Heart, Lung and Circulation (2023) **32**, 166–174
1443-9506/22/$36.00
https://doi.org/10.1016/j.hlc.2022.08.012

ORIGINAL ARTICLE

Harmonising Individual Patient Level Cardiac Registry Data Across the Asia Pacific Region—A Feasibility Study of In-Hospital Outcomes of STEMI Patients From the Asia Pacific Evaluation of Cardiovascular Therapies (ASPECT) Network

Christopher M. Reid, PhD [a,b,*], HuiJun Chih, PhD [a], Stephen J. Duffy, MBBS, PhD [b,c], Angela L. Brennan, CCRN [b], Andrew E. Ajani, MBBS, MD [b,d], John Beltrame, MBBS, PhD [e], Rosanna Tavella, PhD [e], Bryan P. Yan, MBBS, MD [f], Diem Dinh, PhD [b], Chee Tang Chin, MBChB [g,h], Loi Doan Do, MD, PhD [i], Quang Ngoc Nguyen, MD, PhD [i], Hoai T.T. Nguyen, MD, PhD [i], Ika Prasetya Wijaya, MD, PhD [j], Muhammad Yamin, MD, PhD [j], Lusiani Rusdi, MD [j], Idrus Alwi, MD, PhD [j], Kui Hian Sim, MBBS [k,l], Alan Yean Yip Fong, MBChB [k,l], Wan Azman Wan Ahmad, MRCP [l,m], Khung Keong Yeo, MBBS [g,h], on behalf of the ASPECT Investigators

[a]School of Population Health, Curtin University, Perth, WA, Australia
[b]School of Public Health and Preventive Medicine, Monash University, Melbourne, Vic, Australia
[c]Department of Cardiology, Alfred Health, Melbourne, Vic, Australia
[d]Department of Cardiology, The Royal Melbourne Hospital, Melbourne, Vic, Australia
[e]Discipline of Medicine, The University of Adelaide, Adelaide, SA, Australia
[f]Division of Cardiology, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong and Prince of Wales Hospital, Hong Kong SAR, China
[g]National Heart Centre Singapore, Singapore
[h]Duke-NUS Medical School, Singapore
[i]Vietnam National Heart Institute, Bach Mai Hospital, Hanoi, Vietnam
[j]Cipto Mangunkusumo National General Hospital, Universitas Indonesia Medical School, Jalan Pangeran Diponegoro, Jakarta, Indonesia
[k]Sarawak Heart Centre, Sarawak, Malaysia
[l]National Heart Association of Malaysia, Kuala Lumpur, Malaysia
[m]University of Malaya Medical Centre, Jalan Universiti, Selangor, Malaysia

Received 15 June 2021; received in revised form 30 June 2022; accepted 2 August 2022; online published-ahead-of-print 20 October 2022

*Corresponding author at: Professor Christopher Reid, Curtin University, Kent Street, Bentley, WA 6102, Australia, Curtin University, GPO Box U1987, Perth, WA 6845, Australia; Email: christopher.reid@curtin.edu.au; Twitter: @profcmreid

Objective The Asia-Pacific Evaluation of Cardiovascular Therapies (ASPECT) collaboration was established to inform on percutaneous coronary intervention (PCI) in the Asia-Pacific Region. Our aims were to (i) determine the operational requirements to assemble an international individual patient dataset and validate the processes of governance, data quality and data security, and subsequently (ii) describe the characteristics and outcