. A meta-analysis of 12 randomized controlled trials concluded that early discharge resulted in cost reduction of 5.2-50.1% (294-1875 EUR) per patient compared with ordinary discharge (Abdelnoor, Andersen et al. 2017).

2.7 Percutaneous coronary intervention registries

2.7.1 Definitions, roles and utility of clinical quality registries

Clinical quality registries (CQRs) have been well recognized as an important platform for monitoring disease and healthcare delivery patterns, providing real world evidence and improving clinical outcomes and healthcare services for many decades (Hoque, Kumari et al. 2017, Biswas, Lefkovits et al. 2018, Lee, Chin et al. 2019). Playing an important role in healthcare research, data derived from CQRs facilitates randomized clinical trials, and contribute to cost and time reduction of prospective data collection. Evidence from real world data supports generating research hypotheses, assist descriptive studies and health service studies (Hickey, Grant et al. 2013). CQRs also provide a powerful opportunity for addressing research questions which are difficult to conduct by randomised controlled trials due to ethical or practical reasons.

Examples for these questions might be the natural history of disease, changing practice patterns, and treatment effectiveness in disease groups (French, Reddy et al. 2012).

There has been a growing trend in utilizing CQRs across numerous healthcare aspects such as improving health care processes, adherence to clinical guidelines, and cost reduction in delivering care (Hoque, Kumari et al. 2017). The adoption of CQRs in the area of PCI registries results in national and major regional PCI registries around the world. While the initial growth of CQRs was initially predominantly seen in high income countries, there has been growing interest in adopting large-scale multicentre PCI registries in LMICs (O'Reilly, Cameron et al. 2012). Greater efforts have also been seen in public reporting placed by healthcare stakeholders and funding agencies to evaluate the clinical performance and outcomes post PCI procedures (Wadhera and Bhatt 2017).

2.7.2 Characteristics of percutaneous coronary intervention registries worldwide

According to a recent literature review regarding characteristics of national and major regional PCI registries, the earliest PCI registry was established in 1990 while the majority of them (73%) was established in or after 2000 (Table 1). It was estimated that over 20 million patients undergoing PCI have been included in PCI registries across the world to date (Biswas, Lefkovits et al. 2018).

There is wide variation among the characteristics of PCI registries in the world, including registry governance, data collection, data definitions, and public reporting. For instance, among 30 registries included in the review, 15 registries (50%) are

associated with a government organisation, which results in generally higher chance of study participation in comparison with others with voluntary participants. Twelve registries (40%) collect data on PCI procedures only, while dataset of others also include information of patients undergoing diagnostic coronary angiography only. Most registries (97%) collect the rate of in-hospital mortality and the results range from 0.5% to 2.5% for all PCI and from 2.5% to 6.9% for PCI in STEMI patients.

To facilitate the comparison of patient outcomes post PCI between countries and overcome the huge variation in outcomes measured and definition, a consensus was reached in term of standard definitions and outcome measures, in which the minimum survival should be assessed at 30 days post discharge (Flynn, Barrett et al. 2005, McNamara, Spatz et al. 2015). In the review, nearly half of these registries (47%) collect the rate of mortality at 30 days, while 37% of them collect mortality rates at 12 months post index PCIs (Table 1). More than half (53%) report bleeding outcomes, even though bleeding definitions varied significantly. Public reports about registries data are available in 13 registries at hospital or operator level (43%), and some of them report identifiable mortality data for either an individual hospital or operator (Biswas, Lefkovits et al. 2018).

Table 2-1. Overview of current national and major regional PCI registries worldwide

(produced by Biswas, S., et al.(Biswas, Lefkovits et al. 2018))

PCI registry name	Location	Year commenced	Includes diagnostic coronary angiography data?	Time points for mortality data collection
National registries				
Spanish Cardiac Catheterization and Coronary Intervention registry	Spain	1990	Yes	In-hospital
Austrian National Cathlab Registry (ANCALAR)	Austria	1992	Yes	In-hospital
Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte (ALKK) Registry	Germany	1992	Yes	In-hospital
Quality Oriented Electronic Registration of Medical Implant Devices (QERMID) Belgian PCI Registry	Belgium	1996	No	In-hospital, 30-day
Swedish Coronary Angiography and Angioplasty Registry (SCAAR)	Sweden Iceland	1998	Yes	In-hospital, 30-day, 12-month
National Cardiovascular Data Registry (NCDR) CathPCI	United States of America	1998	Yes	In-hospital
Danish Heart Register	Denmark	2000	Yes	In-hospital, 30-day
Singapore Cardiac Data Bank Cath/PCI module	Singapore	2000	Yes	In-hospital, 30-day, 12-month
British Cardiovascular Intervention Society (BCIS) registry	United Kingdom	2000	No	In-hospital, 30-day, 12-month
Portuguese National Registry of Interventional Cardiology (RNCI)	Portugal	2002	No	In-hospital
Lebanese Interventional Coronary Registry (LICOR)	Lebanon	2002	Yes	In-hospital
ORPKI registry	Poland	2004	Yes	In-hospital
ONACI registry	France	2004	Yes	In-hospital
Italian National Registry of Interventional Cardiology	Italy	2004	Yes	No outcome data
National Interventional Council Registry	India	2006	No	In-hospital
Malaysian National Cardiovascular Disease Database-PCI registry	Malaysia	2007	No	In-hospital, 30-day, 12-month
Japan-PCI (J-PCI) Registry	Japan	2008	No	In-hospital
Netherlands Heart Registry	Netherlands	2008	No	In-hospital, 30-day, 12-month
Integrated PCI Data System in Brazil (ICP-BR) Registry	Brazil	2009	No	In-hospital
Ministry of Health Cardiovascular Intervention Online Registry	China	2009	No	In-hospital
All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) CathPCI registry	New Zealand	2010	Yes	In-hospital, 30-day, 12-month
Norwegian Registry for Invasive Cardiology (NORIC)	Norway	2012	Yes	In-hospital
Swiss Working Group of Interventional Cardiology PCI survey	Switzerland	2014	Yes	In-hospital
Korea PCI (K-PCI) registry	Korea	2015	No	In-hospital
Regional registries				
British Columbia Cardiac Registry	British Columbia, Canada	1994	Yes	In-hospital, 30-day, 12-month
Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease PCI registry (APPROACH)	Alberta, Canada	1995	Yes	In-hospital, 30-day, 12-month
Cardiac Care Network of Ontario	Ontario, Canada	2003	No	In-hospital, 30-day, 12-month
Victorian Cardiac Outcomes Registry (VCOR)	Victoria, Australia	2012	No	In-hospital, 30-day
Coronary Angiogram Database of South Australia (CADOSA)	South Australia, Australia	2012	Yes	In-hospital, 30-day, 12-month
Queensland Cardiac Outcomes Registry (QCOR)	Queensland, Australia	2014	Yes	In-hospital, 30-day, 12-month

2.7.3 Percutaneous coronary intervention registries in the Asia-Pacific region

The APAC region comprises approximately 50 countries and is home for around 60% of the world's population. Over the past 50 years, tremendous achievements which surpassed expectations were seen in areas of economic development, structural transformation, health and education improvement (Nakao 2020). These rapid transitions have caused a major shift in the key public health concerns, from focusing on infectious being the leading causes of mortality to a situation where non-communicable diseases have become relatively dominant (Gersh, Sliwa et al. 2010). Recent data reported that increasing risk factors such as obesity, diabetes and hypertension, smoking rates and decreasing physical activity together with population aging across the region fuelled the spread of CVDs and put the management and prevention of these diseases into major focus (Reid, Yan et al. 2014, Asia-Pacific ACS Medical Management Working Group, Huo et al. 2015, Chan, Du et al. 2016). PCI registries received significant attention in this region and were implemented in a number of countries with the aim of optimizing CHD patient outcomes. The earliest PCI registries in the region were established in the year of 2004-2006, specially in Australia, Japan, South Korea, India and Malaysia (Ajani, Szto et al. 2006, Lee, Jeong et al. 2007, Liew, Rosli et al. 2008, Hoshida, Yuasa et al. 2011). However, PCI data derived from registry is still limited in a number of developing countries such as Nepal, Mongolia, and Vietnam.

There is a wide variation between these registries due to regional differences on service levels, availability, facilities, training and ethnicity. Some countries managed nation-wide registries such as Japan, China, South Korea, India, and Thailand, while the

others implemented the regional, multi-centres or single centre one. Other differences include the time of outcome evaluation (from in-hospital to 2 years follow-up) and time of registry implement (some are ongoing while majority of them already finished data collection) (Lee, Jeong et al. 2007, Song, Yu et al. 2016). There is one collaboration in the region, namely The Asia Pacific Evaluation of Cardiovascular Therapies (ASPECT) established in 2011 which included existing registries in Australia, Hong Kong, Malaysia and Singapore on patients undergoing PCI (Reid, Yan et al. 2014). According to their recent data, there were differences across countries in terms of patient characteristics, pre-procedural risk factors, and clinical presentations. However, procedural success rates were high and similar across the region (>95%) (Reid, Yan et al. 2014).

In summary, the APAC region has experienced a major epidemiological transition in most its member countries. Significant effort has been made to establish PCI registries which may indirectly enhance the quality of life of CHD patients following PCIs. Despite the optimistic outcomes of PCI in current registries, there remains limited information in less developed countries, which requires more efforts to develop PCI models there.

Chapter 3 METHODOLOGY

3.1 Overview

This chapter provides the description of the methodology used to achieve the study objectives. Detailed methods used are described in the following eight sections. Specifically, section 3.2 describes the study design. Section 3.3 gives information on the study settings. Section 3.4 defines participants and sample size calculation. Section 3.5 describes the procedure of data collection while study tools and outcome measurements are presented in section 3.6. Section 3.7 and section 3.8 discuss data management and statistical analysis, respectively. Finally, section 3.9 outlines some ethical considerations. Some materials described in this chapter have been published in one of the peer-reviewed journal articles resulting from this thesis (Vu, Nguyen et al. 2020).

3.2 Study design

A single centre, hospital-based registry study was conducted among patients undergoing PCI at the leading cardiac centre in Vietnam. Baseline data were collected from September 2017 to May 2019, while follow-up data were collected at 30 days and 12 months after discharge.

3.3 Study settings

The study was undertaken at the VNHI. Located in Hanoi, the capital city of Vietnam, VNHI is the leading cardiac centre in the country for over 30 years. With a focus on cardiovascular intervention and surgery, intensive care and emergency for CVDs, VNHI is providing the highest quality of healthcare services and acting as the referral

centre for cardiovascular patients in the country. To date, a variety of advanced cardiac-based therapies have become routine clinical treatments for patients at VNHI, such as complex coronary stenting, aortic stent grafting, transcatheter cardiac structural interventions, etc. The workload in VNHI remains extremely high, with around 17,000 inpatients and 80,000 out-patients annually, from across Northern Vietnamese provinces. For 20 years, VNHI has witnessed a significant increase in the number of cardiac interventional procedures performed, from approximately 2,800 in 2004 to 12,000 in 2018 (Vietnam National Heart Institue 2017). In addition, VNHI acts as an education and training centre for medical students and staff from other hospitals in Northern Vietnam, providing transition of cardiovascular technologies and therapies into practice at other lower level medical institutions. VNHI was therefore selected for implementing the pilot PCI registry to reflect the gold-standard contemporary practice of PCI in Vietnam. Figure 3.1 shows the location of the city involved in the study.

Figure 3-1 Location of the registry study

3.4 Participants and sample size calculation

3.4.1 Selection criteria for participants

3.4.1.1 Inclusion criteria:

- ✓ Participants were patients undergoing PCI who satisfied the following criteria:
- ✓ Vietnamese residents aged 18 years and over.
- ✓ Have at least one phone contact number.
- ✓ Undergo PCI in VNHI during the period of the study.
- ✓ Able to communicate, understand the information sheet and have not opted-out of future follow-ups by the time of discharge from the hospital.

3.4.1.2 Exclusion criteria

There are no exclusion criteria for this study.

3.4.2 Sample size

The formula for calculating sample size in prevalence studies was used in our study, in which the details are below:

$n=Z^2 *P (1- P)/ d^2$

n = sample size; Z = Z statistic for a level of confidence; P = expected prevalence or proportion (in proportion of one; if 20%, P = 0.2), and d = precision (Arya, Antonisamy et al. 2012, Pourhoseingholi, Vahedi et al. 2013).

According to the annual report of the national PCI registry in Malaysia, the mortality rate at 12 months was estimated to be 6.8% in 2016 (National Cardiovascular Disease Database 2016), thus, the value of P=0.068 was used. The value of d was recommended being half of P when P less than 0.1 (10%), then we had d= 0.034. The Z here equalled 1.96. This produced a value for n of 210. After accounting for an assumed opt-out rate of 10% and 20% of lost to follow-up at 12 months, a minimum sample size of 273 was required.

3.5 Study procedure

3.5.1 Screening and recruitment

Recruitment started in September 2017 and ended in May 2018. During that period, all patients undergoing PCI at VNHI satisfying the inclusion criteria were approached and invited to participate in the study. Participants were consecutively recruited at VNHI following the sample collecting strategy until the desired sampling quota was reached.

3.5.2 Baseline collection

A paper-based form was used to collect baseline information, which was obtained via interviewing patients, visiting the catheterization laboratory and extracting information from medical records. From the patients list for PCI in catheterization laboratory, eligible patients were identified and approached for interviewing to provide information regarding demographic characteristics, risk factors, medical history and clinical presentation. When patients were medically well enough, as assessed by the responsible physician, interviews were conducted in wards following the index PCI and prior to discharge. At the catheterization laboratory, data regarding the index PCI such as indication, adjunctive devices and procedural details was captured. Images of coronary lesions were stored on protected disks, and printed, read and coded by a cardiologist. Medical records were abstracted to obtained information such as time of admission, in-hospital management, medications used, clinical tests and pre-discharge complications (e.g. renal impairment, cardiogenic shock, bleeding [classified by the Bleeding Academic Research Consortium (BARC)]) (Mehran, Rao et al. 2011) , stroke, new or current MI, target vessel or lesion revascularisation after the procedure (PCI or CABG). It took approximately one hour to complete a case report form (CRF)

on average. Clinical audit processes were conducted by trained staff to ensure the compliance with the project protocol. The data manager at VNHI and research assistants were responsible for conducting these activities.

3.5.3 30 days and 12 months follow-ups

After discharge, at 30 days and 12 months, participants were contacted to obtain follow-ups data. The endpoint of major adverse cardiac and/or cerebrovascular events was captured in both the 30-day and 12-month follow-up surveys [such as all cases of death, new or recurrent MI or stent thrombosis, target vessel revascularisation or stroke; bleeding (BARC) (Mehran, Rao et al. 2011); rehospitalisation; medication use and health quality of life (using the 3-level EQ-5D Quality of life instrument to collect information on mobility, personal care, usual activities, pain/discomfort, anxiety/depression, and own health state today) of participants after the index PCI].

At 30 days, information was obtained via either face-to-face interviews or phone interviews depending on whether the participant was physically present at VNHI. According to current practices, patients were recommended to revisit the hospital after 30 days of discharge, however, many of them were unable to do so. The interviews were undertaken in approximately 15 -30 minutes by the data manager or research assistants.

At 12-months, a 15-minute phone interview was undertaken by trained research assistants to obtain information from the patients directly. First-degree relatives were used as the proxy if the participants were not contactable. At least three attempts were made to contact the participants. If patients have additional concerns regarding their health, then consultation will be available upon request following the interview.

The process of collecting data is illustrated in the Figure 3.2 below

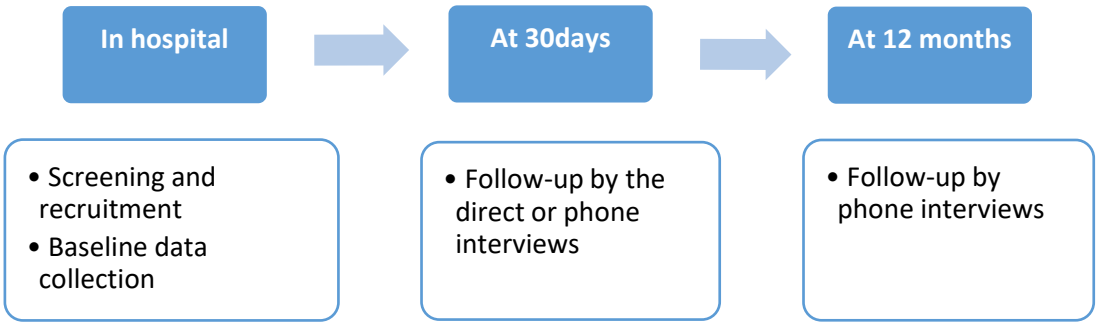

Figure 3-2 Flow chart of data collection

3.6 Questionnaire and measurements

3.6.1 Establishment of dataset

This study adapted the current versions of standardised data abstraction forms developed for the Victorian Cardiac Outcomes Registry (VCOR), Australia (Victorian Cardiac Outcomes Registry 2013), including the standard case report form (CRF) and dataset definitions for all fields. The state-wide VCOR was built on the Melbourne Interventional Group registry (Stub, Lefkovits et al. 2018), in which PCI data elements are in line with a number of current interventional registries worldwide, for instance, the American College of Cardiology - National Cardiovascular Data Registry (Ajani, Reid et al. 2008). The standard dataset aimed to collect the minimum standard data and avoid cumbersome management:

(1) The three-page baseline survey, administered at time of presentation for procedures, contains 13 sections: patient details, admission data, clinical symptoms, clinical presentation, pre-procedural left ventricular function, risk factors, renal status, medication, procedure details, post-procedural cardiac biomarkers, in-hospital complications, discharge details and medications.

(2) The one-page survey for 30-day and 12-month follow-up, includes four sections: patient details, outcomes, medications and quality of life at 30 days and 12 months.

The specific questions for all three data collection points are presented in the Appendix.

The VCOR data collection forms were translated into Vietnamese, and revised by two Vietnamese clinical cardiologists to reflect local practice. After discussion, consensus was reached around the addition of some new elements into the Vietnamese data collection forms, such as patient details (e.g. medical record number, ethnic group, poverty status, educational level, occupation, and income) and risk factors (e.g. smoking, dyslipidaemia). The Vietnamese data collection forms were designed in the TELEFORM software (Electric Paper 2017) and printed in paper records.

3.6.2 Description of variables and instruments

The major variables and instruments of the study are presented in the Table 3.1 below.

Table 3-1 Description of study variables and instruments

Variables	Instrument/ source of data	Assessment
Demographics such as name, gender, phone number, height, weight	Baseline form	Baseline
Admission data: date and time of admission and the index PCI	Medical records	Baseline
Risk factors associated with PCI: diabetes, history of cerebrovascular disease and peripheral vascular disease	Medical records and baseline form	Baseline
Clinical symptoms and presentation: acute coronary syndrome, cardiogenic shock, cardiac arrest	Medical records	Baseline
Left ventricular (LV) function and renal status: LV test type and result, chronic renal failure	Medical records	Baseline
Procedural details: PCI indication, entry location, details of lesion and stent used, cardiac biomarkers	The catheterization laboratory and medical records	Baseline
Medications use: in hospital and after discharge	Medical records and baseline form	Baseline, 30 days, 12 months
In-hospital deaths and complications: renal impairment, bleeding, stroke and stent thrombosis	Medical records	Baseline

30 days and 12 months outcomes: mortality, new heart failure, new MI, stroke and re-hospitalization	Follow-up form	30 days, 12 months
Quality of life	EQ-5D Quality of life	30 days, 12 months

3.7 Data management

Data from the completed forms were coded and entered into Epi-data twice. While the software allows logical errors, missing information, or incorrect coding could be automatically checked, double entering data provided the opportunity to reduce typing errors by comparing two version and checking with paper versions. Then, the final data sets were transferred to SPSS for cleaning and analysis. All variables were checked to detect missing data and outliers. All electronic data were securely stored in a personal computer and backed up at protected University drive, password protected, and accessible by the chief investigators only. Data were de-identified prior to statistical analysis. Only aggregated data were reported. Hard copy of data collection forms was kept in a locked filing cabinet in an office accessible to the investigators only.

3.8 Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences software (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL). Categorical variables were expressed as number and percentages for groups and the continuous variables were expressed as mean ± standard deviation (SD) for normally distributed variables or medians for skewed variables. For the comparisons, Fisher exact or Chi-square tests were undertaken to compare categorical variables. Parametric continuous variables were compared by unpaired (independent samples) student's t-tests for comparison of means, while non-parametric continuous variables were compared by Mann-Whitney U testing.

Univariable and multivariable analyses were conducted to establish factors associated with clinical outcomes/ hospital costs. All variables were tested for association with clinical outcomes/ hospital costs, with those showing association on univariable analysis at $p < 0.1$ included in multivariable analysis.

Forward stepwise logistic regression was used for multivariable analysis. Independent variables were selected by criteria of clinical relevance and evidence of significance or trends towards significance on univariate analysis. All p values (2-sided where appropriate) of less than 0.05 were considered statistically significant for all analyses. Statistical analysis for each study is explained more in each chapter.

3.9 Ethical considerations

Ethics for the study was approved by the Curtin University Human Research Ethics Committee (HRE 2017-0378). Every participant was provided with a Patient Information Sheet in which the purpose of the study, activities and rights of participants were described clearly. Participating in this study was voluntary and participants had the right to decline their participation or withdraw from the study at any time without any consequence via an 'opt-out' consent. A unique ID was assigned to each participant and linkable to the private information such as name, age, address, and phone numbers for follow-ups. All information that identifies participants was coded and stored confidentially.

Chapter 4 A FRAMEWORK/MODEL OF PERCUTANEOUS CORONARY INTERVENTION REGISTRY IN VIETNAM

This chapter addresses objective 1, presenting the rationale, methodology and the real experience of establishing the first PCI registry in Vietnam. From the conducted registry, we also report on the viability of the strategy as a model for the nation. The following peer-reviewed publication based on this chapter was accepted in Global Heart in March 2020:

Vu TTH, Nguyen TTH, Pham MH, Do DL, Nguyen NQ, Norman R, et al (2020). Establishment of a percutaneous coronary intervention registry in Vietnam: rationale and methodology. Global Heart 2020; 15:30.

Other dissemination: This chapter was presented in Mark Liveris Seminar, Health Science Faculty, Curtin University, 11 May 2020.

The PDF of the published paper can be found in Appendix A. For the ease of reading, the paper is reproduced formatted for the thesis below.

4.1 Introduction

CHD is consistently the leading cause of death worldwide, responsible for approximately 16.6 % of total deaths in 2016 and places a large economic burden on the population (World Health Organization 2017, Thomas, Diamond et al. 2018). Since its inception in 1977, PCI has been recognised as a valuable procedure for treating CHD patients and has become a common part of routine practice worldwide (Ahmad, Ali et al. 2011, Kumar, Walters et al. 2013). The APAC region is home to nearly 60% of the world's population, where CHD is now a leading cause of mortality (Finegold, Asaria et al. 2013, World Health Organization 2016) and the development of PCI registries is of growing interest (Ahmad, Ali et al. 2013, A, Mathew et al. 2017, Krittayaphong, Boonbaichaiyapruck et al. 2017). As a clinical quality registry, a PCI database is an important mechanism for monitoring and benchmarking the performance of clinical care, improving safety and outcomes, contributing to reducing treatment cost and regulating guidelines (McNeil, Evans et al. 2010, Gliklich, Dreyer et al. 2018). Nonetheless, there remains wide geographic variation in terms of the organisation, operation, management, sustainability and utilisation of data collected of PCI registries in Asia. Additionally, data are limited regarding the participation of less economically developed countries, particularly those in the South-East Asia region, including Vietnam (Liew, Rosli et al. 2008, Li, Dharmarajan et al. 2014, Reid, Yan et al. 2014, Krittayaphong, Boonbaichaiyapruck et al. 2017).

As a nation undergoing rapid economic and epidemiological transition, Vietnam has experienced a high burden of CHD, causing more than 58,000 deaths (11.6% of all mortality) in 2017 (World Health Rankings 2017). Vietnam began to adopt PCI in 1995 at the VNHI, and has to date introduced this procedure to approximately 70

cardiac centres nationwide (Thai 2012). The annual number of PCI procedures is relatively large and increasing; for instance, there were 2,250 patients receiving this technique in 2013 in a single national centre and there is a 15 % increase annually (Vietnam National Heart Institue 2017). Notwithstanding its widespread use, there has been no PCI registry in Vietnam.

This paper presents the rationale, design and conduct of a pilot PCI registry model in Vietnam. The viability of implementing routine collection of PCI data was also assessed and documented. If viable, this would be the initial step in developing a model for an expanded PCI registry in Vietnam. The major objectives of this pilot study are 1) to describe the implementation experience at a large cardiac centre in Vietnam; 2) to describe the methodology for developing the PCI registry in Vietnam; and 3) to report on the viability of the strategy as a model for the nation.

4.2 Methods

To avoid significant overlap with Chapter 3: Methodology, we only mention the names of sections which are already described there, including *4.2.1 Study setting; 4.2.2. Establishment of dataset; 4.2.3, Data collection; 4.2.6: Ethics approval*. Please find the detailed contents in Chapter 3.

4.2.1 Study setting

4.2.2 Establishment of dataset

4.2.3 Data collection

4.2.4 Perspectives from VNHI

We also conducted an online survey with qualitative open-ended questions to explore perspectives on the implementation of the registry and identify key factors associated with successful implementation of this new model at VNHI. We approached all clinical, nursing and leadership staff involved in coronary interventional activity. The survey that contained 10 questions was administered using Qualtrics Research Suite (Qualtrics, Provo, UT), a web-based tool that allows researchers to build, distribute, and analyse online surveys in real time. Analysis of qualitative data was guided by the principles of the conventional and summative content analysis (Hsieh and Shannon 2005). Briefly, responses obtained from participants were coded to identify and categorise different themes together with performing word counts. The interpretation focused on the several key factors that may influence the development and implementation of PCI registry in Vietnam.

4.2.5 Registry viability

This is the first study focusing on developing a model to collect data on the contemporary practice of PCI at the largest cardiac institute in Vietnam. The viability of the pilot PCI registry as a model for a national registry in Vietnam was determined by the following elements:

a) Being able to recruit a representative sample into the registry.
b) The quality of data collected, determined by data completeness and audit activities.
c) Costs and time taken to collect the data by hospital staff.
d) The level of support for the activity from patients, clinical staff and the cardiac institute.

4.2.6 Ethics approval

4.3 Results

4.3.1 Implementation experience

During the study period (from September 2017 to May 2018), patients who underwent PCI at VNHI and met the inclusion criteria were approached and invited to take part in the study. Three strategies were used to enrol patients as the pilot study progressed, with changes applied to recruitment and the corresponding results (Figure 1). The modification of the data collection strategy was implemented to ensure that, in the absence of resources to capture all cases, we were able to capture a representative sample and minimise the potential for selection bias in registry enrolment when a single data manager was responsible.

For the first period of data collection (September and October 2017), 6-7 patients were randomly selected from the total number admitted of each day. However, to eliminate the potential bias of choosing only good prognosis patients (i.e., without complications prior to and after the procedure), we moved to second approach (from November 2017 to March 2018) which aimed to collect all cases in two weekdays. Two particular weekdays (Monday and Tuesday) were chosen to capture data from all operators including two teams of interventionists who performed PCI at VNHI on alternate days during the week. Notably, this second period of data collection coincided with Tet (Lunar New Year's holiday), the biggest cultural event in the year, which may explain a reduction in the number of patient visits. The actual number of patients recruited in the period one and three may be generalizable to the rest of the year (i.e., from June to August) because there were no similar events in the year. Finally, the last period (from April to mid-May 2018) included all patients undergoing PCI on two weekdays and

the weekend, which was designed to capture both the normal practice (weekdays) and acute cases (weekend).

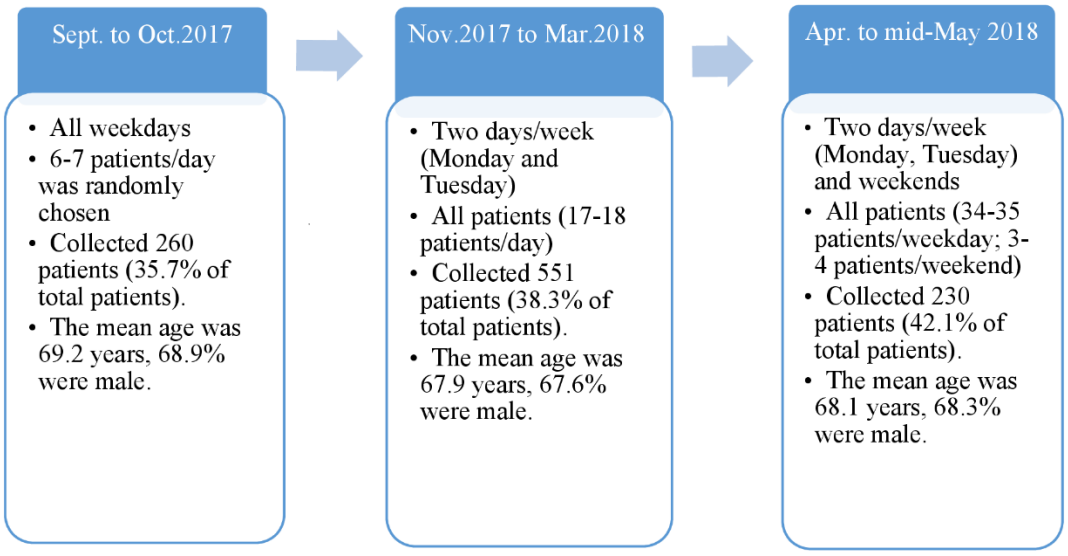

Figure 4-1 The data collection strategies

A total of 1,028 eligible coronary patients were approached and invited from a total of approximately 2,800 patients undergoing PCI at VNHI during the study period. Six patients refused to participate in the study by opt-out consent and thus 1,022 patients remained in the baseline study sample, which included 1,041 individual PCIs (as 19 patients underwent PCI twice at VNHI). There was an extremely high rate of data completeness, with only information of one lesion missed due to a lost disk (0.1%). Ninety-eight percent of fields were fully filled, with the exception of oral anti-coagulant therapy as patients had difficulty recognising the kinds of drug used and unknown information about their referral to cardiac rehabilitation. The successful follow-up rate at 30 days was high, with 993 patients followed-up (97.2%).

Of the 25 invited cardiovascular professionals, 12 consented to participate in the qualitative survey (response rate: 48%). These 12 respondents included 5 cardiologists with administrative leadership at VNHI, 3 clinical cardiologists and 4 nurses. Several key additional factors concerning the successful implementation of a PCI registry in Vietnam were raised. Nine respondents agreed with the importance of standardised data collection forms as used in the registry. Other key facilitating factors were also emphasized, including well-trained investigators, the use of professional clinical audit, and strong support from leaders of target cardiac institutions. They also raised concerns regarding the sustainability of such a study at VNHI, including lack of data storage systems, sufficient funding for infrastructure and human resources, and strong commitment from hospital leaders.

4.3.2 Registry viability

The viability of the pilot PCI registry in VNHI was determined by the following elements:

a) Being able to recruit a representative sample into the registry. After several amendments, the data collection strategy captured all patients undergoing PCI at VNHI four days per week (2 weekdays with routine practice and weekend with emergency cases only). Thus, the sample recruited into the registry could be considered to be representative of coronary patients treated with PCI at VNHI when there were not sufficient resources to collect all cases.

b) Data quality. In total, we collected information on 99 data fields, and overall we had 98% data completeness. The reasons for this high completeness were the strong cooperation of patients and the availability of data resources (e.g.,

medical records, disks and machines in the catheterization laboratory). Additionally, the local clinical audit was performed monthly by well-trained staff, including case ascertainment (checking the collection of eligible data) and data quality assessment (reviewing source of data collection). Overall, 2% of cases were randomly checked and there were no significant errors in choosing patients and medical records. Thus, the quality and accuracy of data collected at VNHI was ensured.

c) Costs for and time taken to collect the data by hospital staff. It took approximately an hour to complete a CRF, including 15 minutes for interviewing patients, abstracting data from medical records and reading procedure information in the secured disks with the cardiologist. In further studies, data collection will be the responsibility of hospital nurses. Therefore, the actual time for completing the data collection form would be around or less than one hour because of the familiarity with routine PCI practice. While hospital nurses will do data collection as part of routine clinical activity, we estimated the cost required for data collection. If we use an average monthly income of a nurse at VNHI, which is approximately 1066 USD a(Vietnam National Heart Institue 2018), then the estimated time-cost of baseline data collection for one case, which is the income of hospital nurse in 1 hour, was equivalent to 1066/ (30*8) = 4.4 USD b. In follow-up survey, approximate 15-30 minutes (phone or direct interviews) will be required for each patient, which was roughly equivalent to 1.1- 2.2 USD.

d) The level of support from patients, clinical staff and the leader team. In the pilot registry, patients at VNHI had shown their strong engagement with the registry and there were no significant difficulties regarding the patients noted. The leader team and the hospital staff were well aware of the necessity to develop such a registry at the VNHI and in Vietnam and shown their universal support. They also belief that the establishment of the registry would be successful if there were sufficient data storing system, sufficient funding for human resources and improving the infrastructure, and strong commitment from hospital leaders.

[a]The exchange rate is 23.150 VND; [b] 30 days were represented for 22 working days and extra shifts of hospital nurses.

4.4 Discussion

In the context of the growing interest in developing clinical quality registries worldwide, this paper reports the development of the first PCI registry in Vietnam, using and adapting experiences from longstanding registries in Australia (Ajani, Szto et al. 2006, Stub, Lefkovits et al. 2018). The work to date has demonstrated a PCI registry to be feasible and suitable for Vietnamese circumstances, providing a significant opportunity to extend the approach to other cardiac centres looking to replicate the model. Importantly, implementing such a model not only provides crucial feedback on the performance of PCI for Vietnamese clinicians and cardiac care providers but also allowing a robust comparison with other regional registries such as those involved in the ASPECT collaboration (Reid, Yan et al. 2014) as well as contributing to the literature on the use of PCI.

In comparison with other regional PCI registries in Thailand, China, India and Malaysia, the methodology in our pilot registry had some similarities, including using a standard abstraction form to collect consecutive patients undergoing PCI, providing sufficient training for investigators prior to data collection, performing clinical audit to ensure data quality and conducting follow-ups at 30 days and 12 months to investigate the outcomes of PCI (Liew, Rosli et al. 2008, Li, Dharmarajan et al. 2014, A, Mathew et al. 2017, Krittayaphong, Boonbaichaiyapruck et al. 2017). Nonetheless, due to resource constraint, we did not approach all the patients undergoing PCI in the study period. The CRF was also completed in a paper format only and data obtained were not transferred to a web-based system as other PCI registries (Liew, Rosli et al. 2008, A, Mathew et al. 2017, Krittayaphong, Boonbaichaiyapruck et al. 2017). Therefore, further studies might apply our methodology if there are limited resources or overcome our drawbacks if there is sufficient funding.

Although it is at an early stage, we are optimistic about the viability of the PCI model that we have implemented at the VNHI. The success of the PCI registry at the VNHI to date, is due to a variety of key factors such as the high number of patients undergoing PCI and their strong engagement with clinicians, the availability of data resources, and the supportive hospital staff team. We also faced several challenges in the first registry implement at VNHI, including high workload which might affect the time spent on data collection by the hospital staff and the lack of electronic record systems which made it difficult to collect comprehensive information when patients revisited the hospital. However, these obstacles can be minimised by providing sufficient training for clinical investigators, specifying sections of the data forms for investigators and conducting more detailed follow-up surveys.

One limitation is that the registry was conducted at VNHI, the leading cardiac centre in Vietnam where there is a highest patient throughput. Therefore, extending the methodology in establishing PCI registries in smaller settings with potentially less experienced staff may require a modified approach to that which we have done, but we believe this current work represents an important first step in doing so. Another potential concern may be bias in data collection, though attempt was made to enrol a representative sample. Thus, where sufficient resources are available, collecting all patients undergoing PCI in the study period would be recommended.

4.5 Conclusion

This paper describes the methodology of establishing the first PCI registry at the leading cardiac centre in Vietnam and reports on the viability of this model. We hope that the successful implementation of a PCI registry at VNHI will encourage other cardiac intervention centres in Vietnam to adopt this model in their daily practice and by doing so, enables the opportunity to develop a nationwide PCI registry.

Chapter 5 PATIENT PROFILES, CLINICAL PRACTICES CHARACTERISTICS AND IN-HOSPITAL OUTCOMES OF PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

This chapter addresses the objective 2, which aimed to investigate the demographic, clinical characteristics and in-hospital outcomes of patients undergoing PCI in the first PCI registry in Vietnam. The following peer-reviewed publication based on this chapter was accepted in International Journal of Cardiology- Heart and Vasculature in August 2020:

Vu TTH, Pham MH, Nguyen TTH, Do DL, Nguyen NQ, Norman R, et al (2020). Novel insights into clinical characteristics and in-hospital outcomes of patients undergoing percutaneous coronary intervention in Vietnam. IJC Heart & Vasculature. Volume 31, December 2020, 100626

Other dissemination: This chapter was presented as a e-poster in The Cardiac Society of Australia and New Zealand Annual Scientific Meeting 2020, December 2020.

The PDF of the published paper can be found in Appendix B. For the ease of reading, the paper is reproduced formatted for the thesis below.

5.1 Introduction

PCI has been demonstrated to be an effective treatment for CHD worldwide since its inception in the late 1970s (Movahed, Ramaraj et al. 2009, Soran, Manchanda et al. 2009). The procedure has become more widely used in Asia, where CHD was the leading cause of death (approximately 16.2% of all deaths in 2016) (World Health Organization 2017, Thomas, Diamond et al. 2018), with around one million PCIs undertaken in 2016 alone (Gao 2017). Notwithstanding the apparent benefits of PCI, post-procedural cardiac complications remain a concern, including death, MI and bleeding (Ricci, Manfrini et al. 2016, Han, Park et al. 2018, Li, Wong et al. 2019, Chacko, J et al. 2020).

Accumulating data in the USA and Europe have shown that the occurrence of these adverse cardiac events differed according to patient characteristics, such as gender, age or comorbidities (Weintraub, Spertus et al. 2008, Akhter, Milford-Beland et al. 2009, Dey, Flather et al. 2009, Ricci, Manfrini et al. 2016). In Asia, cardiac registries in some high-income countries have also reported similar findings (Li, Rha et al. 2010, Kaneko, Yajima et al. 2014), while relevant data remains limited in LMICs. Additionally, most medical care provided for CHD patients in Asian countries is based on the European or North American guidelines developed from large domestic registries (Hasdai, Behar et al. 2002, Budaj, Brieger et al. 2003, Asia-Pacific ACS Medical Management Working Group, Huo et al. 2015). It is not clear whether the non-Asian data reflects the Asian experience, nor whether the guidelines are well suited to the Asian population. Thus, data from real-world practice in less developed countries are very important to establish current benchmarks and determine appropriate management and preventive strategies for these populations.

Vietnam is a L-MIC in South-East Asia, where PCI has been widely used in modern cardiac based treatments for CHD, the second leading cause of death (World Health Rankings 2017). Data pertinent to PCI is scare on the epidemiology, management and outcomes of patients undergoing the procedure in Vietnam (Vietnam National Heart Institue 2017). The aim of this paper is to provide novel insights concerning the clinical characteristics and in-hospital outcomes of patients undergoing PCI in Vietnam based on the first PCI registry conducted at a leading cardiac hospital in Vietnam.

5.2 Methods

5.2.1 Study setting

Data were derived from a registry, which was established at the VNHI, Hanoi, Vietnam during September 2017-May 2018. Full details of this PCI registry was previously described (Vu, Nguyen et al. 2020). As the leading cardiac centre nationwide, VNHI provides the highest quality of healthcare services for around 17,000 cardiovascular inpatients and 80,000 out-patients annually. In 2018, the total number of cardiac interventional procedures undertaken at VNHI was approximately 12,000 (Vietnam National Heart Institue 2017). Initial discussions were held with clinical leaders in cardiology to ensure there was support for the implementation of the registry by senior clinical and executive staff.

5.2.2 Data collection

This single-centre, hospital-based registry adapted the data collection forms currently used in the Victorian Cardiac Outcomes and Melbourne Interventional Group registries, Australia (Yeoh, Yudi et al. 2017, Stub, Lefkovits et al. 2018). Information

on demographic, clinical and procedural information, and outcomes of patients who underwent PCI was recorded on standardised data abstraction forms with standard definitions for all fields. The study protocol was approved by the Curtin University Ethics Committee before the commencement of data collection (HRE 2017-0378). Patients had the right to opt out of the study without impacting on their care. Data collection was conducted by a team of specifically trained local investigators at VNHI.

5.2.3 Patient characteristics

Information on participant demographics, medical history, cardiovascular risk factors (diabetes, hypertension, dyslipidemia, cerebrovascular disease), clinical symptoms and presentation (ACS, cardiogenic shock, cardiac arrest), left ventricular ejection fraction, and pre-procedural renal status was collected via both patient interviews and medical records. ACS includes unstable angina (UA), non-ST-elevation myocardial infraction (NSTEMI) or ST-elevation myocardial infraction (STEMI). STEMI was defined as the presence of at least 0.1-mV ST-segment elevation or new pathological Q waves in ≥ 2 contiguous ECG leads or new left bundle branch block with elevation of cardiac enzyme levels above the reference range. NSTEMI was defined if either of the following was present: elevated cardiac enzyme levels above the reference range, ST-segment depression, T-wave abnormalities or ischemic symptoms. UA was named in the presence of prolonged chest pain without cardiac enzyme elevation.

5.2.4 Procedures and medications

The strategy for the specific coronary intervention (e.g. choice of stent, medication) was at the discretion of the interventionists. Injured lesion segments were coded following the classification of the Syntax Score (Syntax score working group 2019)

and guidelines for the lesion type of American College of Cardiology/ American Heart Association (ACC/AHA) (Levine, Bates et al. 2016). A procedure was considered successful if there was a residual stenosis of less than 10% following coronary stenting and the rate of coronary blood perfusion of thrombosis in MI 2 or 3 flow. Pre and post procedural medical therapies such as oral antiplatelet, aspirin, anti-thrombin, and glycoprotein IIb/IIIa inhibitors were evaluated according to the 2016 ACC/AHA guidelines (Levine GN, Bates ER et al. 2016). Medications and procedural data were obtained by extracting medical records and reading secured procedural disks.

5.2.5 Clinical outcomes

Medical records were extracted to document in-hospital complications including death, new or recurrent MI, cardiogenic shock, bleeding, post-procedural renal impairment, new requirement for dialysis, unplanned target vessel revascularisation (revascularisation for the previously cured coronary artery) by PCI or coronary artery bypass grafts (CABG), stent thrombosis, and stroke. MI was defined as an elevation of cardiac biomarkers more than 5 the upper limit of normal, and evolutionary ST-segment elevations or development of new Q-waves in at least 2 contiguous ECG leads. Cardiogenic shock was defined by hypotension (systolic BP <90 mmHg lasted from 30 minutes and over, evidence of end-organ hypo perfusion or elevated filling pressures).

Bleeding was classified by the Bleeding Academic Research Consortium (Mehran, Rao et al. 2011), and major bleeding was defined by any transfusion or by a drop in haemoglobin ≥ 3.0 g/dl. Acute renal impairment was defined as a rise of creatinine ≥ 44.2μmol/L or ≥ 25% up to 5 days after the index PCI, compared to baseline creatinine.

Stroke was defined as the patient's persistent loss of neurological function due to an ischaemic or haemorrhagic event (Sacco, Kasner et al. 2013). Stent thrombosis was defined as the occurrence of a thrombus or angiographic documentation of vessel occlusion within a pre-existing stent or within 5mm of the proximal or distal stent edges (Lemesle, Delhaye et al. 2008). Medical records were reviewed to identify these cardiac events.

5.2.6 Statistical analysis

Data on demographic, clinical, procedures and outcomes were presented as numbers (and percentages) for categorical variables, and means (with standard deviations) for continuous variables. Descriptive statistics were used to summarise characteristics of the study participants. Fisher exact or Chi-square tests were undertaken to compare categorical variables, and Student's t tests or analysis of variance (ANOVA) were applied to compare continuous variables. All p-values were two-tailed with significance defined as $p \leq 0.05$. All statistical analyses were performed using the SPSS statistical package (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL).

5.3 Results

5.3.1 Patient characteristics

A total of 1,022 patients were enrolled into the registry. Of these, 19 patients had a second PCI, meaning a total of 1,041 procedures, treating 1,276 lesions. Demographics and clinical characteristics of participants are summarized in Table 5.1. Two-thirds of the study population were male. The participants' mean age (±SD) was 68.3 years (10.3) and females were approximately 4 years older than men ($p<0.0001$). The majority of patients were Kinh (96.7%), the largest ethnic group in Vietnam, and

those living in other provinces outside Hanoi accounted for nearly 80%. The proportions of participants with college or higher education, conducting office work and with a low income were 39.9%, 38.1% and 74.5%, respectively.

In total, 54.4% of the patients presented with ACS, with the respective prevalence of STEMI, NSTEMI and UA being 14.5%, 16.2% and 23.7% (Table 5.1). Only 1.1% of the participants experienced cardiogenic shock, and 0.6% had cardiac arrest before PCI. The prevalence of overweight or obesity (BMI ≥ 23.0 kg/m^2) was 38.8%. The prevalence of hypertension, previous PCI and hyperlipidaemia were 67.2%, 35.1% and 29.9%, respectively (Fig. 5.1).

Compared with males, females had a lower education level, monthly income and were more likely to do manual work ($p<0.0001$). Additionally, females also had a higher prevalence of risk factors such as hypertension, diabetes, and hyperlipidaemia ($p<0.05$) with the exception of current smoking and previous PCI ($p<0.05$) compared to males.

Table 5-1 Clinical characteristics of patients undergoing PCI in Vietnam by gender

	Overall	**Female**	**Male**	**P value***
Patients	1022	326 (31.9)	696 (68.1)	_
Age (years), mean ± SD	68.3 ± 10.3	70.9 ± 9.4	67.0 ± 10.5	<0.0001 †
Kinh people	989 (96.7)	321 (98.5)	667 (95.8)	0.045
From provinces outside Hanoi	796 (77.9)	233 (71.5)	563 (80.9)	0.001
Education				

Primary school and lower	83 (8.1)	47 (14.4)	36 (5.2)	<0.0001
Secondary school	367 (35.9)	122 (37.4)	245 (35.2)	
High school	164 (16.0)	40 (12.3)	124 (17.8)	
College and higher	408 (39.9)	117 (35.9)	291 (41.8)	
Current/ past occupation				
Officer worker	389 (38.1)	120 (36.8)	269 (38.6)	<0.0001
Manual worker	163 (15.9)	67 (20.6)	96 (13.8)	
Farmer	255 (25.0)	107 (32.8)	148 (21.3)	
Tradesperson	64 (6.3)	17 (5.2)	47 (6.8)	
Others	151 (14.8)	15 (4.6)	136 (19.5)	
Poverty [a]	44 (4.3)	19 (5.8)	25 (3.6)	0.175
Low income [b]	762 (74.5)	279 (85.6)	483 (69.4)	<0.0001
Body mass index (kg/m^2)				
Low (<18.5)	107 (10.5)	38 (11.7)	69 (9.9)	0.071
Normal (18.5- 22.9)	518 (50.7)	178 (54.6)	340 (48.9)	
High (≥ 23.0)	397 (38.8)	110 (33.7)	287 (41.2)	
ST-elevation myocardial infarction	148 (14.5)	38 (11.7)	110 (15.8)	0.097
Non-ST-elevation myocardial infarction	166 (16.2)	57 (17.5)	109 (15.7)	0.518
Unstable angina	242 (23.7)	83 (25.5)	159 (22.8)	0.402
Non-acute coronary syndrome	466 (45.6)	148 (45.4)	318 (45.7)	0.931
Left ventricular ejection fraction (%), mean ± SD	59.4 (± 14.7)	61.7 (± 14.6)	58.2 (± 14.7)	0.001 †
Moderate to severe renal impairment [c]	25 (2.4)	5 (1.5)	20 (2.9)	0.283
Cardiogenic shock	11 (1.1)	3 (0.9)	8 (1.1)	>0.999

Cardiac arrest	6 (0.6)	2 (0.6)	4 (0.6)	>0.999

Data are presented as n (%), otherwise specified.

**Comparing female and male subjects; [a] Having certificates of poor and near poor household; [b] Individual monthly income < 216 USD with the exchange rate of 23.150 VND; [c] Creatinine > 200µmol/L*

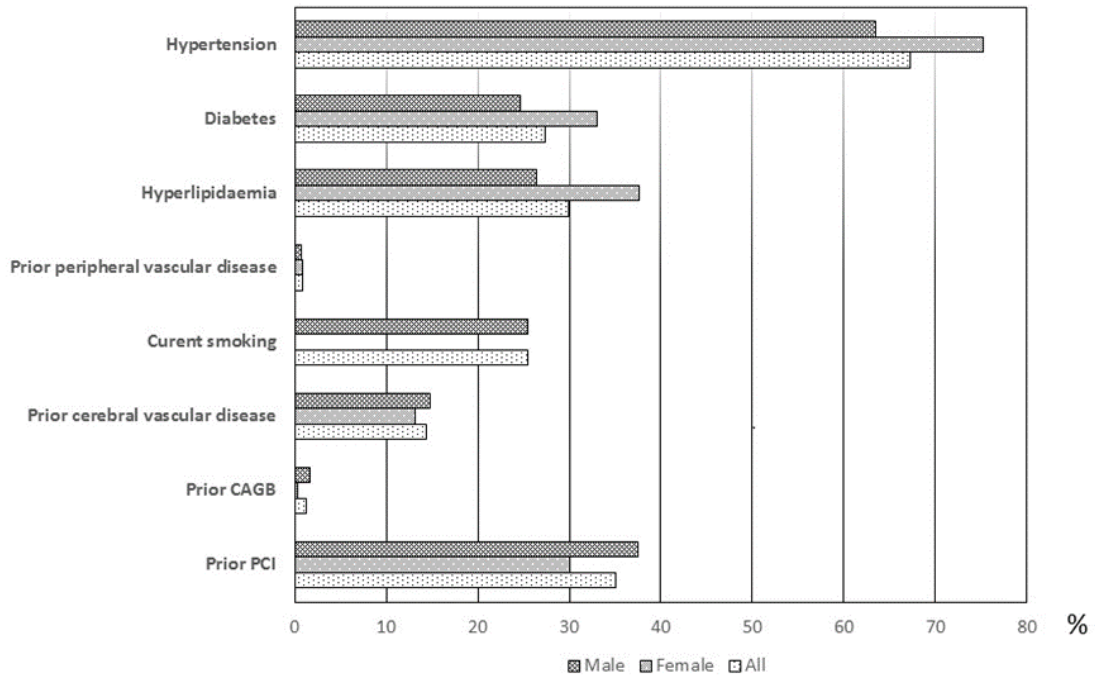

Figure 5-1 Risk factors of study participants by gender

5.3.2 Lesion, procedural characteristics and medications prior to PCI

There were 1,276 lesions which required subsequent treatment within 1041 procedures (Table 5.2). A total of 1,275 lesions was used for analysis due to missing information of one lesion. Radial artery and left anterior descending (LAD) were the most common procedural entry and target vessel (79.2% and 46.7%, respectively). Although 94.2% of the lesions were type B2 and C according to ACC/AHA classification, there was a high rate of angiographic success (99.4%). Just above one-third of the lesions required

at least 2 stents and almost 96% of stents used were over 20 mm in length. Drug eluting stents (DES) were used in all cases. Common agents used prior to PCI were antithrombin, clopidogrel and aspirin, accounting for 36.2%, 80.0% and 97.5%, respectively.

Compared with females, males were more likely to have disease in the left main coronary artery, chronic total occlusions, stent restenosis, and ≥ 2 stents per lesion ($p<0.05$). They tended to receive ticagrelor, while their female counterparts were relatively more likely to be prescribed with clopidogrel prior to PCI (both $p<0.05$).

Table 5-2 Lesion, procedural characteristics and medications prior to PCI by gender

	Overall	**Female (n=406)**	**Male (n=870)**	**P value**
Lesions	1276	406 (31.8)	870 (68.2)	_
Percutaneous entry location				
Radial	824 (79.2)	263 (79.2)	561 (79.1)	>0.999
Femoral	217 (20.8)	69 (20.8)	148 (20.9)	
Target vessel				
Left main	152 (11.9)	29 (7.1)	123 (14.2)	<0.0001
Left anterior descending	596 (46.7)	208 (51.2)	387 (44.5)	0.030
Right coronary	406 (31.8)	118 (29.1)	288 (33.1)	0.164
Circumflex	271 (21.2)	80 (19.7)	191 (22.0)	0.394
PCI with ≥ 2 lesions	218 (17.1)	69 (17.0)	149 (17.1)	>0.999
Type B2 and C lesions	1202 (94.2)	381 (93.8)	821 (94.5)	0.745

Chronic total occlusion	61 (4.8)	10 (2.5)	51 (5.9)	0.012
Restenotic lesions	64 (5.0)	11 (2.7)	53 (6.1)	0.014
Stents used for each lesion				
≤ 1	788 (61.8)	271 (66.7)	517 (59.5)	0.015
≥ 2	487 (38.2)	135 (33.3)	352 (40.5)	
Mean (± SD)	1.5 (± 0.71)	1.42 (± 0.64)	1.54 (± 0.74)	0.002
Stent length > 20mm	1181 (95.9)	375 (95.2)	806 (96.2)	0.502
Mean stent length (± SD)	34.6 (± 8.7)	34.5 (± 8.9)	34.7 (± 8.7)	0.656
Angiographic success	1267 (99.4)	405 (99.8)	862 (99.2)	0.448
Drug-eluting stent use	1231 (96.5)	394 (97.3)	837 (97.1)	0.998
Balloon only	36 (2.8)	11 (2.7)	25 (2.9)	
Guidance of IVUS	46 (3.6)	13 (3.2)	33 (3.8)	0.654
Medications				
Fibrinolytic therapy	2 (0.2)	1 (50.0)	1 (50.0)	0.536
Glycorprotein IIb/ IIIa	0 (0.0)			
Antithrombin therapy	377 (36.2)	111 (34.3)	266 (37.5)	0.227
Ticagrelor	176 (16.9)	35 (10.5)	141 (19.9)	<0.0001
Clopidogrel/ Ticlopidine	833 (80.0)	284 (85.5)	549 (77.4)	0.003
Aspirin	1015 (97.5)	320 (96.4)	695 (98.0)	0.172

**missing information of one lesion*

Data are presented as n (%), unless specified. IVUS: Intravascular Ultrasound

5.3.3 In-hospital outcomes and medications post PCI

Complications following PCI during hospital stay were rarely observed, with a relatively small proportion of new renal impairment and post-procedural bleeding

(3.2% and 2.0%, respectively) (Table 5.3). Median length of hospital stay was 2 days and over 92% of patients were treated with aspirin, antiplatelet, angiotensin receptor blockers and statin post PCI as recommended in the ACC/AHA guideline (Levine GN, Bates ER et al. 2016).

Major bleeding rate was higher in females than males ($p<0.05$). Ticagrelor was commonly used in males, while clopidogrel was frequently prescribed in the latter ($p<0.0001$).

Table 5-3 In-hospital outcomes and medications post PCI

Outcomes	**All (n=1041)**	**Female (n=332)**	**Male (n=709)**	**p**
New renal impairment	33 (3.2)	11 (3.3)	22 (3.1)	>0.999
New dialysis	9 (0.9)	1 (0.3)	8 (1.1)	0.286
Cardiogenic shock	4 (0.4)	1 (0.3)	3 (0.4)	>0.999
New/ recurrent MI	3 (0.3)	2 (0.6)	1 (0.1)	0.24
Unplanned PCI	2 (0.2)	1 (0.3)	1 (0.1)	>0.999
Stent thrombosis	2 (0.2)	2 (0.6)	0 (0.0)	0.102
Major bleeding	21 (2.0)	12 (3.6)	9 (1.3)	0.023
Stroke	5 (0.5)	1 (0.3)	4 (0.6)	>0.999
Death	8 (0.8)	3 (0.9)	3 (0.4)	0.39
Hospital length (day), median	2.0	2.0	2.0	0.69
Hospital length > 2 days	33.0	34.3	32.4	0.59
Medications				
Aspirin	1033 (99.7)	329 (99.7)	704 (99.7)	>0.999

Clopidogrel/ Ticlopidine	835 (80.5)	290 (87.8)	545 (77.2)	<0.0001
Ticagrelor	201 (19.5)	40 (12.2)	161 (22.9)	<0.0001
Beta Blockers	397 (38.5)	138 (41.8)	259 (37.0)	0.125
Angiotensin-receptor blockers	952 (92.2)	308 (93.6)	644 (91.6)	0.317
Statin	1033 (99.7)	330 (100.0)	703 (99.6)	0.556
Other lipid lowering therapy	3 (0.3)	3 (0.9)	0 (0.0)	0.032
Oral anticoagulation therapy	4 (0.4)	2 (0.6)	2 (0.3)	0.956

Data are presented as n (%), unless specified.

5.4 Discussion

This study was the first to provide novel insights into demographic and clinical characteristics as well as in-hospital outcomes of patients undergoing PCI at a leading cardiac interventional centre in Vietnam. The results indicated gender differences in several demographic and socioeconomic factors, clinical presentation and treatment which may be potentially important in the design of optimal care.

5.4.1 Demographic and clinical characteristics

The mean age of patients received PCI in our study was eight year younger than the overall national life expectancy in 2016 of 76.3 (World health rankings 2018). However, this age is higher than average ages of other PCI populations, including neighbouring countries with similar life expectancy such as China, Thailand and Malaysia (62.0, 62.7 and 57.0 years old, respectively) (Ahmad, Ali et al. 2013, Zheng, Curtis et al. 2016, Krittayaphong, Boonbaichaiyapruck et al. 2017) and countries with more economical development and higher life expectancy such as Australia, Japan and

South Korea (approximately 63.0- 65.0 years old) (Yeoh, Yudi et al. 2017, Han, Park et al. 2018, Numao, Suzuki et al. 2019). As patients at VNHI were largely transferred from lower level hospitals, our study population tended to have more comorbidities and older age. Potential barriers to receive timely care such as medical awareness of patients, economic resource and family constraints should be further investigated.

The prevalence of non ACS (45.6%), STEMI (14.5%), NSTEMI (16.2%) and UA (23.7%) were generally comparable to data derived from a recent study of the national PCI registry in Thailand (Kiatchoosakun S 2010). However, ACS presentation was more common in other PCI registries, especially with the proportion of STEMI patients (over 30%) (Ahmad, Ali et al. 2013, Yeoh, Yudi et al. 2017). For instance, the China PEACE registry reported that the prevalence of STEMI, NSTEMI and UA in patients undergoing PCI was 34.8%, 8.1% and 41.8% respectively (Zheng, Curtis et al. 2016). One possible explanation is that acute patients were more likely to receive medical therapy or PCI in district or provincial hospitals, and only more severe patients were referred to VNHI.

Consistent with previous studies, including the Asia-Pacific Evaluation of Cardiovascular Therapies collaborative study (Reid, Yan et al. 2014), our study participants generally presented with common-cardiovascular disease risk factors such as hypertension, diabetes, dyslipidaemia, past PCI, prior stroke and smoking. It is interesting that the prevalence of most those risk factors in our study was similar, despite a much lower proportion of dyslipidaemia (30%). For instance, some recent studies in China, Thailand, Malaysia and Australia showed that approximately two thirds of their patients experienced hyperlipidaemia (Kiatchoosakun S 2010, Ahmad,

Ali et al. 2013, Zheng, Curtis et al. 2016, Yeoh, Yudi et al. 2017). Reasons for such difference are not clear, but it may be due, in part, to a conceivably healthy and low-fat diet of our study participants (Nguyen, Strizich et al. 2013). Indeed, the prevalence of prior stroke and prior PCI in our study were among the highest in comparison with other studies (Kiatchoosakun S 2010, Ahmad, Ali et al. 2013, Zheng, Curtis et al. 2016, Yeoh, Yudi et al. 2017). The rapid expansion of PCI in recent years and strokes remain the leading cause of death in Vietnam might explain for this difference (World health rankings 2018).

Patterns of gender differences in demographic, socioeconomic and clinical factors are consistent with prior research (Akhter, Milford-Beland et al. 2009, Al-Fiadh, Andrianopoulos et al. 2011, Park, Kim et al. 2014). For example, our study showed females receiving PCI accounted for nearly one-third of total participants, those females were generally older and had more comorbidities than males. In our data, the female to male ratio was 0.47, which contrasts with the general Vietnamese population group age 64 and above which has a female to male ratio of 1.6 (Vietnam Population 2019). This lower incidence of PCI in females might be explained by the relatively lower priority in families of females compared to males in Vietnamese culture. This may be exacerbated by the high cost requirement of the procedure itself and other hospital treatments in the national centre as VNHI. More males were transferred from other provinces to VNHI for PCI in comparison to females ($p= 0.001$), which may support this theory. Additionally, presenting females were on average 4 years older than males ($p< 0.0001$). The protective impact of oestrogen in females in delaying the onset of cardiovascular disease is likely to be part of the explanation (Spary, Maqbool et al. 2009). The 4-year age gap also partly explains more comorbidities seen in

females such as hypertension, diabetes and hyperlipidaemia in our study. The Global Registry of Acute Coronary Events (GRACE) indicated that, in the group of patients undergoing cardiac intervention, females had higher rates of diabetes, hypertension, but were less likely to smoke (Dey, Flather et al. 2009). Data from several systematic review with meta-analysis also confirmed that females with cardiovascular risk factors were more likely to have incident CHD than males (Peters, Huxley et al. 2014, Peters, Singhateh et al. 2016).

5.4.2 Lesion, procedural characteristics and medications prior to PCI

The radial artery was the most common entry site of PCI procedures, which is similar to the practice in China (Zheng, Curtis et al. 2016), but different from Australia, Japan and Malaysia where the femoral access is quite popular (Al-Fiadh, Andrianopoulos et al. 2011, Ahmad, Ali et al. 2013, Numao, Suzuki et al. 2019). The prevalence of treated lesions classified as ACC/AHA type B2 and C in our study (94%) is higher than data in previous studies (60-70%) (Kiatchoosakun S 2010, Yeoh, Yudi et al. 2017). VNHI is the largest provider of cardiac intervention nationwide, where patients with PCI may have advanced coronary lesions subsequent to milder lesions being treated at other hospitals with potential less experienced interventionists. Greater number of type B2 and C lesions might also be attributed to the use of longer stents in our study. The use of DES was universal, which contrasts with a more mixed picture elsewhere (Akhter, Milford-Beland et al. 2009, Al-Fiadh, Andrianopoulos et al. 2011, Park, Kim et al. 2014). Regarding medication used, our patients were less likely to receive glycoprotein IIb/ IIIa, but tended to be prescribed with ticagrelor when compared to their counterparts in other studies (Al-Fiadh, Andrianopoulos et al. 2011, Lee, Hairi et al. 2013). Similar to some regional countries (Ahmad, Ali et al. 2013, Yeoh, Yudi et al.

2017, Han, Park et al. 2018), our data showed the left anterior descending and the right coronary artery were the most common lesion locations and the rate of in-stent restenosis was low (5%). The procedural success rate was as high as other countries in the Asia Pacific (APAC) region, despite some differences in clinical practices (Reid, Yan et al. 2014).

It is worth mentioning some gender differences observed in the present study. In general, females receiving PCI had lower procedural risks relative to males. Results from the GRACE registry indicated that females were more likely to have normal/mild diseases and less likely to have injured lesion in left main vessel (Dey, Flather et al. 2009). Although this is not direct comparison as GRACE contained patients undergoing catheterization only, our finding is in line with that result. Similarly, a nationwide study in patients undergoing PCI in South Korea reported that males had more chronic lesions in left main vessel, and required a higher number of stents than females (Park, Kim et al. 2014). Data from a national cardiovascular registry in America also revealed that females had a lower risk of angiographic features, and needed shorter stents (Akhter, Milford-Beland et al. 2009).

5.4.3 In-hospital outcomes and medications post PCI

Overall, our data showed lower rates of in-hospital outcomes among patients undergoing PCI compared with other countries in the APAC region (Reid, Yan et al. 2014). For instance, the rate of in-hospital death (0.6%) was the lowest when compared to the corresponding data in other studies in China (2.2%), South Korea (2.3%) and Australia (2.2%) (Zheng, Curtis et al. 2016, Jang, Han et al. 2017, Yeoh, Yudi et al. 2017). Our PCI participants were also more likely to have shorter hospital stay (2 days)

than their counterparts in China (10 days) and Australia (4.2 days) (Zheng, Curtis et al. 2016, Yeoh, Yudi et al. 2017). The observed differences were partly attributed to the higher proportion of non-ACS patients in our cohort in comparison with other databases. Previous evidence also confirmed that patients with more acute symptoms and server morbidities often stay in hospital longer than non-acute coronary patients (Chambers, Dehmer et al. 2009, Seto, Shroff et al. 2018). Shorter duration of hospital stay may also indicate a low mortality rate before discharge in this study, and such a potential relationship will be investigated in the future. Regarding post procedural medication use, our results are in line with some other reports in Asia. For instance, aspirin was immediately provided to most patients after PCI procedure and remained until post discharge (Asia-Pacific ACS Medical Management Working Group, Huo et al. 2015). Despite the wide variation of DAPT in the region, aspirin and clopidogrel were also used as the most common DAPT in our study, so were studies from South Korea and China (Zheng, Curtis et al. 2016, Han, Park et al. 2018).

Previous studies have largely reported that, females were at a higher risk of having complications or worse PCI-specific outcomes, e.g. death, bleeding or cardiogenic shock than males (Akhter, Milford-Beland et al. 2009, Al-Fiadh, Andrianopoulos et al. 2011, Chua, Shyu et al. 2014). Likewise, females in our study were more likely to have major bleeding relative to males. It is possible that females were older, had a higher prevalence of coronary risk factors, and a smaller body size as well as smaller arteries than males at the time of PCI procedure (Akhter, Milford-Beland et al. 2009, Park, Kim et al. 2014). It is also worth noting that most current PCI-based devices and medication therapies have been designed relatively equally between males and females, without a specific gender indication (Lansky, Hochman et al. 2005). Thus,

more focused efforts should be taken to prevent and reduce bleeding complications in female patients with PCI.

5.4.4 Study limitations

There are some limitations to our study. Despite data was collected at the national and biggest cardiac interventional centre in Vietnam, our findings might not be representative of the whole nation, particularly in terms of lesion type and uptake of cutting-edge interventions as VNHI is a single centre only. Furthermore, some uncertainties and recall errors of patients in self-reporting the socioeconomic status as well as cardiovascular risk factors might occur, which can contribute to the differences observed. Additional dedicated studies should be conducted to provide more overall views of PCI practices in Vietnam.

5.5 Conclusion

Our study based on the first Vietnamese PCI registry provides an opportunity to understand current insights of clinical characteristics and in-hospital outcomes of patients undergoing PCI in Vietnam. It also indicated gender differences in demographic and clinical characteristics together with procedural performance and in-hospital outcomes. The findings may contribute to evaluating PCI-related practices, identifying the gaps in sex-specific care for cardiovascular health, and potentially developing appropriate treatment guidelines.

Chapter 6 OUTCOMES FOLLOWING THE PERCUTANEOUS CORONARY INTERVENTION IN CONTEMPORARY VIETNAMESE PRACTICE: INSIGHT FROM THE INITIAL REGISTRY EXPERIENCE

This chapter addresses objectives 3 and 4 of the thesis, which examines the PCI outcomes of patients undergoing PCI in Vietnam at discharge, 30 days and 12 months. The predictors for adverse PCI outcomes at 12 months are also investigated. The following publication based on this chapter is currently under revision at a peer-reviewed journal.

Outcomes following the percutaneous coronary intervention in contemporary Vietnamese practice: insight from the initial registry experience.

6.1 Introduction

CHD remains the leading cause of death worldwide. Management of CHD continues to evolve; advanced myocardial revascularisations such as PCI have long been considered an important method for the treatment of CHD (Windecker, Stortecky et al. 2014, Verdoia, Barbieri et al. 2018), but uncertainty remains about their effectiveness across different settings and patient groups. Improving outcomes for patients following PCI is still a major focus of contemporary clinical practice, especially when patients present with severe symptoms such as AMI or ACS prior to the procedure (Tong, Xiang et al. 2016, Bhattarai, Ibrahim et al. 2020). Data from previous studies have shown that outcomes post PCI among AMI patients were much worse than among other patient cohorts. For instance, the death rate in the AMI group has been estimated to be approximately 3 times higher than in non-AMI groups (National Cardiovascular Disease Database 2016, Biswas, Duffy et al. 2018, Han, Park et al. 2018). It has also been reported that outcomes post PCI might differ according to various patient factors including demographics, co-morbidities, clinical presentation and angiographic characteristics (Ajani, Reid et al. 2008, Koh, Khin et al. 2011, Yap, Singh et al. 2018). In Southeast Asia, previous studies from some countries have identified a number of factors associated with outcomes post PCI such as ethnicity, gender, and age. However, information from many countries in the region remains limited, especially in relatively lower-income countries (Tungsubutra, Tresukosol et al. 2007, Koh, Khin et al. 2011, Lee, Hairi et al. 2013). Identifying these factors would be beneficial for benchmarking performance, understanding clinical outcomes and developing a reliable prediction model for outcomes of patients undergoing PCI in contemporary clinical practices.

This paper, using data from the first PCI registry in Vietnam, aims to report outcomes post PCI of patients and identify key factors associating with cardiovascular outcomes at 12 months.

6.2 Methods

6.2.1 Study setting

Data were derived from a registry, established at the Vietnam National Heart Institute (VNHI), Hanoi, Vietnam during September 2017-May 2018. Full details of this PCI registry were previously described (Vu, Pham et al. 2020, Vu, Nguyen et al. 2020). Briefly, this is a prospective cohort study. The main outcomes are death and MACCE following PCI and main exposure is the PCI. The hypothesis is that the demographic and clinical factors would be adversely associated with death and/or MACCE post procedures. Information on demographic, clinical and procedural information, and outcomes of patients who underwent PCI was recorded on standardised data abstraction forms with standard definitions for all fields. Data collection was conducted by a team of specifically trained local investigators at VNHI. In hospital, patients' outcomes were collected via extracting medical records, while outcomes of patients at 30 days were collected in person or via phone interview, depending on the availability of patients. At 12 months, phone interviews were conducted to investigate the outcomes of patients. Patients had the right to opt out of the study without impacting on their care. In fact, six patients took the opt out consent in total of 1028 patients approached. From an initial sample of 1022 at baseline, 96 patients (9.4%) were lost to follow-up after 12 months. Thus, the remaining 926 patients were included in this study.

6.2.2 Definitions

Before reporting outcomes at 30 days and 12 months, a number of definitions are required. For the purposes of this work, acute myocardial infarction (AMI) was defined as an increase of cardiac biomarker values [ideally cardiac troponin (cTn)] above the 99th percentile upper reference limit and with at least one of following presentations: symptoms of ischemia; new pathological Q waves; new or presumed new significant ST-segment-T wave changes or new left bundle branch block; confirmed imaging evidence of new loss of viable myocardium or new abnormality in regional wall motion (Thygesen, Alpert et al. 2012). Additionally, based on the electrocardiographic manifestation, patients have new ST-segment elevation at the J point in two contiguous leads with the cut-points: ≥ 0.1mV in all leads other than leads V2-V3 where the following cut points apply: ≥ 0.2mV in men ≥ 40 years; ≥ 0.25mV in men < 40 years; or ≥ 0.15mV in women will be considered as an "ST elevation MI-STEMI" (Thygesen, Alpert et al. 2012). Non-ST-elevation myocardial infraction (NSTEMI) was defined if either of the following was present: ST-segment depression, T-wave abnormalities or ischemic symptoms, and an increase in creatine kinase or creastine kinase-MB ≥3 times the upper limit of normal (Thygesen, Alpert et al. 2012). Unstable angina (UA) was identified in the presence of prolonged chest pain without cardiac enzyme elevation (Victorian Cardiac Outcomes Registry 2015). The AMI group refers to STEMI and non-STEMI, while the ACS group includes AMI and UA. The strategy for the specific coronary intervention (e.g. choice of entry location, stent, medication) was at the discretion of the interventionists. Injured lesion segments were identified and coded following the definition of the coronary tree segments developed in the SYNTAX study (Sianos, Morel et al. 2005) and guidelines for the lesion type of ACC/AHA (Levine, Bates et al. 2016). A procedure was considered successful if there

was a residual stenosis of less than 10% following coronary stenting and the rate of coronary blood perfusion of thrombosis in myocardial infarction 2 or 3 flow.

6.2.3 Clinical outcomes

In-hospital outcomes included all-cause mortality, MACCEs, and major bleeding. Bleeding events were classified by BARC (Mehran, Rao et al. 2011) dividing bleeding into five levels according to clinical, laboratory, imaging evidence and healthcare required. Major bleeding was defined by any transfusion or by a fall in haemoglobin ≥ 3.0 g/dl. MACCEs was a composite outcome consisting of death, myocardial infarction, cerebrovascular accident or stroke and coronary revascularisation. At 30 days and 12 months, together with death and MACCEs, data on all rehospitalisation and unplanned cardiac rehospitalisation were recorded. Cardiac rehospitalisation was confirmed if patients need to re-admit hospital for cardiac reasons regardless the time of hospital admissions. 12 months data is the cumulative one of hospital and 30 days data, with an exception for cardiac rehospitalisation and unplanned cardiac rehospitalisation.

6.2.4 Statistical analysis

Categorical variables (e.g., medical history, procedural characteristics and outcomes) were first presented as numbers and percentages, while continuous variables were expressed as mean ± SD unless otherwise specified. Characteristics of study participants according to AMI status were compared using chi-square or Fisher exact tests and Independent samples t-test as appropriate. To identify independent predictors of worse outcomes at 12 months, multivariable Cox proportional hazards model and logistic regression model were estimated for mortality and MACCEs events,

respectively due to the only availability of time of death. Variables of the baseline characteristics were analysed in univariate regression, and significant variables with p <0.1 were included in the multivariate model. All p-values were two-tailed with statistical significance being defined as p ≤0.05. All statistical analyses were performed in SPSS (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL).

6.3 Results

6.3.1 Overall cohort

In 9-month study period, 1022 patients underwent PCI were included in the baseline survey. For follow-ups, 43 patients were lost to follow-up (4.2%) at 30 days and this figure increased to 96 (9.4%) at 12 months. This left a total of 926 patients for this analysis. An insight of the differences in baseline characteristics between groups of lost to follow-up and other patients in the cohort was also conducted and provided in the Appendix C. For the same period, 60 coronary artery bypass grafting were performed at VNHI.

Table 6.1 presents the characteristics of patients. In total, approximately one third of patients were aged ≥ 75 years, while two third were male. Hypertension, hyperlipidaemia and diabetes were the most common co-mobilities of patients in the cohort (67.3%, 30.2% and 27.8%, respectively). 34.7% of patients had the history of previous PCI. Among tests done prior to PCIs, 12.5 % of patients had a left ventricular ejection fraction ≤ 40%, while only 2.2% had moderate to severe renal impairment (defined as having Creatinine > 200µmol). The majority of procedures were performed via radial access site (78.7%). Most lesions were categorised as type B2 and C and only ten percent of them was located in the left main artery. The mean number of

treated lesions per PCI was 1.23 ± 0.5 and the mean number of stents used per lesion was 1.52 ± 0.7. Only drug-eluting stents were used for PCI procedures at VNHI.

Table 6-1 Baseline clinical characteristics of patients undergoing PCI by AMI status

	All (n=926)	**Non-AMI (n=643)**	**AMI (n=283)**	**p**
Age ≥ 75 (years)	240 (25.9)	159 (24.7)	81 (28.6)	0.244
Male	640 (69.1)	439 (68.3)	201 (71.0)	0.449
BMI (kg/m^2), mean ± SD	22.19 ± 2.9	22.43 ± 2.9	21.65 ± 3.1	<0.001
Medical history				
Hypertension	623 (67.3)	459 (71.4)	164 (58.0)	<0.001
Diabetes mellitus	257 (27.8)	205 (31.9)	52 (18.4)	<0.001
Hyperlipidaemia	280 (30.2)	230 (35.8)	50 (17.7)	<0.001
Current smoking	115 (25.4)	66 (22.3)	49 (31.2)	0.050
Prior cerebral vascular disease	135 (14.6)	96 (15.0)	39 (13.8)	0.716
Previous CABG	11 (1.2)	9 (1.4)	2 (0.7)	0.570
Previous PCI	321 (34.7)	279 (43.4)	42 (14.8)	<0.001
Tests prior to PCI				
Left ventricular ejection fraction ≤ 40%	103 (12.5)	64 (10.7)	39 (17.5)	0.012
Moderate to severe renal impairment [a]	20 (2.2)	10 (1.6)	10 (3.6)	0.094
Procedural characteristics				
Radial access site	729 (78.7)	506 (78.7)	223 (78.8)	>0.999
Left main disease	101 (10.9)	71 (11.0)	30 (10.6)	0.933
Lesion type B2 and C	881 (95.1)	602 (93.6)	279 (98.6)	0.002

Restenotic lesions	49 (5.3)	40 (6.2)	9 (3.2)	0.081
Number of stents used, mean ± SD	1.52 ± 0.7	1.51 ± 0.7	1.55 ± 0.7	0.420
Number of treated lesion, mean ± SD	1.23 ± 0.5	1.23 ± 0.5	1.25 ± 0.6	0.618
Stent used	914 (98.7)	635 (98.8)	279 (98.6)	>0.999
Balloon used only	3 (0.3)	2 (0.3)	1 (0.4)	>0.999
Procedural success	918 (99.1)	637 (99.1)	281 (99.3)	>0.999

[a] *Creatinine > 200µmol/l; BMI: body mass index; AMI: acute myocardial infarction, including ST-elevation and Non-ST-elevation; CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention*

6.3.2 Outcomes: In-hospital, 30 days and 12 months

Outcomes post PCI are presented in Table 6.2. In-hospital events in the total cohort were rare, including mortality (0.9%), MACCEs (1.6%) and major bleeding (1.9%). At 30 days, data revealed a cumulative mortality rate of 1.9%, a MACCEs probability of 3.8%, The corresponding rates at 12 months were 6.5%; 10.8% respectively. Patients tent to re-admit hospital for cardiac reason at 30 days (13.4%) rather than later period (from 2nd month to 12th month) (6.2%). The reason for re-hospitalization was not likely related to restenosis due to low rate of PCI procedures provided for unplanned cardiac re-hospitalization at 30 days (6/53 cases) and 12 months (9/38 cases), and there were no target lesion or vessel revascularization recorded.

Table 6-2 Outcomes in-hospital, 30 days and 12 months according to different subgroups

Outcomes	Total (926)	Non-AMI (n=644)	AMI (n=282)	p
In hospital				
Death	8 (0.9)	1 (0.2)	7 (2.5)	0.01
MACCEs	15 (1.6)	4 (0.6)	11 (3.9)	0.01
Major bleeding	18 (1.9)	12 (1.9)	6 (2.1)	>0.999
At 30 days				
Death	18 (1.9)	5 (0.8)	13 (4.6)	<0.001
MACCEs	35 (3.8)	15 (2.3)	20 (7.1)	0.001
Cardiac rehospitalisation	124 (13.4)	81 (12.6)	43 (15.2)	>0.999
Unplanned cardiac rehospitalisation	53 (5.7)	32 (5.0)	21 (7.4)	0.419
At 12 months				
Death	60 (6.5)	27 (4.2)	33 (11.7)	<0.001
MACCEs	100 (10.8)	47 (7.3)	53 (18.7)	<0.001
Cardiac rehospitalisation	58 (6.2)	41 (6.3)	17 (5.9)	0.955
Unplanned cardiac rehospitalisation	38 (4.1)	25 (3.9)	13 (4.61)	0.136

MACCEs: Major Adverse Cardiac and Cerebrovascular Events (composite of death, MI, cerebrovascular accident or stroke, or target vessel revascularisation); AMI: Acute myocardial infarction, including ST-elevation and not; 12 months data is the cumulative one of hospital and 30 days data, with an exception for cardiac rehospitalisation and unplanned cardiac rehospitalisation.

6.3.3 Predictors of outcomes at 12 months

Independent predictors of mortality at 12 months included patient age ≥ 75 years old (hazard ratio [HR], 0.38 [95% CI, 0.21–0.69]; p=0.001); being male (HR, 0.43 [95% CI, 0.20–0.90]; p=0.025); AMI (HR, 0.27 [95% CI, 0.10- 0.71]; p=0.008); left ventricular ejection fraction ≤ 40 % (HR, 0.39 [95% CI, 0.21-0.72]; p=0.003); unsuccessful procedure (HR, 0.14 [95% CI, 0.03–0.60]; p=0.008) (Figure 6.1).

Regarding MACCEs at 12 months, some similar factors were found to be independent factors, including age ≥ 75 years old (hazard ratio [HR], 0.54 [95% CI, 0.33-0.89]; p=0.015); AMI (HR, 0.29 [95% CI, 0.14-0.59]; p=0.001); left ventricular ejection fraction ≤ 40 % (HR, 0.41 [95% CI, 0.23-0.72]; p=0.002). The history of cerebral vascular disease (HR, 0.48 [95% CI, 0.28-0.85]; p=0.011) also was found to have significant impact on MACCEs at 12 months (Figure 6.1).

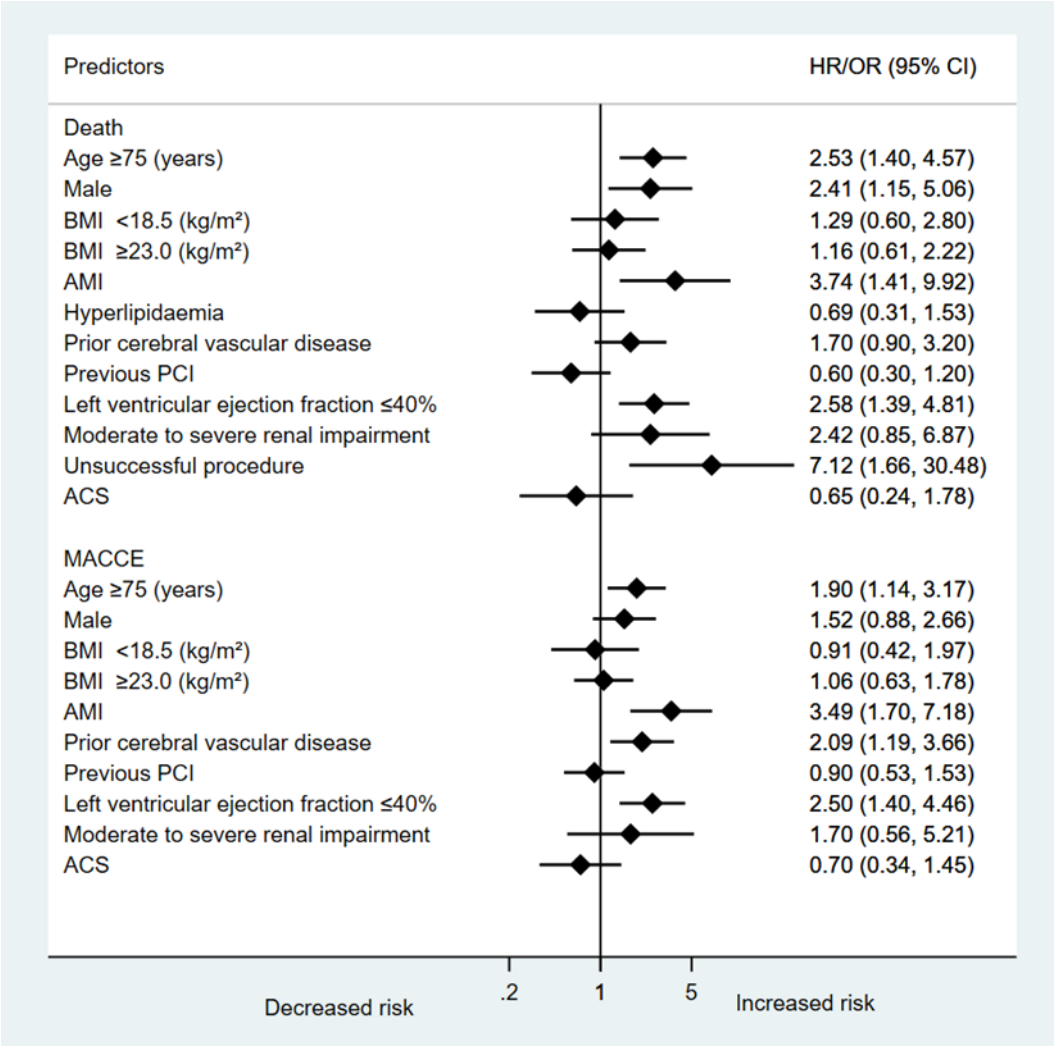

Figure 6-1 Association of demographic and clinical factors with death and MACCE at 12 months following PCI.

BMI: Body mass index; AMI: Acute myocardial infarction, including ST-elevation and not; PCI: Percutaneous coronary intervention; Moderate to severe renal impairment: Creatinine > 200µmol/l before the index PCI; MACCEs: Major Adverse Cardiac and Cerebrovascular Events (composite of death, MI, cerebrovascular accident or stroke, or target vessel revascularisation). ACS: Acute coronary syndromes, including myocardial infarction and unstable angina.

6.3.4 Comparison of subgroups

As shown in Table 6.1, non-AMI and AMI have the most differences in medical history, in which patients without AMI appeared to experience higher rates of risk factors than the AMI group, including morbidities such as hypertension, diabetes mellitus, hyperlipidaemia ($p<0.001$) and mean of BMI and previous PCI ($p<0.05$). Other differences were seen in tests conducted prior to PCI procedures and procedural characteristics, in which the AMI group had poorer left ventricular function and higher rate of lesions type B and C ($p=0.012$ and $p=0.002$, respectively). Similar pattern was seen in comparison of non-ACS and ACS group (Appendix C). Patients with non-ACS had more risk factors such as higher mean BMI, diabetes, hyperlipidaemia, and previous PCI in comparison with ACS group (all $p<0.05$). However, there were no differences in other variables.

Regarding comparison of the outcomes post PCI between the two groups, the AMI group had worse death and MACCEs rates in all time frames, including in-hospital, 30 days and 12 months (all $p<0.05$). (Table 6.2). Patients with ACS had worse death and MACCEs at 30 days and MACCEs at 12 months in comparison with non-ACS counterparts (all $p<0.05$) (Appendix C). There were no differences of cardiac rehospitalisation and unplanned cardiac rehospitalisation between subgroups.

6.4 Discussion

This study is the first to document the outcomes post PCI for Vietnamese patients across discharge, 30 days and 12 months and identify the independent factors for these cardiac outcomes at 12 months. The main findings are that worse outcomes of patients undergoing PCI were relatively low in the whole cohort; AMI and ACS patients had

worse outcomes than other counterparts; a number of factors such as being older than 75, being male, having AMI, left ventricular ejection fraction ≤ 40%, prior cerebral vascular disease and unsuccessful procedures were associated with worse outcomes at 12 months post PCI. These findings contribute to the literature concerning PCI outcomes in low and middle-income countries and be beneficial for benchmarking PCI practices in order to improve the quality of cardiac care as well as developing the prediction model of outcomes post PCI in Vietnam.

Our mortality rates were among the lowest in the APAC region both in-hospital and at 30 days. At discharge, our death rate was 0.9%, which was much lower than that rates reported by national PCI registries in Malaysia, Thailand, Korea or multi centres PCI registry in Australia (2.3%; 2.9%; 2.6% and 2.2%, respectively) (National Cardiovascular Disease Database 2016, Krittayaphong, Boonbaichaiyapruck et al. 2017, Yeoh, Yudi et al. 2017, Han, Park et al. 2018). This result was supported by the lower cardiogenic shock rate in our cohort compared with that in other studies (Krittayaphong, Boonbaichaiyapruck et al. 2017, Yeoh, Yudi et al. 2017). Another possible reason might be related to the culture in Vietnam, in which people want their relatives to pass away at home rather than at hospitals. However, a similar pattern was seen as the death rate of Vietnamese patients at 30 days remained low (1.9%) relative to that of Malaysia (2.8%) and Australia (2.6%) (National Cardiovascular Disease Database 2016, Yeoh, Yudi et al. 2017). Although our data was obtained only in VNHI, the leading hospital where might include the most experienced interventionists and advanced technology in Vietnam, these results still confirmed the initial success in managing the treatment of CHD patients via PCIs. At 12 months, it is noteworthy that our mortality rate was actually higher (6.5%) than that observed in Australia

(4.8%) and quite similar with that rate of Malaysia and Korea (6.8% and 6.0%, respectively) (National Cardiovascular Disease Database 2016, Yeoh, Yudi et al. 2017, Han, Park et al. 2018). One possible explanation might be that our patients who were mostly transferred from lower level hospitals to VNHI had a relative high prevalence of risk factors and co-morbidities. In addition, long distances from their hometowns might prevent them from returning to VNHI for intensive follow-ups. A second explanation might be that, while hospital care was comparable or superior in terms of preventing short-term events, follow-up might be sub-optimal and could be explored as a possible area of improvement in future.

Available studies often reported poorer outcomes for patients with AMI or ACS relative to the other counterparts, and these findings are reinforced in our study. Although our AMI patients seemed to have less cardiovascular risk factors and co-morbidities than other patients, their outcomes at all time frames were significantly worse. We anticipated, the development of atherosclerotic plaque might get triggered and promoted by the inflammatory markers in our AMI patients (Angiolillo, Biasucci et al. 2004, Elhajj, Haydar et al. 2004, Libby, Tabas et al. 2014). When compare with other studies in Australia and Korea, the mortality rates of our AMI patients were still lower at discharge and 30 days, and quite similar at 12 months (Biswas, Duffy et al. 2018, Han, Park et al. 2018). This pattern seemed to be similar to the pattern of mortality observed in the whole cohort relative to other registries in the region. Our ACS patients were also reported to have worse outcomes than non-ACS counterparts, similar to findings in previous studies (Izadnegahdar, Mackay et al. 2016, Hyun, Jeong et al. 2017).

Finding the independent factors for outcomes post PCI is essential for informing clinical practices and improving outcomes of patients undergoing PCI. In our cohort, being older than 75 years old, having AMI and left ventricular ejection fraction ≤ 40 % were found to predict both mortality and MACCEs events at 12 months, which have also been documented in previous studies across countries. For instance, older age was found to be the most common risk factor for worse cardiac outcomes at 12 months (Moonen, van 't Veer et al. 2010, Al-Fiadh, Andrianopoulos et al. 2011, Topaz, Finkelstein et al. 2017). Besides that, studies in Australia and Korea also identified AMI status and low grade of left ventricular ejection as independent predictors of mortality and MACCEs events at 1 year (Al-Fiadh, Andrianopoulos et al. 2011, Park, Kim et al. 2014, Yeoh, Yudi et al. 2017). Although the association of gender on cardiac outcomes remained controversial in current practices (Shrestha, Gami et al. 2013, Guo, Yin et al. 2018), our male participants seemed to have worse mortality outcomes than female counterparts (HR, 0.43 [95% CI, 0.20-0.90]; p=0.025). The potential reason was that male patients might have other characteristics predictive of poor outcomes, such as worse angiographic characteristics. National studies in Korea and America previously reported male patients had more chronic lesions in the left main vessel, required a higher number and longer stents than females (Akhter, Milford-Beland et al. 2009, Park, Kim et al. 2014). Other factors such as unsuccessful procedures and cerebral vascular disease prior to PCI were not found to associate with outcomes post PCI at 12 months in other studies. Although this is the first report regarding factors associating with outcomes with relatively small sample size, Vietnamese cardiologists and interventionists should recognise these factors in daily cardiac practices in the nation.

There are some limitations in our study. The first concern is that entire data in our study was collected in one leading cardiac hospital in Vietnam, therefore the findings might not generalise to the rest of Vietnam. Another limitation is that a number of patients lost to follow-up in our study, mostly due to the failure in contacting them by phone interviews, which might lead to the potential bias in reporting outcomes post PCIs. Further studies should explore more intensive methods to ensure that follow-up rates are maximised.

6.5 Conclusion

This study concludes that adverse outcomes in patients undergoing PCI in Vietnam are relatively low in comparison with those reported in other centres/registries across the APAC region. Several factors were identified to be associated with worse outcomes at 12 months such as being older than 75, being male, having AMI, left ventricular ejection fraction ≤ 40%, prior cerebral vascular disease and unsuccessful procedures. The findings have the potential to contribute to the development of PCI-related practices in Vietnam and elsewhere, identifying the gaps in clinical care for cardiovascular health, and potentially developing appropriate treatment guidelines.

Chapter 7 ACCESS ROUTES FOR PERCUTANEOUS CORONARY INTERVENTION AMONG VIETNAMESE PATIENTS: IMPLICATIONS FOR IN-HOSPITAL COSTS AND OUTCOMES

This chapter addresses objective 5, which estimates the in-hospital cost associated with PCI of patients undergoing PCI in the first PCI registry in Vietnam. The comparison between cost of two popular access routes are analysed to give an overall view of cost benefits for Vietnamese patients. The following peer-reviewed publication based on this chapter was accepted in The Lancet Regional Health-Western Pacific journal in 2021.

Vu TTH, Norman R, Pham NM, Pham MH, Nguyen TTH, Nguyen NQ, et al (2021). Access route selection for percutaneous coronary intervention among Vietnamese patients: implications for in-hospital costs and outcomes. The Lancet Regional Health-Western Pacific journal **(forthcoming).**

7.1 Introduction

Percutaneous coronary intervention (PCI) has been recognized as an effective treatment for individuals with coronary heart disease (CHD). While transfemoral access (TFI) is the traditional approach in cardiac catheterization, the use of transradial access (TRI) has grown significantly in the last two decades (Anjum, Khan et al. 2017). A number of randomized clinical trials and literature reviews have demonstrated favourable cardiac outcomes, shorter hospital stay, and better patient satisfaction for TRI relative to TFI (Agostoni, Biondi-Zoccai et al. 2004, Brueck, Bandorski et al. 2009, Jolly, Yusuf et al. 2011, Anjum, Khan et al. 2017). Nonetheless, data regarding differences in hospital cost incurred by PCI patients according to PCI entry sites are limited. The few studies that have examined this issue have been conducted in high and upper-middle -income countries and have suggested a cost saving associated with TRI in comparison with TFI, mostly because of the reduction in length of hospital stay (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016). As healthcare practice varies greatly by regions, it is unclear that the evidence from these cost evaluations can be generalized to other countries, especially those less economically developed for which there are limited data, and potentially quite significant differences in standards of care. Investigating the cost saving for PCI procedures is also crucial in those countries as it can contribute to reducing the very high economic burden of CHD patients and potentially reform the current PCI practices. Being aware of the cost differences in clinical practice, cardiac interventionists can make their choices about access routes of PCI to reduce the financial burden on patients and healthcare systems.

In Asia, where CHD is the leading cause of death (World Health Organization 2017, Thomas, Diamond et al. 2018) the use of PCI for CHD patients is of growing interest

in the region (Gao 2017). The widespread use of TRI in PCI procedures has been documented in recent studies (Jin, Li et al. 2016, Ahn, Lee et al. 2019), while the impact of PCI access sites on hospital cost and procedural outcomes has not been adequately reported. This paper, uses data from the first PCI registry in Vietnam, assessed in-hospital costs and post-procedural outcomes according to access sites and identified potential factors associated with in-hospital costs among patients undergoing PCI.

7.2 Methods

7.2.1 Study population

The study population was derived from a consecutive cohort of patients undergoing PCI from September 2017 to May 2018 at the Vietnam National Heart Institute (VNHI), Hanoi, Vietnam. Full details of the registry have been described elsewhere (Vu, Pham et al. 2020, Vu, Nguyen et al. 2020). A total of 1,022 patients were recruited in the registry from among 2,800 patients undergoing PCI at VNHI in the same period. Briefly, information on demography, cardiac status, procedure, and in-hospital cost of the participants was recorded by interviewing patients, extracting medical records, reading procedural discs and exploring the admission system. From the total pool of patients, those who underwent >1 PCI (n=78) were excluded, as it is difficult to attribute the bleeding events to a single procedure with certainty. Patients with cardiogenic shock (n=11) and those with missing cost data (n=66) were also excluded as these groups were associated with extremely high outlier costs or no information on total cost, respectively. When >1 entry location was used in one PCI, the primary access site was the one allowing the completion of the procedure. After these exclusions, our study population consisted of 868 patients with 694 TRIs and 174 TFIs.

7.2.2 In-hospital cost and outcomes

The primary outcome was total in-hospital costs from the day of admission to discharge. Our cost data were obtained from the hospital admission system and classified under the following categories: PCI costs (guide wire, IVUS, balloons and stents); medication costs; examination/ laboratory costs; hospital bed costs; operation costs (electrocardiogram in the ward and angiography); and medical supplies (syringes and needles).

In-hospital outcomes were defined as major adverse cardiac events (MACE), major bleeding events and length of stay (LOS, measured in days). MACE was a composite of in-hospital death, myocardial infarction, and coronary revascularisation. Bleeding events were classified by the Bleeding Academic Research Consortium-BARC (Mehran, Rao et al. 2011) indicating bleeding into five types according to clinical, laboratory, imaging evidence and health care required. Major bleeding was defined as BARC 3. Medical records were extracted to document these in-hospital outcomes.

7.2.3 Statistical analysis

Categorical variables (e.g., clinical, procedures, cost and outcomes) were presented as numbers and percentages, while continuous variables were expressed as mean ± SD unless otherwise specified. Unlike the randomized clinical trials, the choice of access point in real-world practice is often based on numerous factors, including patients' clinical characteristics and prognostic factors, therefore characteristics of study participants according to the two access sites were compared to see if there were any differences, using chi-square or Fisher exact tests and Independent samples t-test as appropriate. Median in-hospital costs and LOS were compared between TRI and TFI

with the Mann-Whitney U test, the unadjusted and adjusted differences were obtained by Median regressions. Characteristic variables with statistical significance (p-value <0.05) were selected for adjusting the cost differences. Logistic regression analyses were undertaken for two binary outcomes (major bleeding and MACE). Costs were converted into US Dollars, based on June 2019 exchange rates where 1USD=23,350 Vietnamese Dong. These costs were then log transformed due to the likely skew in cost data, and the normality of this logged data was explored by both graphical and analytical methods such as skewness, kurtosis, box plot, Shapiro-Wilk and Kolmogorov-Smirnov test (Ghasemi and Zahediasl 2012). Multiple linear regressions were performed to identify the influence of different independent variables on the independent variable-log total in-hospital cost. Independent variables included age (year, continuous), sex (male vs. female), level of support from health insurance (>80 and ≤80%), acute coronary syndrome (yes vs. no), hypertension (yes vs. no), diabetes (yes vs. no), current smoking (yes vs. no), prior stroke (yes vs. no), prior coronary artery bypass grafting (CABG) (yes vs. no), prior PCI (yes vs. no); trans-radial PCI (yes vs. no), left ventricular ejection fraction (<40% vs. ≥40%), moderate to severe renal impairment (yes vs. no), intravascular ultrasound (yes vs. no), left main disease (yes vs. no), PCI with ≥ 2 lesions (yes vs. no), PCI with ≥ 2 stents (yes vs. no), major bleeding (yes vs. no), and MACE (yes vs. no). Variables with p<0.1 in univariate regression analyses were included in the multivariable regression model. To assess potential predictors of in-hospital costs percentage changes were computed by exponentiating unstandardized coefficients and subtracting one from the resultant number and multiplying by 100. Relative importance of possible predictors of total hospital costs was evaluated using standardised regression coefficients. Subgroup analyses according to the presence or absence of ACS were also conducted to evaluate

cost and outcome differences All p-values were two-tailed with statistical significance being defined as $p \leq 0.05$. All statistical analyses were performed in SPSS (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL).

7.2.4 Ethics approval

The study received ethical approval from the Curtin University Human Research Ethics Committee (HRE 2017-0378) and Vietnam National Heart Institute provided reciprocal approvals for the study to be conducted and data analysed in Australia. A Patient Information Sheet was provided for every participant, which described clearly the purpose of the study, activities and rights of participants. It was voluntary to participate in the study and it is the right of participants to decline their participation or withdraw from the study via an 'opt-out' consent. The withdraw could occur at any time without any consequence. Each participant was assigned a unique ID which linked to the private information such as name, age, address, and phone numbers for follow- ups. All information that could be used to identify participants was coded and stored confidentially.

7.2.5 Role of the funding source

The funding source had no role in either study design, data collection, data analysis or interpretation and drafting the report. The corresponding author have full access to all data obtained from the study and have the final responsibility for publication submission.

7.3 Results

7.3.1 Clinical and procedural characteristics

Among the 868 patients in the eligible study population, TRI was the dominant access for PCI in our registry (694 patients, 79.9%). Table 7.1 compares demographic, clinical and procedural characteristics of TRI and TFI. Overall, the two target comparison groups had few differences in medical history and procedural characteristics. Patients undergoing TRI were relatively less likely to have previous coronary revascularization such as PCI and CABG (p=0.024 and p=0.005). They also tended to have less disease in the left main artery (p<0.001).

Table 7-1 Clinical and procedural characteristics of the study population by access location group

	TRI (n=694)	**TFI (n= 174)**	**P value**
Age (year), mean ± SD	68.3 ± 9.7	69.3 ± 10.6	0.209[a]
Male	469 (67.6)	117 (67.2)	>0.999
Percentage of health insurance (HI) support			0.337
Non-HI	13 (1.9)	4 (2.3)	
<60%	24 (3.5)	2 (1.1)	
60-80%	133 (19.2)	39 (22.4)	
>80%	524 (75.5)	129 (74.1)	
BMI ≥ 23.0 kg/m^2	264 (38.0)	73 (42.0)	0.390
Presentation			

ST-elevation myocardial infarction	93 (13.4)	18 (10.3)	0.341
Non-ST-elevation myocardial infarction	105 (15.1)	24 (13.8)	0.746
Unstable angina	165 (23.8)	42 (24.1)	0.999
Non-acute coronary syndrome	331 (47.7)	90 (51.7)	0.386
Medical history			
Hypertension	462 (66.6)	122 (70.1)	0.423
Diabetes mellitus	191 (27.5)	59 (33.9)	0.116
Hyperlipidaemia	209 (30.1)	62 (35.6)	0.189
Current smoking	75 (10.8)	19 (10.9)	>0.999
Prior cerebral vascular disease	94 (13.5)	25 (14.4)	0.874
Prior peripheral vascular disease	4 (0.6)	2 (1.1)	0.761
Previous CABG	4 (0.6)	5 (2.9)	0.024
Previous PCI	218 (31.4)	75 (43.1)	0.005
Tests prior to PCI			
Left ventricular ejection fraction <40%	68 (11.1)	14 (8.9)	0.513
Moderate to severe renal impairment [b]	12 (1.7)	6 (3.4)	0.268
Procedural characteristics			
Left main disease	45 (6.5)	35 (20.1)	<0.001
Restenotic lesions	30 (4.3)	11 (6.3)	0.478
PCI with ≥ 2 lesions	49 (7.1)	11 (6.3)	0.860
PCI with ≥ 2 stents	257 (37.0)	76 (43.7)	0.127
Drug-eluting stent use	683 (100.0)	168 (100.0)	_

Balloon only	7 (1.0)	2 (1.1)	0.871
Intravascular ultrasound	28 (4.0)	12 (6.9)	0.13

[a] Independent samples T test; [b] Creatinine > 200µmol/L; Otherwise were Fisher exact or chi-square tests; TRI =Transradial intervention; TFI =Transfemoral intervention; BMI = body mass index; CABG = Coronary artery bypass grafts.

7.3.2 In-hospital cost and outcomes

The median total hospital costs were 4132 and 5910 USD for patients undergoing TRI and TFI in our study (unadjusted cost difference: -1778 USD, approximately 30%). After accounting for baseline differences between the two groups (i.e. history of CABG and PCI, and left main disease), the adjusted difference was -1526.3 USD, indicating that the cost of TRI is lower than that for TFI by 25.8% ($p < 0.001$) (Table 7.2). While health insurance contribution was high (60-70%) in both groups, the out of pocket expenses of participants were 1093 and 1980 USD in TRI and TFI groups, respectively. The majority of in-hospital cost was driven by the particular PCI cost (over 80%) in both groups (Table 7.2). TFI was associated with higher costs in all particular cost categories such as PCI cost, medication cost, laboratory cost, hospital bed cost and medical supplies cost ($p<0.001$). Additionally, patients undergoing TFI were also more likely to have longer LOS, and procedural complications such as major bleeding ($p<0.001$).

Table 7-2 Hospital costs and clinical outcomes between transradial (TRI) and transfemoral (TFI) percutaneous coronary intervention (PCI)

	TRI (n=694)	**TFI (n= 174)**	**Unadjusted differences (95% CI) (TRI versus TFI)**	**Adjusted differences [d] (95% CI) (TRI versus TFI)**	**P value**
Hospital cost (USD [c]), Median					
Total hospital cost	4132.0	5910.1	- 1778.1 (-2253.3; -1302.8)	-1526.3 (-1996.2; -1056.3)	<0.001
Out of pockets	1093.4	1980.6	- 887.2 (-1130.3; -644.3)	-830.4 (-1075.7; -585.0)	<0.001
Health insurance support	3047.3	3661.2	- 613.9 (-723.9; -503.8)	-506.1 (-649.7; -362.4)	<0.001
PCI cost	3482.9	5077.8	- 1594.9 (-2053.1; -1136.5)	-1397.5 (-1875.7; -919.2)	<0.001
Medication cost	37.6	56.2	- 18.6 (-28.3; -9.0)	-18.4 (-26.2; -10.5)	<0.001
Examination/ laboratory cost	96.5	107.9	- 11.4 (-22.0; -1.3)	-12.2 (-24.1; -0.3)	0.020

Operation cost	293.0	296.2	- 3.2 (-5.0; -1.2)	-2.9 (-4.7; -0.9)	<0.001
Hospital bed cost	59.9	102.8	- 42.9 (-56.9; -28.7)	-38.8 (-50.5; -27.1)	<0.001
Medical supplies cost	30.6	31.4	- 0.8 (-1.7; -0.0)	-0.7 (-1.3; -0.1)	0.011
Length of stay (day), Median	4.0	6.0	- 2.0 (-2.9; -1.0)	-2.0 (-2.8; -1.2)	<0.001
Major adverse cardiac events (MACE) [b], n (%)	4 (0.6)	0 (0.0)	_	_	0.589
Major bleeding, n (%)	5 (0.7)	14 (8.0)	-7.3 (-11.4; -3.2)	-7.2 (-11.4; -2.9)	<0.001

[b] MACE was the composite of death, myocardial infarction, and coronary revascularisation; [c] One US dollar is approximately equivalent to 23,350 Vietnam dong (20 June 2019); [d] Factors adjusted for the difference: previous coronary artery bypass grafts; previous percutaneous coronary intervention; left main disease; stent used per lesion.

7.3.3 Impact of clinical, procedural and outcomes on in-hospital total cost

Procedural characteristics had the largest impact on total hospital cost, including trans-radial PCI, left main disease, PCI with ≥ 2 lesions and PCI with ≥ 2 stents (the standardized coefficients were -0.252; 0.121; 0.156; and 0.417, respectively) (all $p<0.05$) (Table 7.3). Additionally, patient's age and prior CABG also had an impact on total in-hospital costs ($p<0.05$).

Table 7-3 Impact of clinical, procedural and outcomes on in-hospital total cost

Characteristics[a]	Percentages changes of total hospital cost (%)	Standardized Coefficients β	P value
Age (5-year increment)	0.7	0.084	0.003
Hypertension	0.4	0.011	0.702
Diabetes	1.9	0.052	0.066
Prior CABG	9.5	0.056	0.048
Transradial PCI	-10.0	-0.252	<0.0001
Left main disease	7.1	0.121	<0.0001
PCI with ≥ 2 lesions	10.7	0.156	<0.0001
PCI with ≥ 2 stents	15.3	0.417	<0.0001
Major bleeding	-0.2	-0.002	0.954

CABG: coronary artery bypass grafting; PCI: percutaneous coronary intervention; MACE composite of death, myocardial infarction, and coronary revascularisation.

[a]With the exception of age variable, all variables are dichotomous and the absence of each variable is taken as the reference.

7.3.4 Subgroup analyses

Of 868 patients, the number of patients with ACS and without ACS who underwent PCI was 447 and 421, respectively (Table 7.4). Results of subgroup analyses by ACS status were consistent with those obtained from the analysis of all subjects. Compared with patients undergoing PCI through TFI, those who received TRI consumed lower in-hospital costs, had a shorter hospital stay and experienced less major bleeding in either ACS or non-ACS (all $p< 0.05$).

Table 7-4 Cost and outcomes differences between ACS and non-ACS group

	TRI	TFI	Unadjusted difference (95% CI)	Adjusted difference [d] (95% CI)	P value
ACS (n=447)					
Total hospital cost (USD [c]) median	4407.5	5422.4	-1014.9 (-1619.5; -410.3)	-1257.7 (-1833.6; -681.7)	<0.0001
Length of stay (day), median	4.0	6.0	-2.0 (-2.9; -1.1)	-1.0 (-1.9; -0.1)	<0.0001
Major bleeding, n (%)	3 (0.8)	8 (9.5)	-8.7 (-15.1; -2.4)	-8.9 (-15.7; -2.1)	<0.0001
MACE, n (%)	3 (0.8)	0 (0.0)	_	_	>0.9999
Non-ACS (n=421)					
Total hospital cost (USD [c]) median	4006.9	6159.3	-2152.4 (-2839.1; -1465.7)	-1965.2 (-2626.5; -1303.9)	<0.0001
Length of stay (day), median	4.0	7.0	-3.0 (-3.9; -2.1)	-2.0 (-2.9; -1.1)	<0.0001
Major bleeding, n (%)	2 (0.6)	6 (6.7)	-6.1 (-11.2; -0.8)	- 5.9 (-11.4; -0.5)	0.002
MACE, n (%)	1 (0.3)	0 (0.0)	_	_	>0.9999

ACS: acute coronary syndrome; MACE was the composite of death, myocardial infarction, and coronary revascularisation; [c] One US dollar is approximately equivalent to 23,350 Vietnam dong (20 June 2019); [d] Factors adjusted for the difference: previous coronary artery bypass grafts; previous percutaneous coronary intervention; left main disease.

7.4 Discussion

This study is the first to quantify in-hospital costs and outcomes between TRI and TFI in Vietnam. TRI was significantly associated with a lower cost of 1526.3 USD than TFI (25.8%), a shorter hospital stays and less major bleeding post procedure. The findings are important evidence in PCI cost saving, especially in this lower-middle-income country, where patients endure hardship for healthcare expenses. The result of this study can also contribute to amending clinical practice guidelines and assisting clinicians in making their decisions on the use of PCI.

7.4.1 In-hospital cost and post procedural outcomes according to the entry sites

Compared with TFI, the use of TRI in PCI practice has received more support partly because it was shown to reduce the bleeding associated with access sites and PCI complications (Rao, Cohen et al. 2010, Anjum, Khan et al. 2017, Batra, Rai et al. 2020). Although few studies have investigated cost differences between two different entry sites, among those reporting costs, similar results were reported. Early previous findings reported that TRI was associated with significant reduction in total hospital costs, e.g., up to 15% reduction relative to TFI (Mann, Cubeddu et al. 1998, Mann, Cowper et al. 2000). Recent data, both in countries where TFI has been the dominant access such as the USA, and countries where TRI was more preferred such as China and UK, also confirmed the favourable cost advantage of TRI relative to TFI (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016, Mamas, Tosh et al. 2017). Despite differences in the data analysis approach across studies, our findings were concordant with these results, suggesting the finding to be robust. The difference in in-hospital costs for the TRI group in our study was among the highest, compared

with other studies in China and USA (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016) (Figure 7.1). The characteristics of the two access site groups might be part of the explanation for this difference. Unlike these previous studies, our TFI patient group was likely to have more stents per lesion than the TRI group, probably due to more left main diseases in the former group. This difference subsequently increased the procedure cost, the major component of hospital cost.

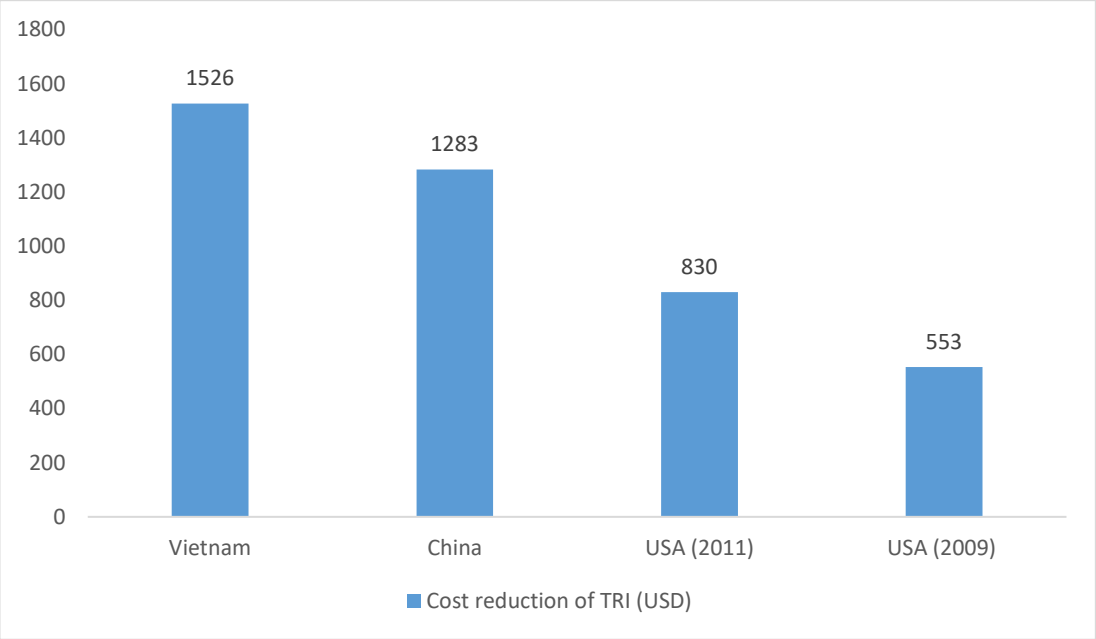

Figure 7-1 Cost reduction of trans-radial in total hospital cost

Comparison was made between Vietnam, China and USA (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016)

The health care system in Vietnam includes both public and private sectors and health care is not free for all people. Our study was conducted in a public hospital where health insurance can cover some components of total expenses that patients incurred in hospital. While health insurance contributed a large proportion of hospital cost of

all PCIs (60-70%), the cost difference in out of pocket expenditure was extremely significant in terms of the economic burden on patients, especially given the average monthly income per capita of Northern Vietnamese people was low (approximately 168 USD in 2016) (Vietnam 2016). Depending on the clinical presentation, diagnosis and prognosis of CHD patients, cardiologists will consider the appropriate care and treatment methods, such as PCI or medical therapy. In some very high cost health care such as PCI, the ability to pay might affect the treatment provided, especially in patients with low income and/or no health insurance. Therefore, identifying the in-hospital costs of patients undergoing PCIs using the two access points is an important consideration for future implementing TRI programs.

Regarding post-procedural outcomes in hospital of patients undergoing PCI, similar findings were found in our study. While the reduction advantage of TRI in bleeding complications was reported in most previous studies (Amin, House et al. 2013, Safley, Amin et al. 2013, Asrar Ul Haq, Tsay et al. 2016, Jin, Li et al. 2016, Batra, Rai et al. 2020), significant reduction of cardiovascular outcomes such as in-hospital mortality and MACE were also found in TRI group (Jin, Li et al. 2016, Batra, Rai et al. 2020). Additionally, patients undergoing TRI in India, China, Australia and USA were found to discharge earlier than their TFI counterparts (from 0.2 day to 2.3 days), which also contribute to the cost reduction (Safley, Amin et al. 2013, Asrar Ul Haq, Tsay et al. 2016, Jin, Li et al. 2016, Batra, Rai et al. 2020). Thus, our findings empirically support the recommendations of recent guidelines on adopting TRI in clinical and add economic evidence to promote the use of this approach in the community practice (Levine, Bates et al. 2011) (Kolh, Windecker et al. 2014).

7.4.2 Factor associated with hospital cost of patients undergoing PCI

Previous studies reported that the cost saving of TRI was related strongly with a reduced LOS and/or a lower rate of post procedural bleeding complication (Amin, House et al. 2013, Jin, Li et al. 2016, Mamas, Tosh et al. 2017). Similar findings were found in our study. Beside the main component of hospital cost (i.e. PCI cost), other cost differences were seen in terms of hospital bed costs, medication and laboratory tests, which indicated the significant contribution of LOS to the total hospital cost. Thus, to explore the potential effect of other factors associated with total hospital cost, we eliminated LOS in our analysis as LOS seemed to be affected by other factors such as post procedural complications. The result revealed total hospital cost was likely to be driven mostly by procedural characteristics, especially PCI with ≥ 2 stents and the PCI access sites. This result reinforced the highest contribution of PCI cost to total hospital costs observed in table 7.2. Findings from a study in China also supported our study, indicating that total hospital cost differences of PCI patients were related mostly to procedural cost, e.g., vascular closure devices (Jin, Li et al. 2016), while two studies in USA indicated that the cost saving of TRI was found only in terms of post procedural costs (Amin, House et al. 2013, Safley, Amin et al. 2013). This observation might be explained by the differences in health care systems in Western and Asian countries, which need to be investigated in further studies. Thus, our study reported that the procedural factors such as number of stents per lesion (≥ 2), PCI access sites having the most impact on the in-hospital cost of patients undergoing PCI. By reporting this finding, we believe that our study made a significant impact on clinical practice of PCI in the country. Even though TRI is the current preferred approach, the valued cost saving of TRI relative to TFI was reported for the first time in a reliable study, which supports the use of this location access in PCI practice at VNHI. The

interventionists and cardiologists might consider the result of this study in managing their practice at VNHI to provide the cost-effective care for patients, especially the ones who have financial hardship or no health insurance. This strategy can also be followed at lower level hospitals in Vietnam given the training and educational roles of VNHI.

There are some limitations in our study. First, cost data were obtained from the hospital admission system, which can reflect only cost incurred by patients during hospitalization, but not indirect costs such as food supplied or accommodation for the patient's families who came to care for the patient. Other costs prior to and after discharge was also not investigated. Second, despite adjustment of the cost and outcome differences, selection bias cannot be ruled out due to the nature of non-randomisation of access sites. In fact, most of the participants characteristics are similar between the TRI and TFI group. Another concern is that our data were only derived from the leading cardiac centre in Vietnam, where the highest technology might be applied, then findings might not be considered as representative for the whole nation, but provided important insight of PCI practices. More dedicated studies should be conducted to give full insights of in-hospital cost for the PCI practices in Vietnam.

7.5 Conclusion

Our study based on the first Vietnamese PCI registry provides an opportunity to understand current insights of in-hospital cost and outcomes of patients undergoing PCI according to entry sites in Vietnam. TRI was the most preferred access site and overall, patients undergoing TRI were associated with lower in-hospital costs, shorter LOS and favourable post-procedural outcomes in comparison with TFI. Procedural

factors such as PCI with ≥2 stents and PCI access sites had the most impact on in-hospital cost of PCI patients.

Chapter 8 DISCUSSION AND RECOMMENDATIONS

This chapter describes the contribution of the thesis, including a summary of the key findings, and a comparison of them with evidence from other studies. In addition, the strengths and limitations together with the significance of the research are presented. Lastly, recommendations for future research and health policies are drawn.

8.1 Contribution of the thesis

In Vietnam, a L-MIC located in Southeast Asia, the epidemiological transition in both mortality and morbidity has been underway for decades. CHD remains the leading cause of death and has placed a large economic and disease burden on the population. PCI has been a key option for many Vietnamese interventionists in this CHD population and the numbers of procedure are increasing annually. There were approximately 2,250 procedures performed in 2013 in a leading cardiac centre in Vietnam. However, understanding of PCI practice in the country remains limited due to the lack of available data. In the APAC region, although a number of studies regarding practices and outcomes post PCI have been conducted, geographic variation between different settings is a major barrier to generalisability of existing findings to the Vietnamese setting. Therefore, conducting research to obtain and report data from real practice of PCI in Vietnam is essential. Clinical quality registries have been well recognized as the corner-stone in quality and safety improvement of clinical care for many years. Using this mechanism, we established a model for a PCI registry in Vietnam with the aim of obtaining quality data, provide clinical insights and contributing to the PCI literature in the APAC region. The focus of this thesis has been: (i) the methodology of the first model for PCI registry in Vietnam and the viability of that model in real practice, (ii) patient profiles and clinical practice of PCI in Vietnam, (iii) outcomes post procedure at one and 12 months, (iv) predictors of worse outcomes post procedures, (v) in-hospital costs associated with PCI.

8.2 The main finding in context with other research

In our study, most of the obtained findings are in line with those of previous studies in the region. However, this thesis contributed to the consistency and generalisability of

the literature in the area of PCI due to reporting real data from a low resource setting in the establishment of a model for a clinical quality registry. Findings of each study in this thesis were discussed in detail in Chapter 4, 5, 6 and 7. This section summaries the main findings in the wider clinical context.

8.2.1 The methodology of the PCI registry

In the first attempt to develop a PCI registry model at a leading cardiac centre in Vietnam, the established model has some similarities with other PCI registries in the region such as using a standard abstraction form to collect consecutive patients undergoing PCI, providing sufficient training for investigators prior to data collection, performing clinical audit to ensure data quality and conducting follow-ups at 30 days and 12 months to investigate the outcomes of PCI (Liew, Rosli et al. 2008, Li, Dharmarajan et al. 2014, A, Mathew et al. 2017, Krittayaphong, Boonbaichaiyapruck et al. 2017). However, there were some specific characteristics in our methodology in conducting this study. We approached and collected patients undergoing PCI 4 days per week instead of all patients in the study period. We completed the CRF in a paper format only and did not transfer data into any web-based system to manage data like other studies (Liew, Rosli et al. 2008, A, Mathew et al. 2017, Krittayaphong, Boonbaichaiyapruck et al. 2017). The main reason for the differences in our study in comparison with others was the limited resource. However, this methodology also provided the opportunity for replicating the same study in other cardiac centres at relatively low cost.

8.2.2 The patient profiles and clinical practices

In comparison with other PCI populations, our patients are relatively older than average ages of other PCI patients in the region (Lee, Hairi et al. 2013, Yeoh, Yudi et al. 2017, Han, Park et al. 2018). Similar to other studies, our patients have relatively high rates of cardiovascular risk factors, the rate of dyslipidaemia is much lower in comparison with other populations. Conceivably, a healthy and low-fat diet in Vietnamese community might be part of the explanation (Nguyen, Strizich et al. 2013). Our participants presented with lower rate of ACS, especially with more popular presence of STEMI than in other studies. We anticipated that the patients at VNHI were mainly transferred from district or provincial hospitals where acute patients were more likely to receive medical therapy or PCI, and only more severe patients were referred to VNHI.

Choosing the optimal entry location for PCI practices has remained controversial for many years. There are some places where radial artery is more preferred such as in China (Zheng, Curtis et al. 2016), similar to our Vietnamese interventionists, but using the femoral artery as the access site is quite popular in Australia, Japan and Malaysia (Al-Fiadh, Andrianopoulos et al. 2011, Ahmad, Ali et al. 2013, Numao, Suzuki et al. 2019). Our patients have more treated lesions classified as ACC/AHA type B2 and C and required longer stents in comparison with other studies. VNHI is the leading cardiac centre and often admits PCI patients with potential advanced coronary lesions subsequent to milder lesions being treated at other hospitals. All the stents used were DES with no utilizing of BMS in our study, which differs with a more mixed picture elsewhere (Akhter, Milford-Beland et al. 2009, Al-Fiadh, Andrianopoulos et al. 2011, Park, Kim et al. 2014). For medications, our patients received less glycoprotein IIb/

IIIa, but more ticagrelor when compared to their counterparts in other studies (Al-Fiadh, Andrianopoulos et al. 2011, Lee, Hairi et al. 2013). Despite some differences in clinical practice, the rate of procedural success was as high as other countries in the Asia Pacific (APAC) region (Reid, Yan et al. 2014).

8.2.3 Outcomes post procedures

From the revealed findings, we can report that our mortality rates following PCI were among the lowest at discharge and 30 days and quite comparable at 12 months in the APAC region. At discharge, our death rate was much lower compared to the rates of 2.3%, 2.9%, 2.6% and 2.2% in Malaysia, Thailand, South Korea and Australia, respectively (National Cardiovascular Disease Database 2016, Krittayaphong, Boonbaichaiyapruck et al. 2017, Yeoh, Yudi et al. 2017, Han, Park et al. 2018). The lower cardiogenic shock rate in our cohort might be part of the explanation (Krittayaphong, Boonbaichaiyapruck et al. 2017, Yeoh, Yudi et al. 2017). Similar pattern was seen at 30 days (1.9% compared to 2.8% in Malaysia and 2.6% in Australia (National Cardiovascular Disease Database 2016, Yeoh, Yudi et al. 2017)). At 12 months, our death rate (6.5%) was quite similar with that rate in Malaysia and South Korea (6.8% and 6.0%, respectively) (National Cardiovascular Disease Database 2016, Yeoh, Yudi et al. 2017, Han, Park et al. 2018). It was attributed to the relative high prevalence of risk factors and co-morbidities of our participants.

Regarding the independent factors for outcomes post PCI, some factors found to be associated with worse outcomes in our cohort were also documented in previous studies across countries. Older age was reported previously to be the most common risk factor for worse cardiac outcomes at 12 months (Moonen, van 't Veer et al. 2010,

Al-Fiadh, Andrianopoulos et al. 2011, Topaz, Finkelstein et al. 2017). AMI status and low grade of left ventricular ejection were identified as independent predictors of mortality and MACCEs events at 1 year (Al-Fiadh, Andrianopoulos et al. 2011, Park, Kim et al. 2014, Yeoh, Yudi et al. 2017). While the impact of gender on cardiac outcomes remained controversial in current literature (Shrestha, Gami et al. 2013, Guo, Yin et al. 2018), we reported that male patients seemed to have worse mortality outcomes than their female counterparts (HR, 0.43 [95% CI, 0.20-0.90]; p=0.025). It is attributed to some characteristics predictive of poor outcomes of male patients, such as worse angiographic characteristics, similar to findings of national studies in South Korea and America (Akhter, Milford-Beland et al. 2009, Park, Kim et al. 2014).

8.2.4 In-hospital cost of PCI

Our findings of cost benefits in TRI group are in line with that of previous study despite the differences in choosing the dominant access artery for PCI procedures. Previous findings reported up to 15% cost reduction relative to TFI TRI (Mann, Cubeddu et al. 1998, Mann, Cowper et al. 2000), similar to recent reports in USA, China and the UK (Amin, House et al. 2013, Safley, Amin et al. 2013, Jin, Li et al. 2016, Mamas, Tosh et al. 2017). The cost difference in 2 common access sites in our study was among the highest, compared with other studies in China and USA (reduction of 1,283 USD and 830 USD per capita, respectively) (Amin, House et al. 2013, Jin, Li et al. 2016). It is partly explained by the differences in characteristics of the two access site groups. PCI procedures of TFI patient group was likely to use more stents per lesion, probably due to more left main diseases than the TRI group. This difference led to the increase in the procedure cost and subsequently the increased hospital cost.

Finding the factors associated with hospital cost is essentially important, especially with a high cost procedure as PCI. Our study revealed that total hospital cost was most likely to be driven by procedural characteristics such as the number of stents per lesion (≥ 2) and the PCI access sites. Similar findings were reported from a study in China, indicating that total hospital cost differences of PCI patients were related mostly to procedural cost, e.g., vascular closure devices (Jin, Li et al. 2016). Two studies in USA indicated that the cost saving of TRI was found to be related to post procedural costs (Amin, House et al. 2013, Safley, Amin et al. 2013). There requires more observation to investigate in further study.

8.3 Strengths and limitations

Throughout the analyses of this thesis, attempts were made to enhance strengths and decrease limitations in each chapter. Below is the overall strengths and limitations of the thesis, which need to be considered when interpreting the findings.

8.3.1 Strengths

This study has a number of strengths. Firstly, it was conducted in the leading cardiac centre in Vietnam, home to the most experienced cardiologists and operators, the highest patient throughput and advanced technology in the country. Given the national leadership role of this centre, pilot-testing the registry in this centre was considered vital for the future expansion across other centres in Vietnam. Additionally, the high volume of patients in the institute and their willingness to contribute their data through questionnaires facilitated the recruitment process. The significant number of PCI procedures performed daily, the availability of essential data in medical records and disks containing procedural images were advantageous for data collection activities

and contributed to a high level of data completeness. Secondly, this study was conducted based on the collaboration of the leader team in VNHI and longstanding registry leaders in Australia. This collaboration allowed the application of experiences of well-known registries in Australia into a lower resource setting and reflected local practices. For instance, the standardised data abstraction forms developed for the Victorian Cardiac Outcomes Registry in Australia were translated and revised by Vietnamese clinical cardiologists. The current dataset is appropriate for collecting sufficient data elements for registry purposes which are informing the practices and outcomes post procedures of patients. Data obtained in the study also can be compared with that of other registries in the region due to the use of standardised data abstraction forms. Avoiding collecting too much data also ensures the feasibility of data management, especially considering the impact of resources for staff time beyond the provision of routine care. Thirdly, the pilot registry was conducted with limited resources, where a single data manager was responsible for data collection at the institute, yet a representative sample was collected. A final data collection strategy included all patients undergoing PCI in 4 days per week (2 weekdays with routine practices and weekend with emergency cases only), which allowed the data collected to be considered as representative of the institute. Finally, a total sample of 1022 patients was recruited and was much larger than required sample size (273 patients), which gave the study more statistical power. From the data obtained in the registry, the study conducted significant data analysis to provide sufficient insights regarding real practices of PCI in Vietnam. Comparative stratification was performed in all data analyses, including sex differences, in hospital cost of PCI between 2 common entry locations, outcomes regarding disease groups. This allowed for better understanding

of group's differences in term of characteristics, clinical factors and outcomes post procedures.

8.3.2 Limitations

There are some limitations of the thesis. Firstly, the study obtained data in a single cardiac centre. Although it is the leading cardiac institute, results obtained might not be representative of the whole country due to the significant demographic variation of leading cardiac centre with lower level hospitals. Future development of the registry in smaller settings with potentially less experienced staff and less advanced technology may require some modifications to the approach used in VNHI. These modifications might include the sample collecting strategy, number of data elements and time and cost for data collection by staff. Secondly, though attempts were made to enrol a representative sample with limited resources, potential sample bias may exist. Therefore, where sufficient resources are available, collecting all patients undergoing PCI in the study period is recommended. Lastly, though all patients were reminded to revisit the hospital for examination, the majority of follow-up data was collected via phone calls which might lead to potential lost to follow-ups. The missing data of patients lost to follow-up might lead to survivor bias and affect the outcomes as well as the comparison with other registries. In further studies, we recommend conducting intensive follow-ups to maximize accuracy and efficacy.

8.4 Significance of the thesis

This study is the first to develop a model PCI registry in Hanoi, Vietnam. The country has experienced a large and growing burden of CHD, and PCI is widely used in cardiac therapy treatments for CHD patients. By adopting experiences of a longstanding PCI

registry in Australia into a different socioeconomic setting and achieving the initial success, this study confirm that such registry can be developed and sustained in the area of PCI. This achievement is an important step for further development of research into PCI in Vietnam. In the country, other cardiac centres can replicate the established model to provide insights of their PCI practices or collaborate for a multiple/ regional centre. Researchers and clinical staff in other fields also can use the experience from our study to develop a clinical quality registry in their clinical setting. From outside the country, this initial achievement encourages collaboration between countries, passing experiences and conducting more dedicated study.

Data obtained from the study were reported for the first insights regarding patient profiles, clinical outcomes post procedures, and cost related to PCI in Vietnam. Within the country, clinical staff and stakeholders have the opportunity to benchmark their daily practices, identify the potential gap in knowledge and might develop appropriate guidelines. Furthermore, these findings contributed significantly to the literature in the area of PCI, allowing comparison between study populations and potential opportunity for collaboration between countries.

8.5 Recommendations

Improving cardiovascular health outcomes post procedures of patients undergoing PCI and reducing cost related to PCI is among the most concern of population, clinical interventionists and stakeholders. From the findings of the study, we suggest some recommendations for patients, clinical staff and future research as follows:

8.5.1 For Vietnamese patients

Participants in our study had high prevalence of cardiovascular risk factors (often modifiable) and relatively high age. We recommend patients aged 60 years and older with cardiovascular risk factors pay more attention to their health status by following necessary treatment from medical staff and maintaining a healthy lifestyle, including smoking cessation. These activities are important to reduce the chance of developing CHD in these patients or contribute to preventing the emergent situations such as cardiac death or acute MI. Male patients should be more aware of the injured lesions even though they have lower rates of risk factors in comparison with females. All patients should know that PCI is a relatively safe procedure with very high rate of success and low rates of complications in choosing the optimal treatment therapy. Nonetheless, female patients might face the chance of developing major bleeding post procedures. Post PCI procedures, patients should be aware of the chance of developing medium and long-term complications post PCI at 30 days and 12 months such as death, acute MI and repeat revascularizations. In an attempt to prevent these complications, they should follow recommendations from cardiologists and procedural interventionists precisely in term of using medicine and attending follow-up at the hospital.

8.5.2 For clinical staff and stakeholders

Health staff and cardiovascular interventionists should be well aware of the patient profiles, clinical characteristics, outcomes post procedures and PCI cost for patients undergoing PCI in their daily practices, especially at VNHI. At admission, some points which need to be considered are the high prevalence of risk factors, old age and long distance from patients' residence to VNHI. During the procedure, interventionists

might consider the use of the radial approach in choosing the PCI access route, especially with patients having no medical insurance or exposing financial risk. Even though cardiac complications are rare in our study, interventionists should be particularly aware of major bleeding in women patients. For preventing medium and long-term adverse outcomes, recommendation of revisiting VNHI should be given to patients at discharge. While PCI procedures in Vietnam have very high procedural success rate and relatively low mortality rates of participants at discharge and follow-ups, cardiac interventionists should be aware of some factors associated with worse outcomes at 12 months, which are being older than 75 years, being male, having AMI, left ventricular ejection fraction ≤40%, prior cerebral vascular disease and unsuccessful procedures.

Health scientists and policy makers should pay more attention to current situation of PCI management in Vietnam, based on our findings in order to formulate intensive guidelines and instructions. These informative documents should be made available nationwide to patients, their families and medical staff.

8.5.3 For further research

Due to the ecologically significant variation in around 70 cardiac centres in Vietnam, patient profiles, clinical practices might differ across regions in the country. In order to make an overall picture of the management of PCI and post procedures outcomes in the nation, more dedicated research is recommended. Research with limited resources might consider our methodology in investigating patient characteristics, PCI managements and outcomes in other coronary interventional centres. Due to the variation in the settings of centres, some modifications should be applied such as

choice of variables collected and days of collecting data. When additional research resources are available, we recommend the following points to optimize the study: collecting all patients undergoing PCI in the study period; using electronic data storage systems; investigating the initial diagnosis with patients transferred from other hospitals; and conducting more rigorous follow-ups surveys. Furthermore, a study based on the collaboration of multi-centres in the country will enable the national model for PCI registry in the country.

Establishing clinical quality registry in other clinical fields is highly recommended. To complete such study, there are some points that might need to be considered: the volume of intervention/ procedure/ disease of the clinical quality registry; the suitability of data collection form; the availability of data elements; the resources in recruiting participants and data collection; the support from patients, clinical staff and leader teams; the financial support.

Study aiming to improve the outcomes post PCI at long term is recommended as we observed an increase in mortality at 12 months in our cohort. The researcher should be aware that patients might encounter some difficulties in readmit the hospital after initial procedures, which lead to limited information for data collection. More thoughtful methods of contacting patients should be considered such as managing them by the commune health stations, choosing patients in one specific province to facilitate the follow-ups.

Reducing cost of PCI procedures has received much attention in current literature reviews. Although our study achieved a first step in estimating the cost of PCI

procedures according to access routes, more dedicated studies are recommended. To overcome our limitations, information collected regarding in-direct cost and cost after discharge should be applied.

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Appendix A Paper 1

GLOBAL HEART

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ORIGINAL RESEARCH

Establishment of a Percutaneous Coronary Intervention Registry in Vietnam: Rationale and Methodology

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Background: In lower- and middle-income countries across Asia there has been a rapid expansion and uptake of percutaneous coronary intervention (PCI). However, there has been limited routine collection of related data, particularly around quality, safety and cost. The aim of this study was to assess the viability of implementing routine collection of PCI data in a registry at a leading hospital in Hanoi, Vietnam.
Method: A Vietnamese data collection form and collection strategy were developed in collaboration with the Vietnam National Heart Institute. Information on patient characteristics, treatments, and outcomes was collected through direct interviews using a standardised form and medical record abstraction, while PCI data was read and coded into paper forms by interventional cardiologists. Viability of the registry was determined by four main factors: 1) being able to collect a representative sample; 2) quality of data obtained; 3) costs and time taken for data collection by hospital staff; and 4) level of support from key stakeholders in the institute.
Results: Between September 2017 and May 2018, 1,022 patients undergoing PCI were recruited from a total of 1,041 procedures conducted during that time frame. The estimated mean time to collect information from patients before discharge was 60 minutes. Of the collected data fields, 98% were successfully completed. Most hospital staff surveyed indicated support for the continuation of the activity following the implementation of the pilot study.
Conclusions: The proposed methodology for establishing a PCI registry in a large hospital in Vietnam produced high quality data and was considered worthwhile by hospital staff. The model has the potential opportunity for replication in other cardiac catheterisation sites, leading to a national PCI registry in Vietnam.

Keywords: methodology; percutaneous coronary intervention; registry; Vietnam

Coronary heart disease (CHD) is consistently the leading cause of death worldwide, responsible for approximately 16.6% of total deaths in 2016 and places a large economic burden on the population [1, 2]. Since its inception in 1977, percutaneous coronary intervention (PCI) has been recognised as a valuable procedure for treating CHD patients and has become a common part of routine practice worldwide [3, 4]. The Asia-Pacific region is home to nearly 60% of the world's population, where CHD is now a leading cause of mortality [5, 6] and the development of PCI registries is of growing interest [7–9]. As a clinical quality registry, a PCI

database is an important mechanism for monitoring and benchmarking the performance of clinical care, improving safety and outcomes, contributing to reducing treatment cost and regulating guidelines [10, 11]. Nonetheless, there remains wide geographic variation in terms of the organisation, operation, management, sustainability and utilisation of data collected of PCI registries in Asia. Additionally, data are limited regarding the participation of less economically developed countries, particularly those in the South-East Asia region, including Vietnam [9, 12–14].

As a nation undergoing rapid economic and epidemiological transition, Vietnam has experienced a high burden of CHD, causing more than 58,000 deaths (11.6% of all mortality) in 2017 [15]. Vietnam began to adopt PCI in 1995 at the Vietnam National Heart Institute (VNHI), and has to date introduced this procedure to approximately 70 cardiac centres nationwide [16]. The annual number of PCI procedures is relatively large and increasing; for instance, there were 2,250 patients receiving this technique in 2013 in a single national centre and there is a 15% increase annually [17]. Notwithstanding its widespread use, there has been no PCI registry in Vietnam.

This paper presents the rationale, design and conduct of a pilot PCI registry model in Vietnam. The viability of implementing routine collection of PCI data was also assessed and documented. If viable, this would be the initial step in developing a model for an expanded PCI registry in Vietnam. The major objectives of this pilot study are 1) to describe the implementation experience at a large cardiac centre in Vietnam; 2) to describe the methodology for developing the PCI registry in Vietnam; and 3) to report on the viability of the strategy as a model for the nation.

Methods

Study setting

This PCI pilot registry project was conducted at the VNHI. Located in Hanoi, the capital city of Vietnam, VNHI is the biggest cardiac and referral centre in the country, providing the highest quality of healthcare services for cardiovascular patients in the country. Numerous advanced catheter-based therapies including complex coronary stenting, aortic stent grafting, transcatheter cardiac structural interventions, have become integrated into routine clinical practice at VNHI. As a 450-bed medical institution, VNHI receives around 17,000 inpatients and 80,000 out-patients annually, from across Northern Vietnamese provinces. The number of cardiac interventional procedures undertaken at VNHI is increasing from approximately 2,800 in 2004 to 12,000 in 2018 [17]. In addition, VNHI is an education and training centre, from which cardiovascular technologies and therapies are transferred into practice at other lower level medical institutions. VNHI was therefore selected for implementing the pilot PCI registry to reflect the contemporary practice of PCI in Vietnam.

Establishment of dataset

This study adapted the current versions of standardised data abstraction forms developed for the Victorian Cardiac Outcomes Registry (VCOR), Australia [18], including the standard case report form (CRF) and dataset definitions for all fields. The state-wide VCOR was built on the Melbourne Interventional Group registry [19], in which PCI data elements are in line with a number of current interventional registries worldwide, for instance, the American College of Cardiology – National Cardiovascular Data Registry [20]. The standard dataset aimed to collect the minimum standard data and avoid cumbersome management:

(1) The three page baseline survey, administered at time of presentation for procedures, contains 13 sections: patient details, admission data, clinical symptoms, clinical presentation, pre-procedural left ventricular function, risk factors, renal status, medication, procedure details, post-procedural cardiac biomarkers, in-hospital complications, discharge details and medications.
(2) The one page survey for 30-day and 12-month follow-up, including four sections: patient details, outcomes, medications and quality of life at 30 days and 12 months.

The VCOR data collection forms were translated into Vietnamese, and revised by two Vietnamese clinical cardiologists to reflect local practice. After discussion, consensus was reached around the addition of some new elements into the Vietnamese data collection forms, such as patient details (e.g. medical record number, ethnic group, poverty status, educational level, occupation, and income) and risk factors (e.g. smoking, dyslipidaemia).

The Vietnamese data collection forms were designed in the TELEFORM software [21] and printed in paper records. The specific questions for all three data collection points are presented in the Appendix.

Data collection

Following the finalisation of the data collection form, data recruitment commenced in September 2017. Potential participants were patients who underwent PCI at VNHI during the study period and met the following criteria: (1) Vietnamese residents aged 18 years and over; (2) Had at least one active phone contact number; and (3) Able to communicate, understand the information sheet and did not opt-out of future follow-ups by the time of discharge. There were no exclusion criteria. Under the strict clinical audit and strategy for data collection, baseline data collection was conducted over a 9 month period (from September 2017 to May 2018), followed by the 30-day follow-up, while the 12-month follow-up is underway.

Baseline survey

Baseline data were collected using a paper-based form through interviewing patients, visiting the catheterization laboratory where PCI was performed and extracting information from medical records. The data manager at VNHI and research assistants were responsible for conducting these activities. Compliance with the project protocol was supervised by staff trained in clinical audit processes. The patient interviews were largely conducted in wards, following the index PCI and prior to discharge when patients were medically well enough, as assessed by the responsible physician. Data on the index PCI (e.g. the PCI indication, entry location, adjunctive devices, lesion characteristics, in-stent restenosis, stent thrombosis, and stents used) were obtained from the catheterization laboratory. Images of coronary lesions were stored on protected disks, and printed, read and coded by a cardiologist. Other information was abstracted from medical records including time of admission, in-hospital management, medications used, clinical tests and pre-discharge complications (e.g. renal impairment, cardiogenic shock, bleeding [classified by the Bleeding Academic Research Consortium (BARC)]) [22], stroke, new or current myocardial infarction, target vessel or lesion revascularisation after the procedure (PCI or coronary artery bypass grafting). It took approximately one hour to complete a CRF on average.

Follow-up surveys

The 30-day and 12-month follow-up surveys were designed to capture data on the combined endpoint of major adverse cardiac and/or cerebrovascular events such as all cases of death, new or recurrent myocardial infarction or stent thrombosis, target vessel revascularisation or stroke; bleeding (BARC) [22]; rehospitalisation; medication use and health quality of life (mobility, personal care, usual activities, pain/discomfort, anxiety/depression, and own health state today) of participants after the index PCI.

At 30 days, a face-to-face interview was conducted by the data manager or research assistants if the participant was physically present at VNHI; otherwise, a phone interview was used. Supplementary information from a heart ultrasound and blood tests was recorded during the face-to-face interviews at VNHI, which lasted approximately 30 minutes.

The 12-month follow-up survey is beyond the scope of the current report, however the planned methods are as follows. A 15-minute phone interview is being undertaken by trained research assistants to obtain information from the patients directly. First-degree relatives are used as the proxy if the participant is not contactable. At least three attempts will be made to contact the participants. If patients have additional concerns regarding their health, then consultation will be available upon request following the interview.

Perspectives from VNHI

We also conducted an online survey with qualitative open-ended questions to explore perspectives on the implementation of the registry and identify key factors associated with successful implementation of this new model at VNHI. We approached all clinical, nursing and leadership staff involved in coronary interventional activity. The survey that contained 10 questions was administered using Qualtrics Research Suite (Qualtrics, Provo, UT), a web-based tool that allows researchers to build, distribute, and analyse online surveys in real time. Analysis of qualitative data was guided by the principles of the conventional and summative content analysis [23]. Briefly, responses obtained from participants were coded to identify and categorise different themes together with performing word counts. The interpretation focused on the several key factors that may influence the development and implementation of PCI registry in Vietnam.

Registry viability

This is the first study focusing on developing a model to collect data on the contemporary practice of PCI at the largest cardiac institute in Vietnam. The viability of the pilot PCI registry as a model for a national registry in Vietnam was determined by the following elements:

a) Being able to recruit a representative sample into the registry.
b) The quality of data collected, determined by data completeness and audit activities.
c) Costs and time taken to collect the data by hospital staff.
d) The level of support for the activity from patients, clinical staff and the cardiac institute.

Ethics approval

Ethics for the study was approved by the Curtin University Human Research Ethics Committee (HRE 2017-0378). Every participant was provided with a Patient Information Sheet in which the purpose of the study, activities and rights of participants were described clearly. Participating in this study was voluntary and participants had the right to decline their participation or withdraw from the study at any time without any consequence via an 'opt-out' consent. A unique ID was assigned to each participant and linkable to the private information such as name, age, address, and phone numbers for follow- ups. All information that identifies participants was coded and stored confidentially.

Results

Implementation experience

During the study period (from September 2017 to May 2018), patients who underwent PCI at VNHI and met the inclusion criteria were approached and invited to take part in the study. Three strategies were used to enrol patients as the pilot study progressed, with changes applied to recruitment and the corresponding results (**Figure 1**). The modification of the data collection strategy was implemented to ensure that, in the absence of resources to capture all cases, we were able to capture a representative sample and minimise the potential for selection bias in registry enrolment when a single data manager was responsible.

For the first period of data collection (September and October 2017), 6–7 patients were randomly selected from the total number admitted of each day. However, to eliminate the potential bias of choosing only good prognosis patients (i.e., without complications prior to and after the procedure), we moved to second approach (from November 2017 to March 2018) which aimed to collect all cases in two weekdays. Two particular weekdays (Monday and Tuesday) were chosen to capture data from all operators including two teams of interventionists who performed PCI at VNHI on alternate days during the week. Notably, this second period of data collection coincided with Tet (Lunar New Year's holiday), the biggest cultural event in the year, which may explain a reduction in the number of patient visits. The actual number of patients recruited in the period one and three may be generalizable to the rest of the year (i.e., from June to August) because there were no similar events in the year. Finally, the last period (from April to mid-May 2018) included all patients undergoing PCI on two weekdays and the weekend, which was designed to capture both the normal practice (weekdays) and acute cases (weekend).

A total of 1,028 eligible coronary patients were approached and invited from a total of approximately 2,800 patients undergoing PCI at VNHI during the study period. Six patients refused to participate in the study by opt-out consent and thus 1,022 patients remained in the baseline study sample, which included 1,041 individual PCIs (as 19 patients underwent PCI twice at VNHI). There was an extremely high rate of data

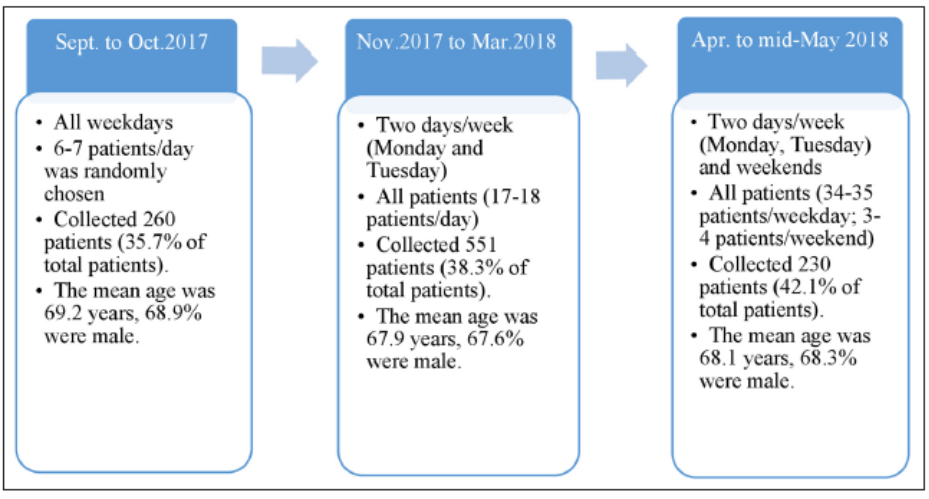

Figure 1: The data collection strategies.

completeness, with only information of one lesion missed due to a lost disk (0.1%). Ninety-eight percent of fields were fully filled, with the exception of oral anti-coagulant therapy as patients had difficulty recognising the kinds of drug used and unknown information about their referral to cardiac rehabilitation. The successful follow-up rate at 30 days was high, with 993 patients followed-up (97.2%).

Of the 25 invited cardiovascular professionals, 12 consented to participate in the qualitative survey (response rate: 48%). These 12 respondents included 5 cardiologists with administrative leadership at VNHI, 3 clinical cardiologists and 4 nurses. Several key additional factors concerning the successful implementation of a PCI registry in Vietnam were raised. Nine respondents agreed with the importance of standardised data collection forms as used in the registry. Other key facilitating factors were also emphasized, including well-trained investigators, the use of professional clinical audit, and strong support from leaders of target cardiac institutions. They also raised concerns regarding the sustainability of such a study at VNHI, including lack of data storage systems, sufficient funding for infrastructure and human resources, and strong commitment from hospital leaders.

Registry viability

The viability of the pilot PCI registry in VNHI was determined by the following elements:

a) Being able to recruit a representative sample into the registry. After several amendments, the data collection strategy captured all patients undergoing PCI at VNHI four days per week (2 week days with routine practice and weekend with emergency cases only). Thus, the sample recruited into the registry could be considered to be representative of coronary patients treated with PCI at VNHI when there were not sufficient resources to collect all cases.

b) Data quality. In total, we collected information on 99 data fields, and overall we had 98% data completeness. The reasons for this high completeness were the strong cooperation of patients and the availability of data resources (e.g., medical records, disks and machines in the catheterization laboratory). Additionally, the local clinical audit was performed monthly by well-trained staff, including case ascertainment (checking the collection of eligible data) and data quality assessment (reviewing source of data collection). Overall, 2% of cases were randomly checked and there were no significant errors in choosing patients and medical records. Thus, the quality and accuracy of data collected at VNHI was ensured.

c) Costs for and time taken to collect the data by hospital staff. It took approximately an hour to complete a CRF, including 15 minutes for interviewing patients, abstracting data from medical records and reading procedure information in the secured disks with the cardiologist. In further studies, data collection will be the responsibility of hospital nurses. Therefore, the actual time for completing the data collection form would be around or less than one hour because of the familiarity with routine PCI practice. While hospital nurses will do data collection as part of routine clinical activity, we estimated the cost required for data collection. If we use an average monthly income of a nurse at VNHI, which is approximately 1066 USD[1] [24], then the estimated time-cost of baseline data collection for one case, which is the income of hospital nurse in 1 hour, was equivalent to 1066/(30*8) = 4.4 USD.[2] In follow-up survey, approximate 15–30 minutes (phone or direct interviews) will be required for each patient, which was roughly equivalent to 1.1–2.2 USD.

d) The level of support from patients, clinical staff and the leader team. In the pilot registry, patients at VNHI had shown their strong engagement with the registry and there were no significant difficulties regarding the patients noted. The leader team and the hospital staff were well aware of the necessity to develop such a registry at the VNHI and in Vietnam and shown their universal support. They also belief that the establishment of the registry would be successful if there were sufficient data storing system, sufficient funding for human resources and improving the infrastructure, and strong commitment from hospital leaders.

Discussion

In the context of the growing interest in developing clinical quality registries worldwide, this paper reports the development of the first PCI registry in Vietnam, using and adapting experiences from longstanding registries in Australia [19, 25]. The work to date has demonstrated a PCI registry to be feasible and suitable for Vietnamese circumstances, providing a significant opportunity to extend the approach to other cardiac

[1] The exchange rate is 23.150 VND.

[2] 30 days were represented for 22 working days and extra shifts of hospital nurses.

centres looking to replicate the model. Importantly, implementing such a model not only provides crucial feedback on the performance of PCI for Vietnamese clinicians and cardiac care providers but also allowing a robust comparison with other regional registries such as those involved in the ASPECT collaboration [14] as well as contributing to the literature on the use of PCI.

In comparison with other regional PCI registries in Thailand, China, India and Malaysia, the methodology in our pilot registry had some similarities, including using a standard abstraction form to collect consecutive patients undergoing PCI, providing sufficient training for investigators prior to data collection, performing clinical audit to ensure data quality and conducting follow-ups at 30 days and 12 months to investigate the outcomes of PCI [8, 9, 12, 13]. Nonetheless, due to resource constraint, we did not approach all the patients undergoing PCI in the study period. The CRF was also completed in a paper format only and data obtained were not transferred to a web based system as other PCI registries [8, 9, 12]. Therefore, further studies might apply our methodology if there is limited resources or overcome our drawbacks if there is sufficient funding.

Although it is at an early stage, we are optimistic about the viability of the PCI model that we have implemented at the VNHI. The success of the PCI registry at the VNHI to date, is due to a variety of key factors such as the high number of patients undergoing PCI and their strong engagement with clinicians, the availability of data resources, and the supportive hospital staff team. We also faced several challenges in the first registry implement at VNHI, including high workload which might affect the time spent on data collection by the hospital staff and the lack of electronic record systems which made it difficult to collect comprehensive information when patients revisited the hospital. However, these obstacles can be minimised by providing sufficient training for clinical investigators, specifying sections of the data forms for investigators and conducting more detailed follow-up surveys.

One limitation is that the registry was conducted at VNHI, the leading cardiac centre in Vietnam where there is a highest patient throughput. Therefore, extending the methodology in establishing PCI registries in smaller settings with potentially less experienced staff may require a modified approach to that which we have done, but we believe this current work represents an important first step in doing so. Another potential concern may be bias in data collection, though attempt was made to enrol a representative sample. Thus, where sufficient resources are available, collecting all patients undergoing PCI in the study period would be recommended.

Conclusion

This paper describes the methodology of establishing the first PCI registry at the leading cardiac centre in Vietnam and reports on the viability of this model. We hope that the successful implementation of a PCI registry at VNHI will encourage other cardiac intervention centres in Vietnam to adopt this model in their daily practice and by doing so, enables the opportunity to develop a nationwide PCI registry.

Abbreviations

ASPECT	Asia Pacific Evaluation of Cardiovascular Therapies
BARC	Bleeding Academic Research Consortium
CHD	Coronary heart disease
CRF	Case reported form
PCI	Percutaneous coronary intervention
VCOR	Victorian Cardiac Outcomes Registry
VNHI	Vietnam National Heart Institute

Additional File

The additional file for this article can be found as follows:

- **Appendix.** PCI Form 1 – Baseline. DOI: https://doi.org/10.5334/gh.782.s1

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Competing Interests

The authors have no competing interests to declare.

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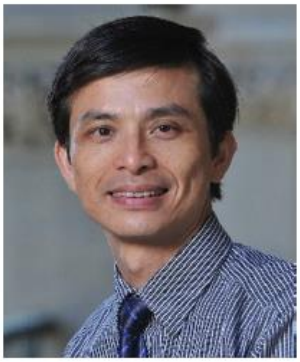

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Appendix B **Paper 2**

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Novel insights into clinical characteristics and in-hospital outcomes of patients undergoing percutaneous coronary intervention in Vietnam

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ABSTRACT

Background: Little is known about percutaneous coronary intervention (PCI) practices and outcomes in low-and middle-income nations, despite its rapid uptake across Asia. For the first time, we report on clinical characteristics and in-hospital outcomes for patients undergoing PCI at a leading cardiac centre in Vietnam.

Methods: Information on characteristics, treatments, and outcomes of patients undergoing PCI was collected into the first PCI registry through direct interviews using a standardised form, medical record abstraction, and reading PCI imaging data on secured disks. Subgroup analysis was also conducted to explore gender differences.

Results: Between September 2017 and May 2018, 1022 patients undergoing PCI were recruited from a total of 1041 procedures. The mean age was 68.3 years and two thirds were male. While 54.4% of patients presented with acute coronary syndromes, the rate of ST-elevation myocardial infarction was 14.5%. The majority of lesions were classified as type B2 and C and the radial artery was the most common access location for PCI (79.2%). The use of drug-eluting stents was universal and the angiographic success rate was 99.4%. Cardiac complications following PCI were rare with the exception of major bleeding (2.0%). Female patients were older with relatively more comorbidities and a higher incidence of major bleeding than males ($p < 0.05$).

Conclusions: Findings of this study provide an opportunity to benchmark current PCI practices in Vietnam, identify possible care gaps and potentially inform the adoption of treatment guidelines as well as use of prevention strategies.

1. Introduction

Percutaneous coronary intervention (PCI) has been demonstrated to be an effective treatment for coronary heart disease (CHD) worldwide since its inception in the late 1970s [1,2]. The procedure has become more widely used in Asia, where CHD was the leading cause of death (approximately 16.2% of all deaths in 2016) [3,4], with around one million PCIs undertaken in 2016 alone [5]. Notwithstanding the apparent benefits of PCI, post-procedural cardiac complications remain a concern, including death, myocardial infarction (MI) and bleeding [6,7].

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ACS, Acute coronary syndrome; APAC, Asia-Pacific; CABG, Coronary artery bypass grafts; CHD, Coronary heart disease; DAPT, Dual-anti platelet therapy; DES, Drug eluting stent; ECG, Electrocardiogram; GRACE, Global Registry of Acute Coronary Events; MI, Myocardial infarction; NSTEMI, Non-ST-elevation myocardial infraction; PCI, Percutaneous coronary intervention; STEMI, ST-elevation myocardial infraction; UA, Unstable angina; VNHI, Vietnam National Heart Institute.

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Accumulating data in the USA and Europe have shown that the occurrence of these adverse cardiac events differed according to patient characteristics, such as gender, age or comorbidities [6,8,9]. In Asia, cardiac registries in some high-income countries have also reported similar findings [10,11], while relevant data remains limited in lower-and middle-income countries. Additionally, most medical care provided for CHD patients in Asian countries is based on the European or North American guidelines developed from large domestic registries [12–14]. It is not clear whether the non-Asian data reflects the Asian experience, nor whether the guidelines are well suited to the Asian population. Thus, data from real-world practice in less developed countries are very important to establish current benchmarks and determine appropriate management and preventive strategies for these populations.

Vietnam is a middle-income nation in South-East Asia, where PCI has been widely used in modern cardiac based treatments for CHD, the second leading cause of death [15]. Data pertinent to PCI is scare on the epidemiology, management and outcomes of patients undergoing the procedure in Vietnam [16]. The aim of this paper is to provide novel insights concerning the clinical characteristics and in-hospital outcomes of patients undergoing PCI in Vietnam based on the first PCI registry conducted at a leading cardiac hospital in Vietnam.

2. Methods

2.1. Study setting

Data were derived from a registry, which was established at the Vietnam National Heart Institute (VNHI), Hanoi, Vietnam during September 2017-May 2018. Full details of this PCI registry was previously described [17]. As the leading cardiac centre nationwide, VNHI provides the highest quality of healthcare services for around 17,000 cardiovascular inpatients and 80,000 out-patients annually. In 2018, the total number of cardiac interventional procedures undertaken at VNHI was approximately 12,000 [16]. Initial discussions were held with clinical leaders in cardiology to ensure there was support for the implementation of the registry by senior clinical and executive staff.

2.2. Data collection

This single-centre, hospital-based registry adapted the data collection forms currently used in the Victorian Cardiac Outcomes and Melbourne Interventional Group registries, Australia [18,19]. Information on demographic, clinical and procedural information, and outcomes of patients who underwent PCI was recorded on standardised data abstraction forms with standard definitions for all fields. The study protocol was approved by the Curtin University Ethics Committee before the commencement of data collection (HRE 2017-0378). Patients had the right to opt out of the study without impacting on their care. Data collection was conducted by a team of specifically trained local investigators at VNHI.

2.2.1. Patient characteristics

Information on participant demographics, medical history, cardiovascular risk factors (diabetes, hypertension, dyslipidemia, cerebrovascular disease), clinical symptoms and presentation (acute coronary syndrome (ACS), cardiogenic shock, cardiac arrest), left ventricular ejection fraction, and pre-procedural renal status was collected via both patient interviews and medical records. ACS includes unstable angina (UA), non-ST-elevation myocardial infraction (NSTEMI) or ST-elevation myocardial infraction (STEMI). STEMI was defined as the presence of at least 0.1-mV ST-segment elevation or new pathological Q waves in ≥ 2 contiguous ECG leads or new left bundle branch block with elevation of cardiac enzyme levels above the reference range. NSTEMI was defined if either of the following was present: elevated cardiac enzyme levels above the reference range, ST-segment depression, T-wave abnormalities or ischemic symptoms. UA was named in the presence of prolonged chest pain without cardiac enzyme elevation.

2.2.2. Procedures and medications

The strategy for the specific coronary intervention (e.g. choice of stent, medication) was at the discretion of the interventionists. Injured lesion segments were coded following the classification of the Syntax Score [20] and guidelines for the lesion type of American College of Cardiology/ American Heart Association (ACC/AHA) [21]. A procedure was considered successful if there was a residual stenosis of less than 10% following coronary stenting and the rate of coronary blood perfusion of Thrombosis in Myocardial Infarction 2 or 3 flow. Pre and post procedural medical therapies such as oral antiplatelet, aspirin, anti-thrombin, and glycoprotein IIb/IIIa inhibitors were evaluated according to the 2016 ACC/AHA guidelines [22]. Medications and procedural data were obtained by extracting medical records and reading secured procedural disks.

2.2.3. Clinical outcomes

Medical records were extracted to document in-hospital complications including death, new or recurrent MI, cardiogenic shock, bleeding, post-procedural renal impairment, new requirement for dialysis, unplanned target vessel revascularisation (revascularisation for the previously cured coronary artery) by PCI or coronary artery bypass grafts (CABG), stent thrombosis, and stroke. MI was defined as an elevation of cardiac biomarkers more than 5 the upper limit of normal, and evolutionary ST-segment elevations or development of new Q-waves in at least 2 contiguous ECG leads. Cardiogenic shock was defined by hypotension (systolic BP <90 mmHg lasted from 30 min and over, evidence of end-organ hypo perfusion or elevated filling pressures).

Bleeding was classified by the Bleeding Academic Research Consortium [23], and major bleeding was defined by any transfusion or by a drop in haemoglobin ≥ 3.0 g/dl. Acute renal impairment was defined as a rise of creatinine ≥ 44.2 μmol/L or $\geq 25\%$ up to 5 days after the index PCI, compared to baseline creatinine. Stroke was defined as the patient's persistent loss of neurological function due to an ischaemic or haemorrhagic event [24]. Stent thrombosis was defined as the occurrence of a thrombus or angiographic documentation of vessel occlusion within a pre-existing stent or within 5 mm of the proximal or distal stent edges [25]. Medical records were reviewed to identify these cardiac events.

2.3. Statistical analysis

Data on demographic, clinical, procedures and outcomes were presented as numbers (and percentages) for categorical variables, and means (with standard deviations) for continuous variables. Descriptive statistics were used to summarise characteristics of the study participants. Fisher exact or Chi-square tests were undertaken to compare categorical variables, and Student's t tests or analysis of variance (ANOVA) were applied to compare continuous variables. All p-values were two-tailed with significance defined as $p \leq 0.05$. All statistical analyses were performed using the SPSS statistical package (SPSS Version 20.0 for Windows; SPSS Inc., Chicago, IL).

Table 1
Clinical characteristics (n = 1022).

	Overall	Female	Male	P value*
Patients	1022	326 (31.9)	696 (68.1)	_
Age (years), mean ± SD	68.3 ± 10.3	70.9 ± 9.4	67.0 ± 10.5	<0.0001 †
Kinh people	989 (96.7)	321 (98.5)	667 (95.8)	0.045
From provinces outside Hanoi	796 (77.9)	233 (71.5)	563 (80.9)	0.001
Education				
Primary school and lower	83 (8.1)	47 (14.4)	36 (5.2)	<0.0001
Secondary school	367 (35.9)	122 (37.4)	245 (35.2)	
High school	164 (16.0)	40 (12.3)	124 (17.8)	
College and higher	408 (39.9)	117 (35.9)	291 (41.8)	
Current/ past occupation				
Officer worker	389 (38.1)	120 (36.8)	269 (38.6)	<0.0001
Manual worker	163 (15.9)	67 (20.6)	96 (13.8)	
Farmer	255 (25.0)	107 (32.8)	148 (21.3)	
Tradesperson	64 (6.3)	17 (5.2)	47 (6.8)	
Others	151 (14.8)	15 (4.6)	136 (19.5)	
Poverty [a]	44 (4.3)	19 (5.8)	25 (3.6)	0.175
Low income [b]	762 (74.5)	279 (85.6)	483 (69.4)	<0.0001
Body mass index (kg/m^2)				0.071
Low (<18.5)	107 (10.5)	38 (11.7)	69 (9.9)	
Normal (18.5–22.9)	518 (50.7)	178 (54.6)	340 (48.9)	
High (≥23.0)	397 (38.8)	110 (33.7)	287 (41.2)	
ST-elevation myocardial infarction	148 (14.5)	38 (11.7)	110 (15.8)	0.097
Non-ST-elevation myocardial infarction	166 (16.2)	57 (17.5)	109 (15.7)	0.518
Unstable angina	242 (23.7)	83 (25.5)	159 (22.8)	0.402
Non-acute coronary syndrome	466 (45.6)	148 (45.4)	318 (45.7)	0.931
Left ventricular ejection fraction (%), mean ± SD	59.4 (±14.7)	61.7 (±14.6)	58.2 (±14.7)	0.001 †
Moderate to severe renal impairment [c]	25 (2.4)	5 (1.5)	20 (2.9)	0.283
Cardiogenic shock	11 (1.1)	3 (0.9)	8 (1.1)	>0.999
Cardiac arrest	6 (0.6)	2 (0.6)	4 (0.6)	>0.999

Data are presented as n (%), otherwise specified.
*Comparing female and male subjects; [a] Obtained certificates of poor and near poor household; [b] Individual monthly income < 216 USD with the exchange rate of 23.150 VND; [c] Creatinine > 200 μmol/L.

3. Results

3.1. Patient characteristics

A total of 1022 patients were enrolled into the registry. Of these, 19 patients had a second PCI, meaning a total of 1041 procedures, treating 1276 lesions.

Demographics and clinical characteristics of participants are summarized in Table 1. Two-thirds of the study population were male. The participants' mean age (±SD) was 68.3 years (10.3) and females were approximately 4 years older than men ($p < 0.0001$). The majority of patients were Kinh (96.7%), the largest ethnic group in Vietnam, and those living in other provinces outside Hanoi accounted for nearly 80%. The proportions of participants with college or higher education, conducting office work and with a low income were 39.9%, 38.1% and 74.5%, respectively.

In total, 54.4% of the patients presented with ACS, with the respective prevalence of STEMI, NSTEMI and UA being 14.5%, 16.2% and 23.7% (Table 1). Only 1.1% of the participants experienced cardiogenic shock, and 0.6% had cardiac arrest before PCI. The prevalence of overweight or obesity (BMI ≥ 23.0 kg/m^2) was 38.8%. The prevalence of hypertension, previous PCI and hyperlipidaemia were 67.2%, 35.1% and 29.9%, respectively (Fig. 1).

Compared with males, females had a lower education level, monthly income and were more likely to do manual work ($p < 0.0001$). Additionally, females also had a higher prevalence of risk factors such as hypertension, diabetes, and hyperlipidaemia ($p < 0.05$) with the exception of current smoking and previous PCI ($p < 0.05$) compared to males.

3.2. Lesion, procedural characteristics and medications prior to PCI

There were 1276 lesions which required subsequent treatment within 1041 procedures (Table 2). A total of 1275 lesions was used for analysis due to missing information of one lesion. Radial artery and left anterior descending (LAD) were the most common procedural entry and target vessel (79.2% and 46.7%, respectively). 11.9% patients were undergone left main PCI. Although 94.2% of the lesions were type B2 and C according to ACC/AHA classification, there was a high rate of angiographic success (99.4%). Just above one-third of the lesions required at least 2 stents and almost 96% of stents used were over 20 mm in length. Drug eluting stents (DES) were used in all cases and IVUS was utilized in 3.6% of cases. Common agents used prior to PCI were antithrombin, clopidogrel and aspirin, accounting for 36.2%, 80.0% and 97.5%, respectively. Prior to procedures, patients were given low-molecular-weight-heparin, while unfractionated heparin was used during PCI.

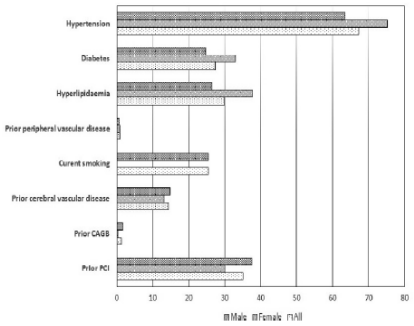

Fig. 1. Risk factors of study participants.

Compared with females, males were more likely to have disease in the left main coronary artery, chronic total occlusions, stent restenosis, and ≥ 2 stents per lesion ($p < 0.05$). They tended to receive ticagrelor, while their female counterparts were relatively

Table 2
Lesion, procedural characteristics and medications prior to PCI (n = 1276*).

	Overall	Female (n = 406)	Male (n = 870)	P value
Lesions	1276	406 (31.8)	870 (68.2)	_
Percutaneous entry location				
Radial	824 (79.2)	263 (79.2)	561 (79.1)	>0.999
Femoral	217 (20.8)	69 (20.8)	148 (20.9)	
Target vessel				
Left main	152 (11.9)	29 (7.1)	123 (14.2)	<0.0001
Left anterior descending	596 (46.7)	208 (51.2)	387 (44.5)	0.030
Right coronary	406 (31.8)	118 (29.1)	288 (33.1)	0.164
Circumflex	271 (21.2)	80 (19.7)	191 (22.0)	0.394
PCI with ≥ 2 lesions	218 (17.1)	69 (17.0)	149 (17.1)	>0.999
Type B2 and C lesions	1202 (94.2)	381 (93.8)	821 (94.5)	0.745
Chronic total occlusion	61 (4.8)	10 (2.5)	51 (5.9)	0.012
Restenotic lesions	64 (5.0)	11 (2.7)	53 (6.1)	0.014
Stents used for each lesion				
≤1	788 (61.8)	271 (66.7)	517 (59.5)	0.015
≥2	487 (38.2)	135 (33.3)	352 (40.5)	
Mean (±SD)	1.5 (±0.71)	1.42 (±0.64)	1.54 (±0.74)	0.002
Stent length > 20 mm	1181 (95.9)	375 (95.2)	806 (96.2)	0.502
Mean stent length (±SD)	34.6 (±8.7)	34.5 (±8.9)	34.7 (±8.7)	0.656
Angiographic success	1267 (99.4)	405 (99.8)	862 (99.2)	0.448
Drug-eluting stent use	1231 (96.5)	394 (97.3)	837 (97.1)	0.998
Balloon only	36 (2.8)	11 (2.7)	25 (2.9)	
Guidance of IVUS	46 (3.6)	13 (3.2)	33 (3.8)	0.654
Medications				
Fibrinolytic therapy	2 (0.2)	1 (50.0)	1 (50.0)	0.536
Glycorprotein IIb/IIIa	0 (0.0)			
Antithrombin therapy	377 (36.2)	111 (34.3)	266 (37.5)	0.227
Ticagrelor	176 (16.9)	35 (10.5)	141 (19.9)	<0.0001
Clopidogrel/Ticlopidine	833 (80.0)	284 (85.5)	549 (77.4)	0.003
Aspirin	1015 (97.5)	320 (96.4)	695 (98.0)	0.172

*missing information of one lesion.
Data are presented as n (%), unless specified. IVUS: Intravascular Ultrasound.

more likely to be prescribed with clopidogrel prior to PCI (both $p < 0.05$).

3.3. In-hospital outcomes and medications post PCI

Complications following PCI during hospital stay were rarely observed, with a relatively small proportion of new renal impairment and post-procedural bleeding (3.2% and 2.0%, respectively) (Table 3). Median length of hospital stay was 2 days and over 92% of patients were treated with aspirin, antiplatelet, angiotensin receptor blockers and statin post PCI as recommended in the ACC/AHA guideline [22].

Major bleeding rate was higher in females than males ($p < 0.05$). Ticagrelor was commonly used in males, while clopidogrel was frequently prescribed in the latter ($p < 0.0001$).

4. Discussion

This study was the first to provide novel insights into demographic and clinical characteristics as well as in-hospital outcomes of patients undergoing PCI at a leading cardiac interventional centre in Vietnam. The results indicated gender differences in several demographic and socioeconomic factors, clinical presentation and treatment which may be potentially important in the design of optimal care.

4.1. Demographic and clinical characteristics

The mean age of patients received PCI in our study was eight year younger than the overall national life expectancy in 2016 of 76.3 [26]. However, this age is higher than average ages of other PCI populations, including neighbouring countries with similar life expectancy such as China, Thailand and Malaysia (62.0, 62.7 and 57.0 years old, respectively) [27–29] and countries with more economical development and higher life expectancy such as Australia, Japan and South Korea (approximately 63.0–65.0 years old) [7,18,30]. As patients at VNHI were largely transferred from lower level hospitals, our study population tended to have more comorbidities and older age. Potential barriers to receive timely care such as medical awareness of patients, economic resource and family constraints should be further investigated.

The prevalence of non ACS (45.6%), STEMI (14.5%), NSTEMI (16.2%) and UA (23.7%) were generally comparable to data derived from a recent study of the national PCI registry in Thailand [31]. However, ACS presentation was more common in other PCI registries, especially with the proportion of STEMI patients (over 30%) [18,28]. For instance, the China PEACE registry reported that the prevalence of STEMI, NSTEMI and UA in patients undergoing PCI was 34.8%, 8.1% and 41.8% respectively [29]. One possible explanation is that acute patients were more likely to receive medical therapy or PCI in district or provincial hospitals, and only more severe patients were referred to VNHI.

Consistent with previous studies, including the Asia-Pacific Evaluation of Cardiovascular Therapies collaborative study [32], our study participants generally presented with common cardiovascular disease risk factors such as hypertension, diabetes, dyslipidaemia, past PCI, prior stroke and smoking. It is interesting that the prevalence of most those risk factors in our study was similar, despite a much lower proportion of dyslipidaemia (30%). For instance, some recent studies in China, Thailand, Malaysia and Australia showed that approximately two thirds of their patients experienced hyperlipidaemia [18,28,29,31]. Reasons for such difference are not clear, but it may be due, in part, to a conceivably healthy and low-fat diet of our study participants [33]. Indeed, the prevalence of prior stroke and prior PCI in our study were among the highest in comparison with other studies [18,28,29,31]. The rapid

Table 3
In-hospital outcomes and medications post PCI (n = 1041).

Outcomes	All (n = 1022)	Female (n = 332)	Male (n = 709)	p
New renal impairment	33 (3.2)	11 (3.3)	22 (3.1)	>0.999
New dialysis	9 (0.9)	1 (0.3)	8 (1.1)	0.286
Cardiogenic shock	4 (0.4)	1 (0.3)	3 (0.4)	>0.999
New/recurrent MI	3 (0.3)	2 (0.6)	1 (0.1)	0.24
Unplanned PCI	2 (0.2)	1 (0.3)	1 (0.1)	>0.999
Stent thrombosis	2 (0.2)	2 (0.6)	0 (0.0)	0.102
Major bleeding	21 (2.0)	12 (3.6)	9 (1.3)	0.023
Stroke	5 (0.5)	1 (0.3)	4 (0.6)	>0.999
Death	8 (0.8)	4 (1.2)	4 (0.6)	0.47
Hospital length (day), median	2.0	2.0	2.0	0.69
Hospital length > 2 days	33.0	34.3	32.4	0.59
Medications				
Aspirin	1033 (99.7)	329 (99.7)	704 (99.7)	>0.999
Clopidogrel/Ticlopidine	835 (80.5)	290 (87.8)	545 (77.2)	<0.0001
Ticagrelor	201 (19.5)	40 (12.2)	161 (22.9)	<0.0001
Beta Blockers	397 (38.5)	138 (41.8)	259 (37.0)	0.125
Angiotensin-receptor blockers	952 (92.2)	308 (93.6)	644 (91.6)	0.317
Statin	1033 (99.7)	330 (100.0)	703 (99.6)	0.556
Other lipid lowering therapy	3 (0.3)	3 (0.9)	0 (0.0)	0.032
Oral anticoagulation therapy	4 (0.4)	2 (0.6)	2 (0.3)	0.956

Data are presented as n (%), unless specified.

expansion of PCI in recent years and strokes remain the leading cause of death in Vietnam might explain for this difference [26].

Patterns of gender differences in demographic, socioeconomic and clinical factors are consistent with prior research [8,34,35]. For example, our study showed females receiving PCI accounted for nearly one-third of total participants, those females were generally older and had more comorbidities than males. In our data, the female to male ratio was 0.47, which contrasts with the general Vietnamese population group age 64 and above which has a female to male ratio of 1.6 [36]. This lower incidence of PCI in females might be explained by the relatively lower priority in families of females compared to males in Vietnamese culture. This may be exacerbated by the high cost requirement of the procedure itself and other hospital treatments in the national centre as VNHI. More males were transferred from other provinces to VNHI for PCI in comparison to females ($p = 0.001$), which may support this theory. Additionally, presenting females were on average 4 years older than males ($p < 0.0001$). The protective impact of oestrogen in females in delaying the onset of cardiovascular disease is likely to be part of the explanation [37]. The 4-year age gap also partly explains more comorbidities seen in females such as hypertension, diabetes and hyperlipidaemia in our study. The Global Registry of Acute Coronary Events (GRACE) indicated that, in the group of patients undergoing cardiac intervention, females had higher rates of diabetes, hypertension, but were less likely to smoke [9]. Data from several systematic review with meta-analysis also confirmed that females with cardiovascular risk factors were more likely to have incident CHD than males [38,39].

4.2. Lesion, procedural characteristics and medications prior to PCI

The radial artery was the most common entry site of PCI procedures, which is similar to the practice in China [29], but different from Australia, Japan and Malaysia where the femoral access is quite popular [28,30,34]. The prevalence of treated lesions classified as ACC/AHA type B2 and C in our study (94%) is higher than data in previous studies (60–70%) [18,31]. VNHI is the largest provider of cardiac intervention nationwide, where patients with PCI may have advanced coronary lesions subsequent to milder lesions being treated at other hospitals with potential less experienced interventionists. Greater number of type B2 and C lesions might also be attributed to the use of longer stents in our study. The use of DES was universal, which contrasts with a more mixed picture elsewhere [8,34,35]. In our study, not all left main PCIs were accompanied with IVUS use, partly due to the high cost and the avaibility of this technique in the centre. Regarding medication used, our patients were less likely to receive glycoprotein IIb/ IIIa, but tended to be prescribed with ticagrelor when compared to their counterparts in other studies [34,40]. Similar to some regional countries [7,18,28], our data showed the left anterior descending and the right coronary artery were the most common lesion locations and the rate of in-stent restenosis was low (5%). The procedural success rate was as high as other countries in the Asia Pacific (APAC) region, despite some differences in clinical practices [32].

It is worth mentioning some gender differences observed in the present study. In general, females receiving PCI had lower procedural risks relative to males. Results from the GRACE registry indicated that females were more likely to have normal/mild diseases and less likely to have injured lesion in left main vessel [9]. Although this is not direct comparison as GRACE contained patients undergoing catheterization only, our finding is in line with that result. Similarly, a nationwide study in patients undergoing PCI in Korea reported that males had more chronic lesions in left main vessel, and required a higher number of stents than females [35]. Data from a national cardiovascular registry in America also revealed that females had a lower risk of angiographic features, and needed shorter stents [8].

4.3. In-hospital outcomes and medications post PCI

Overall, our data showed lower rates of in-hospital outcomes among patients undergoing PCI compared with other countries in the APAC region [32]. For instance, the rate of in-hospital death (0.8%) was the lowest when compared to the corresponding data in other studies in China (2.2%), Korea (2.3%) and Australia (2.2%) [18,29,41]. Our PCI participants were also more likely to have shorter hospital stay (2 days) than their counterparts in China (10 days) and Australia (4.2 days) [18,29]. Shorter duration of hospital stay may indicate a low mortality rate before discharge in this study, and such a potential relationship will be investigated in the future. Regarding post procedural medication use, our results are in line with some other reports in Asia. For instance, aspirin was immediately provided to most patients after PCI procedure and

remained until post discharge [14]. Despite the wide variation of dual-anti platelet therapy (DAPT) in the region, aspirin and clopidogrel were also used as the most common DAPT in our study, so were studies from Korea and China [7,29].

Previous studies have largely reported that, females were at a higher risk of having complications or worse PCI-specific outcomes, e.g. death, bleeding or cardiogenic shock than males [8,34,42]. Likewise, females in our study were more likely to have major bleeding relative to males. It is possible that females were older, had a higher prevalence of coronary risk factors, and a smaller body size as well as smaller arteries than males at the time of PCI procedure [8,35]. It is also worth noting that most current PCI-based devices and medication therapies have been designed relatively equally between males and females, without a specific gender indication [43]. Thus, more focused efforts should be taken to prevent and reduce bleeding complications in female patients with PCI.

4.4. Study limitations

There are some limitations to our study. Despite data was collected at the national and biggest cardiac interventional centre in Vietnam, our findings might not be representative of the whole nation, particularly in terms of lesion type and uptake of cutting-edge interventions as VNHI is a single centre only. Furthermore, some uncertainties and recall errors of patients in self-reporting the socioeconomic status as well as cardiovascular risk factors might occur, which can contribute to the differences observed. Additional dedicated studies should be conducted to provide more overall views of PCI practices in Vietnam.

5. Conclusion

Our study based on the first Vietnamese PCI registry provides an opportunity to understand current insights of clinical characteristics and in-hospital outcomes of patients undergoing PCI in Vietnam. It also indicated gender differences in demographic and clinical characteristics together with procedural performance and in-hospital outcomes. The findings may contribute to evaluating PCI-related practices, identifying the gaps in sex-specific care for cardiovascular health, and potentially developing appropriate treatment guidelines.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

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Appendix C Supplement tables for Chapter 6

Table 1: Baseline clinical characteristics difference between ACS - Non-ACS

	All (n=926)	Non-ACS (n=422)	ACS (n=504)	p
Age ≥ 75 (years)	240 (25.9)	105 (24.9)	135 (26.8)	0.560
Male	640 (69.1)	291 (69.0)	349 (69.2)	0.981
BMI (kg/m^2), mean ± SD	22.19 ± 2.9	22.50 ± 2.9	21.94 ± 2.9	0.004
Medical history				
Hypertension	623 (67.3)	292 (69.2)	331 (65.7)	0.286
Diabetes mellitus	257 (27.8)	139 (32.9)	118 (23.4)	0.002
Hyperlipidaemia	280 (30.2)	145 (34.4)	135 (26.8)	0.015
Current smoking	115 (25.4)	41 (22.0)	74 (27.7)	0.210
Prior cerebral vascular disease	135 (14.6)	62 (14.7)	73 (14.5)	0.992
Previous CABG	11 (1.2)	7 (1.7)	4 (0.8)	0.365
Previous PCI	321 (34.7)	192 (45.5)	129 (25.6)	<0.001
Tests prior to PCI				
Left ventricular ejection fraction ≤ 40%	103 (12.5)	43 (10.9)	60 (14.0)	0.211
Moderate to severe renal impairment [a]	20 (2.2)	7 (1.7)	13 (2.6)	0.453
Procedural characteristics				
Radial access site	729 (78.7)	334 (79.1)	395 (78.4)	0.837

Left main disease	101 (10.9)	47 (11.1)	54 (10.7)	0.920
Lesion type B2 and C	881 (95.1)	397 (94.1)	484 (96.0)	0.221
Restenotic lesions	49 (5.3)	24 (5.7)	25 (5.0)	0.730
Number of stents used, mean ± SD	1.52 ± 0.7	1.52 ± 0.8	1.53 ± 0.7	0.966
Number of treated lesion, mean ± SD	1.23 ± 0.5	1.24 ± 0.5	1.23 ± 0.6	0.890
Stent used	914 (98.7)	416 (98.6)	498 (98.8)	0.985
Balloon used only	3 (0.3)	1 (0.2)	2 (0.4)	>0.999
Procedural success	918 (99.1)	417 (98.8)	501 (99.4)	0.542

[a] *Creatinine > 200µmol/l; BMI: body mass index; ACS: acute coronary syndrome, including myocardial infarctions and unstable angina;*

CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention

Table 2: Outcomes in-hospital, 30 days and 12 months between ACS - Non-ACS

Outcomes	Total (926)	Non-ACS (n=422)	ACS (n= 504)	p
In hospital				
Death	8 (0.9)	1 (0.2)	7 (1.4)	0.078
MACCEs	15 (1.6)	3 (0.7)	12 (2.4)	0.081
Major bleeding	18 (1.9)	8 (1.9)	10 (2.0)	>0.999
At 30 days				
Death	18 (1.9)	2 (0.5)	16 (3.2)	0.006
MACCEs	35 (3.8)	9 (2.1)	26 (5.2)	0.026
Cardiac rehospitalisation	124 (13.4)	46 (10.9)	78 (15.5)	0.365
Unplanned cardiac rehospitalisation	53 (5.7)	18 (4.3)	35 (6.9)	0.663
At 12 months				
Death	60 (6.5)	20 (4.7)	40 (7.9)	0.067
MACCEs	100 (10.8)	34 (8.1)	66 (13.1)	0.019
Cardiac rehospitalisation	58 (6.2)	26 (6.1)	32 (6.3)	>0.999
Unplanned cardiac rehospitalisation	38 (4.1)	16 (3.8)	22 (4.4)	0.681

MACCEs: Major Adverse Cardiac and Cerebrovascular Events (composite of death, MI, cerebrovascular accident or stroke, or target vessel revascularisation);

ACS: Acute coronary syndrome, including myocardial infarctions and unstable angina; 12 months data is the cumulative one of hospital and 30 days data,

with an exception for cardiac rehospitalisation and unplanned cardiac rehospitalisation.

Table 3: Baseline characteristics according to lost to follow-up status

(n=1022)	Non- Lost to FU (n=926)	Lost to FU (n=96)	p
Age ≥ 75 (years)	240 (25.9)	41 (42.7)	0.001
Male	640 (69.1)	56 (58.3)	0.041
BMI (kg/m^2), mean ± SD	22.19 ± 2.9	22.16 ±3.0	0.919
Medical history			
AMI	283 (30.6)	31 (32.3)	0.815
Hypertension	623 (67.3)	64 (66.7)	0.994
Diabetes mellitus	257 (27.8)	22 (22.9)	0.372
Hyperlipidaemia	280 (30.2)	27 (28.1)	0.754
Current smoking	115 (25.4)	9 (22.0)	0.760
Prior cerebral vascular disease	135 (14.6)	11 (11.5)	0.497
Previous CABG	11 (1.2)	1 (1.0)	>0.999
Previous PCI	321 (34.7)	38 (39.6)	0.396
Tests prior to PCI			
Left ventricular ejection fraction ≤ 40%	103 (12.5)	12 (13.6)	0.895
Moderate to severe renal impairment [a]	20 (2.2)	5 (5.2)	0.139
Procedural characteristics			
Radial access site	729 (78.7)	82 (85.4)	0.159
Left main disease	101 (10.9)	9 (9.4)	0.773
Lesion type B2 and C	881 (95.1)	90 (93.8)	0.764

Restenotic lesions	49 (5.3)	4 (4.2)	0.817
Number of stents used, mean ± SD	1.52 ± 0.7	1.52 ± 0.7	0.960
Number of treated lesion, mean ± SD	1.23 ±0.5	1.23±0.4	0.926
Stent used	914 (98.8)	95 (99.0)	>0.999
Balloon used only	3 (0.3)	1 (1.0)	0.831
Procedural success	918 (99.1)	96 (100)	0.760

[a] *Creatinine > 200µmol/l; BMI: body mass index; AMI: acute myocardial infarction, including ST-elevation and Non-ST-elevation;*

CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention

Appendix D Study instruments

D.1 Patient information sheet (English version)

Vietnam Cardiac Outcomes Registry
Participant Information Statement

For patients undergoing Percutaneous Coronary Intervention (PCI)

Principal Investigators: Prof. Christopher Reid, Prof. Do Doan Loi, Prof. Pham Manh Hung, Dr. Nguyen Thi Thu Hoai, Dr. Nguyen Ngoc Quang

Data manager: Mrs Vu Thi Thanh Hoa

Introduction

The Vietnam Cardiac Outcomes Registry (VNCOR) is a population-based clinical quality registry that aims to improve the quality of care provided to cardiovascular patients. Clinical registries are large databanks of health information used to assess and report on the quality of care. Quality indicators collected by clinical registries assess whether care is safe and effective and delivered in a timely and appropriate manner. To achieve this, VNCOR has been set up to collect information about cardiovascular treatments and interventions (e.g. Percutaneous Coronary Intervention: PCI).

We ask that you participate in the Vietnam Cardiac Outcomes Registry (VNCOR) by allowing VNCOR to document information relevant to you, your procedure and its outcomes.

1. What Information is needed?

The information we intend to collect includes your full name, date of birth, contact information, hospital identification number, the reason you had the PCI procedure and other very basic information directly related to your health before, during and after the procedure.

2. How is the Information Collected?

You are not required to do anything to participate in the Registry. If you do not contact us to withdraw, the researcher will access your medical records to collect information about you and your PCI after you have been discharged from hospital. Follow-up information (at 30 days and 12 months) may be collected by accessing your medical records, or by calling you to ask a few, simple questions about how you have been since your procedure (this will take no more than 15-20 minutes of your time).

3. How is the Information Stored?

Data obtained will be stored securely by the researcher and her supervisors at the Vietnam National Heart Institute (VNHI) and Curtin University who have experience managing registries for a period of 7 years. The information will be entered onto a secure database by researcher and backed up daily. The hard copy will be kept securely in a locked cabinet at VNHI, which allows access by only researchers.

4. How will the Information be used?

We will produce general reports on cardiac outcomes for public, government, clinical and academic audiences. We anticipate that these publications will help to inform the community about common trends and/or gaps that may exist in service provision. **No publication or report will ever contain any identifying information about you**.

Researchers may use unidentified, group data for future research projects. Any further research undertaken using VNCOR data will require approval by a Human Research Ethics Committee.

5. We Will Keep Your Information Confidential and Private

Any information obtained that can identify you will be treated as confidential and stored securely. Identifying information is protected by privacy legislation and would only be disclosed with your permission, or in compliance with the law. We will ensure that there is no unauthorized access.

6. Potential Risks and Benefits to You

There is no harm of harm or discomfort to you. Having your information stored in the Registry will not affect any future health care or your relationship with doctors, surgeons or clinical staff at the VNHI. Your treating physician(s) will not necessarily know whether your information has been recorded in the Registry.

7. Is it Compulsory to Participate?

No. Participation in any research project is voluntary. If you do not wish to take part you don't have to. If you decide to allow your information to be recorded in the Registry but later change your mind, you are free to withdraw your consent at any stage by contacting VNCOR directly. This will not affect your relationship with any hospital staff or healthcare providers.

If you do not want your information recorded in the Registry, please contact the VNCOR researcher on* +84 915 530 789 *(Mailing address below).

Please be aware your information will be collected in the Registry unless you contact VNCOR to advise that you **do not** want your details recorded. If you do contact VNCOR to opt-out of the Registry, we will ask for some identifying information so we can accurately remove your details from our records. Alternatively, you can write to the VNCOR researcher at:

VNCOR Project
Researcher: Hoa Vu Thi Thanh
Vietnam National Heart Institute, 78 Giai Phong street, Dong Da group, HaNoi

Please provide enough information for VNCOR to identify your records and remove them.

8. Who Can I Contact?

If you want any additional information about this Registry, you can contact:

- **Professor Christopher Reid**

Department of Health Policy and Management, Curtin University

Phone: +61 8 9266 7123 Email: Christopher.Reid@curtin.edu.au

- **Or Vu, Thi Thanh Hoa,** PhD student

Curtin University

Phone: +84 915 530 789 Email: T.vu18@postgrad.curtin.edu.au

The Vietnam National Heart Institute and Curtin University Human Research Ethics Committee (HREC) has approved this study (HREC HRE2017-0378). Should you wish to discuss the study with someone not directly involved, in particular, any matters concerning the conduct of the study or your rights as a participant, or you wish to make a confidential complaint, you may contact:

- **Vietnam National Heart Institute's office**: +84 436290881
- **Ethics Officer at Curtin University** on (08) 9266 9223 or the Manager, Research Integrity on (08) 9266 7093 or email: hrec@curtin.edu.au

D.2 Baseline data collection form (English version)

5282451658

Patient ID

Curtin University | CCRE Centre of Clinical Research and Education | VIỆN TIM MẠCH VIỆT NAM

PCI Form 1 - Baseline

Patient Details

1.1.1 Medical record number

1.1.2 Surname

1.1.3 First name

1.1.4 Middle name

1.1.5 Gender ○ Male ○ Female

1.1.6 Date of Birth d d / m m / y y y y

1.1.7 ID number OR ○ Patient has no ID number

1.1.8 Province code OR ○ Patient has no province code

1.1.9 Primary Phone No.

1.1.10 Alternate Phone No. OR ○ Patient has no alternate phone No

1.1.11 Ethnic group OR ○ Patient has no ethnic code

1.1.12 Poor status ○ Poor ○ Near poor ○ Other

1.1.13 Educational level ○ Primary school ○ Secondary school ○ High school ○ Higher

1.1.14 Occupation ○ Official worker ○ Manual worker ○ Farmer ○ Others

1.1.15 Monthly income/ person VND

Admission Data

2.1.1 Admission date at PCI hospital d d / m m / y y y y

2.1.2 Time of arrival at PCI hospital h h : m m

2.1.3 PCI Procedure date d d / m m / y y y y

2.1.4 PCI Procedure time h h : m m

2.1.5 Patient height cm

2.1.6 Patient weight kg

Version 1.0 2017

0794451651 Patient ID

Clinical Symptoms

2.2.1 Acute coronary syndrome (ACS) ○ NO ○ YES → **if NO** *proceed to Clinical Presentation* ***2.3.1***

2.2.2 Date of ACS symptom onset (ACS onset must be <7 days ago) d d / m m / y y y y Accuracy Code

2.2.3a Time of ACS symptom onset h h : m m 2.2.3b Time estimated? ○ NO ○ YES *OR* ○ Onset time not available

2.2.4 Type of ACS ○ Unstable angina ○ NSTEMI ○ STEMI

For STEMI Patients ONLY:

2.2.5 Inter hospital transfer ○ NO ○ YES 2.2.7 Balloon / device time h h : m m

2.2.6 Pre hospital notification ○ NO ○ YES

Clinical Presentation

2.3.1 Cardiogenic shock ○ NO ○ YES

2.3.2 Out of hospital cardiac arrest ○ NO ○ YES

2.3.3 In-hospital pre-procedure cardiac ○ NO ○ YES

2.3.4 In-hospital pre-procedural intubation ○ NO ○ YES

Pre-Procedural LV Function

3.1.1a LVEF test performed ○ NO ○ YES → **if YES** *complete 3.1.1b - 3.1.3*

3.1.1b Date of most recent LVEF test d d / m m / y y y y Accuracy Code

3.1.2 Most recent LVEF test type ○ Echocardiography ○ Gated cardiac blood pool scan ○ Myocardial perfusion scan ○ Angiography ○ Magnetic resonance imaging (MRI) ○ Not stated/inadequately described

3.1.3 Most recent ejection fraction: Digitally derived % *OR* Estimated ○ Normal (> 50%) ○ Moderate (35 - 44%) ○ Mild (45 - 49%) ○ Severe (< 35%)

Pre-Procedural Risk Factors

3.2.1a Diabetes medication ○ NO ○ YES → *if YES* 3.2.1b Medication type ○ Oral ○ Insulin

3.2.2 Hypertension medication ○ NO ○ YES

3.2.3 Dyslipidemia medication ○ NO ○ YES

3.2.4 Peripheral vascular disease history ○ NO ○ YES

3.2.5 Cerebrovascular disease history ○ NO ○ YES

3.2.6 Chronic oral anti-coagulant therapy ○ NO ○ YES

3.2.7a Previous CABG ○ NO ○ YES → **if YES** 3.2.7b Date most recent CABG d d / m m / y y y y Accuracy Code

3.2.8a Previous PCI ○ NO ○ YES → **if YES** 3.2.8b Date of most recent PCI d d / m m / y y y y Accuracy Code

Pre-Procedural Renal Status

3.3.1a Last pre-procedure creatinine ____ µmol/L OR ○ Creatinine results not available

3.3.1b Date of test (cannot be >60days prior to PCI) __ __ / __ __ / __ __ __ __ (d d / m m / y y y y) Accuracy Code ___

3.3.2 Dialysis therapy (chronic renal failure) ○ NO ○ YES **if NO**

3.3.3 Functioning renal transplant ○ NO ○ YES

3.3.4 Acute renal replacement therapy ○ NO ○ YES

Peri-procedural Medication

3.4.1a Fibrinolytic therapy ○ NO ○ YES **if YES**

3.4.1b Fibronolytic therapy <= 24 ○ NO ○ YES

3.4.2 Medications given <= 24 hours prior to and during the PCI procedure (Check ALL that apply)

☐ Glycoprotein IIb/IIIa inhibitor therapy ☐ Antithrombin therapy ☐ Ticagrelor ☐ Clopidogrel/Ticlopidine ☐ Aspirin

Procedure Details

4.1.1 PCI indication - select ONE *(PCI Indication must not contradict ACS presentation coding on page 1)*

- ○ Primary PCI for STEMI < 12hrs
- ○ PCI for STEMI >12hr (unstable)
- ○ PCI for STEMI >12hr (stable)
- ○ STEMI (stable after full-dose thrombolytics)
- ○ STEMI (unstable after full-dose thrombolytics) non-rescue PCI
- ○ Rescue PCI for STEMI (failed thrombolytics)
- ○ PCI post cardiac arrest/cardiogenic shock (non MI)
- ○ PCI for NSTEMI
- ○ PCI for unstable angina
- ○ PCI for ACS >7days ago (stable)
- ○ PCI for stable angina
- ○ Staged PCI
- ○ No angina / angina equivalent
- ○ Other (give reason) _____

4.1.2 Reason for PCI (non-acute / non-ACS patients)
(Answer if PCI indication is not coded as acute STEMI, NSTEMI, Unstable Angina or Recent ACS)

- ○ High Grade Stenosis (>70%)
- ○ Medium Grade Stenosis (50-70%)
- ○ Low Grade Stenosis (< 50%)
- ○ Function test positive (+)
- ○ Functional test negative (-)
- ○ Functional test equivocal (?)
- ○ Functional test not done (x)

4.2.1 Percutaneous entry location ○ Brachial ○ Radial ○ Femoral

4.2.2a Adjunctive device required ○ NO ○ YES **if YES**

4.2.2b Type of adjunctive device(s) (check ALL that apply)

- ☐ Intravascular Ultrasound
- ☐ Optical coherence tomography
- ☐ Thrombus aspiration device
- ☐ Distal or proximal protection device
- ☐ Rotational arthrectomy
- ☐ Fractional flow reserve
- ☐ Other (specify) _____

4.2.3 Procedural intubation required ○ NO ○ YES

4.2.4a Mechanical ventricular support required ○ NO ○ YES **if YES**

4.2.4b Type of mechanical support required ○ IABP ○ ECMO ○ LVAD

Lesion 1 - Procedure Details (Lesion & Device Data)

The following questions are to be answered for lesion 1 ONLY.

4.3.1 Lesion Location Code [ ][ ][ ] *Refer to Lesion Location Map*

4.3.2 Lesion Type ○ A ○ B1 ○ B2 ○ C

4.3.3 Chronic total occlusion (CTO) ○ NO ○ YES

4.3.4a In-stent restenosis (ISR) ○ NO ○ YES → **if YES** 4.3.4b Stent thrombosis ○ NO ○ YES

4.3.5 Lesion successfully treated ○ NO ○ YES

4.4.1a Total number of stents (current lesion) [ ] **if = 0** → 4.4.2 **Type of balloon(s) deployed**
if > 0 *continue to 4.4.1 b & c*

4.4.1b Total length of stents (current lesion) [ ][ ][ ] mm

4.4.1c Type of stent(s) implanted

- ○ Bare metal stents (BMS)
- ○ BVS (non-drug scaffold)
- ○ Drug-eluting stents (DES)
- ○ Drug eluting BVS (DE-BVS)
- ○ Mixed stents (BMS & DES)
- ○ Other (specify) _____

4.4.2 **Type of balloon(s) deployed**
- ○ No balloon / stent used
- ○ Plain balloon
- ○ Drug-eluting balloon

Lesion 2 - Procedure Details (Lesion & Device Data)

The following questions are to be answered for lesion 2 ONLY.

4.3.1 Lesion Location Code [ ][ ][ ] *Refer to Lesion Location Map*

4.3.2 Lesion Type ○ A ○ B1 ○ B2 ○ C

4.3.3 Chronic total occlusion (CTO) ○ NO ○ YES

4.3.4a In-stent restenosis (ISR) ○ NO ○ YES → **if YES** 4.3.4b Stent thrombosis ○ NO ○ YES

4.3.5 Lesion successfully treated ○ NO ○ YES

4.4.1a Total number of stents (current lesion) [ ] **if = 0** → 4.4.2 **Type of balloon(s) deployed**
if > 0 *continue to 4.4.1 b & c*

4.4.1b Total length of stents (current lesion) [ ][ ][ ] mm

4.4.1c Type of stent(s) implanted

- ○ Bare metal stents (BMS)
- ○ BVS (non-drug scaffold)
- ○ Drug-eluting stents (DES)
- ○ Drug eluting BVS (DE-BVS)
- ○ Mixed stents (BMS & DES)
- ○ Other (specify) _____

4.4.2 **Type of balloon(s) deployed**
- ○ No balloon / stent used
- ○ Plain balloon
- ○ Drug-eluting balloon

Lesion 3 - Procedure Details (Lesion & Device Data)

The following questions are to be answered for lesion 3 ONLY.

4.3.1 Lesion Location Code [ ][ ][ ] *Refer to Lesion Location Map*

4.3.2 Lesion Type ○ A ○ B1 ○ B2 ○ C

4.3.3 Chronic total occlusion (CTO) ○ NO ○ YES

4.3.4a In-stent restenosis (ISR) ○ NO ○ YES → **if YES** 4.3.4b Stent thrombosis ○ NO ○ YES

4.3.5 Lesion successfully treated ○ NO ○ YES

4.4.1a Total number of stents (current lesion) [ ] **if = 0** → 4.4.2 **Type of balloon(s) deployed**
if > 0 *continue to 4.4.1 b & c*

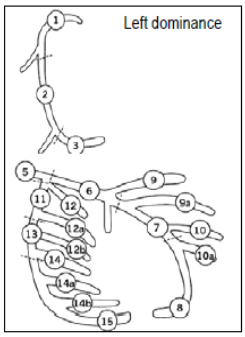
4.4.1b Total length of stents (current lesion) [ ][ ][ ] mm

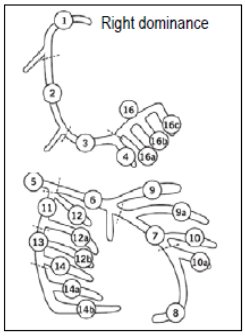
4.4.1c Type of stent(s) implanted

- ○ Bare metal stents (BMS)
- ○ BVS (non-drug scaffold)
- ○ Drug-eluting stents (DES)
- ○ Drug eluting BVS (DE-BVS)
- ○ Mixed stents (BMS & DES)
- ○ Other (specify) _____

4.4.2 **Type of balloon(s) deployed**
- ○ No balloon / stent used
- ○ Plain balloon
- ○ Drug-eluting balloon

Lesion Location Map





Coronary Artery Segment Codes

1	RCA proximal
2	RCA mid
3	RCA distal
4	PDA
5	Left main
6	LAD proximal
7	LAD mid
8	LAD apical (distal)
9	D1 First diagonal
9a	D1a First diagonal a
10	D2 Second Diagonal
10a	D2a Second Diagonal a
11	Proximal circumflex
12	Intermediate / anterolateral
12a	Obtuse marginal a
12b	Obtuse marginal b
13	Distal cirumflex
14	Left posterolateral
14a	Left posterolateral a
14b	Left posterolateral b
15	Posterior descending
16	Posterolateral from RCA
16a	Posterolateral from RCA a
16b	Posterolateral from RCA b
16c	Posterolateral from RCA c
17	Internal mammary graft
18	Radial artery graft
19	Saphenous vein graft

Note: *Where serial stenoses are treated with overlapping stents / devices, classify as ONE lesion.*

Lesion 4 - Procedure Details (Lesion & Device Data)

The following questions are to be answered for lesion 4 ONLY.

4.3.1 Lesion Location Code ☐☐☐ *Refer to Lesion Location Map*

4.3.2 Lesion Type ○ A ○ B1 ○ B2 ○ C

4.3.3 Chronic total occlusion (CTO) ○ NO ○ YES

4.3.4a In-stent restenosis (ISR) ○ NO ○ YES → **if YES** 4.3.4b Stent thrombosis ○ NO ○ YES

4.3.5 Lesion successfully treated ○ NO ○ YES

4.4.1a Total number of stents (current lesion) ☐ **if = 0** → 4.4.2 **Type of balloon(s) deployed**
if > 0 *continue to 4.4.1 b & c*

4.4.1b Total length of stents (current lesion) ☐☐☐ mm

- ○ No balloon / stent used
- ○ Plain balloon
- ○ Drug-eluting balloon

4.4.1c Type of stent(s) implanted
- ○ Bare metal stents (BMS)
- ○ BVS (non-drug scaffold)
- ○ Drug-eluting stents (DES)
- ○ Drug eluting BVS (DE-BVS)
- ○ Mixed stents (BMS & DES)
- ○ Other (specify) _____

Lesion 5 - Procedure Details (Lesion & Device Data)

The following questions are to be answered for lesion 5 ONLY.

4.3.1 Lesion Location Code ☐☐☐ *Refer to Lesion Location Map*

4.3.2 Lesion Type ○ A ○ B1 ○ B2 ○ C

4.3.3 Chronic total occlusion (CTO) ○ NO ○ YES

4.3.4a In-stent restenosis (ISR) ○ NO ○ YES → **if YES** 4.3.4b Stent thrombosis ○ NO ○ YES

4.3.5 Lesion successfully treated ○ NO ○ YES

4.4.1a Total number of stents (current lesion) ☐ **if = 0** → 4.4.2 **Type of balloon(s) deployed**
if > 0 *continue to 4.4.1 b & c*

4.4.1b Total length of stents (current lesion) ☐☐☐ mm

- ○ No balloon / stent used
- ○ Plain balloon
- ○ Drug-eluting balloon

4.4.1c Type of stent(s) implanted
- ○ Bare metal stents (BMS)
- ○ BVS (non-drug scaffold)
- ○ Drug-eluting stents (DES)
- ○ Drug eluting BVS (DE-BVS)
- ○ Mixed stents (BMS & DES)
- ○ Other (specify) _____

Post-Procedural Cardiac Biomarkers

5.1.1 Post-procedural cardiac biomarker levels measured within 24 hours ○ NO ○ YES
→ **if NO** *go straight to 5.3.1*

5.2.1a Peak Troponin <= 24 hours ☐☐☐☐.☐☐ ○ Tn-I ng/L ○ Tn-T ng/L OR ○ Not measured

5.2.1b Date and time of Troponin levels measured ☐☐ / ☐☐ / ☐☐☐☐ ☐☐:☐☐
(d d / m m / y y y y h h : m m)

5.2.2a Peak CK-MB <= 24 hours (U/L) ☐☐☐☐ U/L OR ○ Not measured

5.2.2b Date and time of CK-MB levels measured ☐☐ / ☐☐ / ☐☐☐☐ ☐☐:☐☐
(d d / m m / y y y y h h : m m)

5.2.3a Peak CK <= 24hours (U/L) ☐☐☐☐ U/L OR ○ Not measured

5.2.3b Date and time of CK levels measured ☐☐ / ☐☐ / ☐☐☐☐ ☐☐:☐☐
(d d / m m / y y y y h h : m m)

D.3 30 days follow-up form (English version)

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PCI Form 2 - 30 days Follow-Up

Patient ID

Patient Details

1.1.1 Medical record number

1.1.7 ID number

1.1.2 Surname

1.1.3 First name

1.1.4 Gender ○ Male ○ Female

1.1.6 Date of birth d d / m m / y y y y

30 Day Outcomes

7.1.1 Date of follow-up d d / m m / y y y y

7.1.2a Follow-up status (30 days) ○ Alive ○ Deceased ○ Unknown → **If patient lost to follow-up** *do not continue*

If deceased *answer 7.1.2b-c and continue through to 7.1.8*

7.1.2b Date of death d d / m m / y y y y Accuracy Code

7.1.2c Primary cause of death ○ Cardiac ○ Non - cardiac ○ Uncertain

7.1.3 New heart failure ○ NO ○ YES ○ UNKNOWN

7.1.4 New myocardial infarction ○ NO ○ YES ○ UNKNOWN

7.1.5 New stent-thrombosis ○ None ○ Probable ○ UNKNOWN ○ Definite ○ Possible

7.1.6 New bleeding event (Please refer to the BARC definition) ○ Type 0 ○ Type 1 ○ Type 2 ○ Type 3a ○ Type 3b ○ Type 3c ○ Type 4 ○ Type 5a ○ Type 5b ○ UNKNOWN

7.1.7a New stroke ○ NO ○ YES → **If yes** 7.1.7b **Stroke type** ○ Haemorrhagic ○ Ischaemic ○ UNKNOWN

7.1.8a Rehospitalisation ○ NO ○ YES → **If yes** *answer Questions 7.1.8b-e in Rehospitalisation Table (for each rehospitalisation up to 6 rehospitalisations)* ○ UNKNOWN → **If UNK** *continue to medications*

30 Day Outcomes (continued...)

Please answer for each rehospitalisation (up to 6 rehospitalisations)

		Rehospitalisation 1	2	3	4	5	6
7.1.8b	Cardiac rehospitalisation **If no** *do not continue with items 7.1.8 c-e*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
		if NO *do not continue with items 7.1.8 c-e*					
7.1.8c	Planned cardiac rehospitalisation	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (i)	PCI rehospitalisation **If no** *continue to 7.1.8e*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (ii)	Target vessel revascularisation (PCI)	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (iii)	Target lesion revascularisation (TLR)	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8e (i)	CABG rehospitalisation **If no** *continue to medications*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8e (ii)	Target vessel CABG	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes

Do not complete sections 7.2 and 7.3 if patient is deceased

Medications at 30 days

7.2.1a Aspirin ○ NO ○ YES ○ Not asked

7.2.1b Clopidogrel/Ticlopidine ○ NO ○ YES ○ Not asked

7.2.1c Ticagrelor ○ NO ○ YES ○ Not asked

Quality of Life (QoL) at 30 days

○ All QoL not asked

7.3.1a Mobility ○ No problem ○ Some problem ○ Confined to bed ○ Not asked

7.3.1b Personal care ○ No problem ○ Some problem ○ Unable to wash/ dress ○ Not asked

7.3.1c Usual activities ○ No problem ○ Some problem ○ Unable to perform usual activities ○ Not asked

7.3.1d Pain/discomfort ○ No problem ○ Some problem ○ Extreme pain/ discomfort ○ Not asked

7.3.1e Anxiety/depression ○ No problem ○ Some problem ○ Extreme anxiety/ depression ○ Not asked

7.3.2 Own health state today ○ Not asked

0 = worst; 100 = best

Version 1.4 October 2015

PCI Follow up Telephone Script (EQ-5D Quality of life)

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Quality of life

It is suggested that the telephone administrator follows the script of the EQ-5D. Although allowance should be made for the interviewer's particular style of speaking, the wording should be followed as closely as possible. **In the case of the EQ-5D descriptive system, the precise wording must be followed**.

It is recommended that the administrator has a copy of the EQ-5D in front of them as it is administered over the telephone.
If the respondent has difficulty with regard to which box to tick, the administrator should repeat the question verbatim and ask the respondent to answer in a way that most closely resembles their thoughts about their health state today.

EQ-5D

"We are trying to find out what you think about your health. I will first ask you a few brief and simple questions about your own health state today. I will then ask you to do a rather different task that involves rating your health on a measuring scale. I will explain the tasks fully as I go along but please interrupt me if you do not understand something or if things are not clear to you. Please remember that there are no right or wrong answers. We are interested here only in your personal view."

"First I am going to read out some questions. Each question has a choice of three answers. Please tell me which answer best describes your own health state today. Do not choose more than one answer in each group of questions."

1. In terms of mobility, would you say you have
- No problem walking around
- Some problems walking around
- Are you confined to bed

2. In term of personal care (washing, dressing), would you say you are
- No problems with personal care
- Some problems washing and dressing myself
- Unable to wash/dress myself

3. In terms of usual activities (e.g. work, study,housework, family of leisure activities), would you say you have
- No problem performing my usual activities
- Some problem performing my usual activies
- Unable to perform my usual activities

4. In terms of pain/ discomfort, would you say you have
- No pain/ discomfort
- Moderate pain/ discomport
- Extreme pain/ discomfort

5. Interm of anxiety/ depression, would you say you are
- Not anxious/depressed
- Moderately anxious/depressed
- Extremely anxious/depressed

6."I would like to ask you to do a rather different task. To help you say how good or bad your health state is, I'd like you to try to picture in your mind a scale that looks a bit like a thermometer. The best health state you can imagine is marked 100 at the top of the scale and the worst state you can imagine is marked zero at the bottom.
Please tell me the point on this scale where you would put your own health state today."

Please indicate numerically, on a scale between 0-100, where the patient visualises theri own health state TODAY.

Record the value as per the patients's answer. Remember, "100" is as good as the interviewee has ever felt in their life.

D.4 12 months follow-up form (English version)

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PCI Form 2 - 12 months Follow-Up

Patient ID ☐☐☐☐

Patient Details

1.1.1 Medical record number ☐☐☐☐☐☐☐☐☐☐

1.1.7 ID number ☐☐☐☐☐☐☐☐☐☐☐☐

1.1.2 Surname ☐☐☐☐☐☐☐

1.1.3 First name ☐☐☐☐☐☐☐

1.1.4 Gender ○ Male ○ Female

1.1.6 Date of birth ☐☐ / ☐☐ / ☐☐☐☐ (d d / m m / y y y y)

12 months Outcomes

7.1.1 Date of follow-up ☐☐ / ☐☐ / ☐☐☐☐ (d d / m m / y y y y)

7.1.2a Follow-up status (12 months) ○ Alive ○ Deceased ○ Unknown → **If patient lost to follow-up** *do not continue*

↓ **If deceased** *answer 7.1.2b-c and continue through to 7.1.8*

7.1.2b Date of death ☐☐ / ☐☐ / ☐☐☐☐ (d d / m m / y y y y) Accuracy Code ☐☐☐

7.1.2c Primary cause of death ○ Cardiac ○ Non - cardiac ○ Uncertain

7.1.3 New heart failure ○ NO ○ YES ○ UNKNOWN

7.1.4 New myocardial infarction ○ NO ○ YES ○ UNKNOWN

7.1.5 New stent-thrombosis ○ None ○ Definite ○ Probable ○ Possible ○ UNKNOWN

7.1.6 New bleeding event (Please refer to the BARC definition) ○ Type 0 ○ Type 1 ○ Type 2 ○ Type 3a ○ Type 3b ○ Type 3c ○ Type 4 ○ Type 5a ○ Type 5b ○ UNKNOWN

7.1.7a New stroke ○ NO ○ YES → **If yes** 7.1.7b **Stroke type** ○ Haemorrhagic ○ Ischaemic ○ UNKNOWN

7.1.8a Rehospitalisation ○ NO ○ YES → **If yes** *answer Questions 7.1.8b-e in Rehospitalisation Table (for each rehospitalisation up to 6 rehospitalisations)* ○ UNKNOWN → **If UNK** *continue to medications*

12 months Outcomes (continued...)

Please answer for each rehospitalisation (up to 6 rehospitalisations)		Rehospitalisation 1	2	3	4	5	6
7.1.8b	**Cardiac rehospitalisation** **If no** *do not continue with items 7.1.8 c-e*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
		if NO *do not continue with items 7.1.8 c-e*					
7.1.8c	**Planned cardiac rehospitalisation**	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (i)	**PCI rehospitalisation** **If no** *continue to 7.1.8e*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (ii)	**Target vessel revascularisation (PCI)**	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8d (iii)	**Target lesion revascularisation (TLR)**	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8e (i)	**CABG rehospitalisation** **If no** *continue to medications*	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes
7.1.8e (ii)	**Target vessel CABG**	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes	○ No ○ Yes

Do not complete sections 7.2 and 7.3 if patient is deceased

Medications at 12 months

7.2.1a **Aspirin** ○ NO ○ YES ○ Not asked

7.2.1b **Clopidogrel/Ticlopidine** ○ NO ○ YES ○ Not asked

7.2.1c **Ticagrelor** ○ NO ○ YES ○ Not asked

Quality of Life (QoL) at 12 months

○ All QoL not asked

7.3.1a **Mobility** ○ No problem ○ Some problem ○ Confined to bed ○ Not asked

7.3.1b **Personal care** ○ No problem ○ Some problem ○ Unable to wash/ dress ○ Not asked

7.3.1c **Usual activities** ○ No problem ○ Some problem ○ Unable to perform usual activities ○ Not asked

7.3.1d **Pain/discomfort** ○ No problem ○ Some problem ○ Extreme pain/ discomfort ○ Not asked

7.3.1e **Anxiety/depression** ○ No problem ○ Some problem ○ Extreme anxiety/ depression ○ Not asked

7.3.2 **Own health state today** ☐☐☐ ○ Not asked

0 = worst; 100 = best

Version 1.4 October 2015

PCI Follow up Telephone Script (EQ-5D Quality of life)

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EQ-5D

"We are trying to find out what you think about your health. I will first ask you a few brief and simple questions about your own health state today. I will then ask you to do a rather different task that involves rating your health on a measuring scale. I will explain the tasks fully as I go along but please interrupt me if you do not understand something or if things are not clear to you. Please remember that there are no right or wrong answers. We are interested here only in your personal view."

"First I am going to read out some questions. Each question has a choice of three answers. Please tell me which answer best describes your own health state today. Do not choose more than one answer in each group of questions."

1. In terms of mobility, would you say you have
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- Some problems walking around
- Are you confined to bed

2. In term of personal care (washing, dressing), would you say you are
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- Some problems washing and dressing myself
- Unable to wash/dress myself

3. In terms of usual activities (e.g. work, study,housework, family of leisure activities), would you say you have
- No problem performing my usual activities
- Some problem performing my usual activies
- Unable to perform my usual activities

4. In terms of pain/ discomfort, would you say you have
- No pain/ discomfort
- Moderate pain/ discomport
- Extreme pain/ discomfort

5. Interm of anxiety/ depression, would you say you are
- Not anxious/depressed
- Moderately anxious/depressed
- Extremely anxious/depressed

6."I would like to ask you to do a rather different task. To help you say how good or bad your health state is, I'd like you to try to picture in your mind a scale that looks a bit like a thermometer. The best health state you can imagine is marked 100 at the top of the scale and the worst state you can imagine is marked zero at the bottom.
Please tell me the point on this scale where you would put your own health state today."

Please indicate numerically, on a scale between 0-100, where the patient visualises theri own health state TODAY.

Record the value as per the patients's answer. Remember, "100" is as good as the interviewee has ever felt in their life.

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1. **Hoa T.T. Vu**, Hoai T.T. Nguyen, Hung M. Pham, Loi D. Do, Quang N. Nguyen, Richard Norman, Rachel R. Huxley, Ngoc M. Pham, Crystal M.Y. Lee, Christopher M. Reid (2020). Establishment of a percutaneous coronary intervention registry in Vietnam: rationale and methodology. *Global Heart*. Article ID 32489803. doi: 10.5334/gh.782

2. **Hoa T.T. Vu**, Hung M. Pham, Hoai T.T. Nguyen, Quang N. Nguyen, Loi D. Do, Ngoc M. Pham, Richard Norman, Rachel R. Huxley, Crystal M.Y. Lee, Christopher M. Reid (2020). Novel insights into clinical characteristics and in-hospital outcomes of patients undergoing percutaneous coronary intervention in Vietnam. IJC Heart & Vasculature. Article ID 32944609. doi:10.1016/j.ijcha.2020.100626

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Appendix F Statement of Contributors

Paper 1: Hoa T.T. Vu, Hoai T.T. Nguyen, Hung M. Pham, Loi D. Do, Quang N. Nguyen, Richard Norman, Rachel R. Huxley, Ngoc M. Pham, Crystal M.Y. Lee, Christopher M. Reid (2020). Establishment of a percutaneous coronary intervention registry in Vietnam: rationale and methodology. *Global Heart*. Article ID 32489803. doi: 10.5334/gh.782

	Concept & design	Acquisition of data& Method	Data conditioning & Manipulation	Analysis & Statistical method	Interpretation & Discussion	Final Approval	Total %contribution
Hoa T.T. Vu	20	30	30	70	30	10	190
	I acknowledge that these represent my contribution to the above research output Signed:						
Hoai T.T. Nguyen		20	10			10	40
	I acknowledge that these represent my contribution to the above research output Signed:						
Hung M. Pham		10	10			10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Loi D. Do		10	10			10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Quang N. Nguyen		10	10			10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Richard Norman				10	30	10	50
	I acknowledge that these represent my contribution to the above research output Signed:						
Rachel R. Huxley	25					10	35
	I acknowledge that these represent my contribution to the above research output Signed:						
Ngoc M. Pham				20	20	10	50
	I acknowledge that these represent my contribution to the above research output Signed:						
Crystal M.Y. Lee	20					10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Christopher M. Reid	35	20	30		20	10	115
	I acknowledge that these represent my contribution to the above research output Signed:						
Total %	100	100	100	100	100	100	

Paper 2: Hoa T.T. Vu, Hung M. Pham, Hoai T.T. Nguyen, Quang N. Nguyen, Loi D. Do, Ngoc M. Pham, Richard Norman, Rachel R. Huxley, Crystal M.Y. Lee, Christopher M. Reid (2020). Novel insights into clinical characteristics and in-hospital outcomes of patients undergoing percutaneous coronary intervention in Vietnam. IJC Heart & Vasculature. Article ID 32944609. doi:10.1016/j.ijcha.2020.100626

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Hoa T.T. Vu	20	30	30	70	30	10	190
	I acknowledge that these represent my contribution to the above research output Signed:						
Hung M. Pham		10	10			10	30
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Hoai T.T. Nguyen		20	10			10	40
	I acknowledge that these represent my contribution to the above research output Signed:						
Quang N. Nguyen		10	10			10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Loi D. Do		10	10			10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Ngoc M. Pham				20	20	10	50
	I acknowledge that these represent my contribution to the above research output Signed:						
Richard Norman				10	30	10	50
	I acknowledge that these represent my contribution to the above research output Signed:						
Rachel R. Huxley	25					10	35
	I acknowledge that these represent my contribution to the above research output Signed:						
Crystal M.Y. Lee	20					10	30
	I acknowledge that these represent my contribution to the above research output Signed:						
Christopher M. Reid	35	20	30		20	10	115
	I acknowledge that these represent my contribution to the above research output Signed:						
Total %	100	100	100	100	100	100	

Paper 3: Hoa T.T. Vu, Richard Norman, Ngoc M. Pham, Hung M. Pham, Hoai T.T. Nguyen, Quang N. Nguyen, Loi D. Do, Rachel R. Huxley, Crystal M.Y. Lee, Tu M. Hoang, Christopher M. Reid. Access route selection for percutaneous coronary intervention among Vietnamese patients: implications for in-hospital costs and outcomes. *The Lancet Regional Health- Western Pacific* journal (forthcoming).

	Concept & design	Acquisition of data& Method	Data conditioning & Manipulation	Analysis & Statistical method	Interpretation & Discussion	Final Approval	Total %contribution
Hoa T.T. Vu	20	30	25	70	30	10	185
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Richard Norman				10	30	10	50
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Ngoc M. Pham				20	20	10	50
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Hung M. Pham		10	10			5	25
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Hoai T.T. Nguyen		20	10			10	40
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Quang N. Nguyen		10	10			10	30
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Loi D. Do		10	10			10	30
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Rachel R. Huxley	25					10	35
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Crystal M.Y. Lee	20					10	30
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Tu Minh Hoang			15			5	20
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Christopher M. Reid	35	20	20		20	10	105
	I acknowledge that these represent my contribution to the above research output						
	Signed:						
Total %	100	100	100	100	100	100	

Appendix G Ethics approval

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Web research.curtin.edu.au

19-Jun-2017

Name: Christopher Reid
Department/School: Department of Health Policy and Management
Email: Christopher.Reid@curtin.edu.au

Dear Christopher Reid

RE: Ethics approval
Approval number: HRE2017-0378

Thank you for submitting your application to the Human Research Ethics Office for the project **Development of a clinical quality registry for percutaneous coronary intervention among coronary heart disease patients in Northern Vietnam: A pilot registry study**.

Your application was reviewed by the Curtin University Human Research Ethics Committee at their meeting on **06-Jun-2017**.

The review outcome is: **Approved**.

Your proposal meets the requirements described in National Health and Medical Research Council's (NHMRC) *National Statement on Ethical Conduct in Human Research (2007)*.

Approval is granted for a period of one year from **19-Jun-2017** to **19-Jun-2018**. Continuation of approval will be granted on an annual basis following submission of an annual report.

Personnel authorised to work on this project:

Name	Role
Reid, Christopher	CI
Vu, Thi Thanh Hoa	Student
Lee, Crystal	Supervisor
Huxley, Rachel	Supervisor

Standard conditions of approval

1. Research must be conducted according to the approved proposal
2. Report in a timely manner anything that might warrant review of ethical approval of the project including:
   - proposed changes to the approved proposal or conduct of the study

Appendix H Presentation from the PhD project

CSANZ VIRTUAL 2020

68TH ANNUAL SCIENTIFIC MEETING OF THE CARDIAC SOCIETY OF AUSTRALIA AND NEW ZEALAND

11 – 13 DECEMBER 2020

WWW.CSANZASM.COM

Certificate of Attendance

This is to certify that

Hoa Thi Thanh Vu

Attended the

CSANZ Annual Scientific Meeting 2020

11 - 13 December 2020
Virtual Meeting
Australia

Clara Chow
Convenor

Peter Psaltis
Chair, Scientific Program

Novel insights into clinical characteristics and in-hospital outcomes of patients undergoing percutaneous coronary intervention in Vietnam

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Introduction

- Rapid uptake of percutaneous coronary intervention (PCI) in Asia
- Understandings of practice of PCI in developing countries is limited

Project aim

To report on the clinical characteristics and in-hospital outcomes for patients undergoing PCI in Vietnam

Methods

- First PCI registry was established in Vietnam
- 1,022 patients were recruited from 09/2017-05/2018
- Adapted dataset from Victorian Cardiac Outcomes Registry, Australia

Findings

Patient profiles

- Mean age 68.3 years
- Male 60%; BMI 22.2 ± 2.9

54.4% patients were acute coronary syndrome; 30.7% myocardial infarction

- Hypertension 67.2%, hyperlipidaemia 29.9%; diabetes 27.3%

Procedure details - In hospital outcomes

- Radial artery 79.2%, 11.9% left main PCI
- Drug eluting stent 96.5%
- Angiographic success 99.4%;
- In-hospital death 0.8%; bleeding 2.0%;

Hospital stay 2 days.

Gender differences

- Female patients were 4 years older and had more risk factors and higher rate of major bleeding
- Male patients had higher rate of smoking and more severe lesions

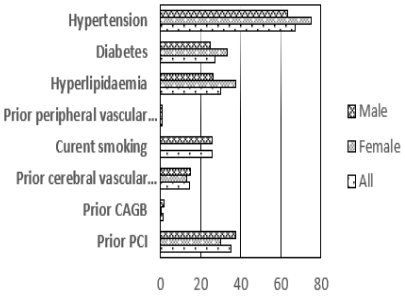

Figure 1: Risk factors of study participants

Conclusions

- Contribute for understanding of current status of PCI in Vietnam
- Provide opportunity to benchmark practices, identify possible care gaps
- Potentially contribute to development of appropriate guidelines and prevention strategies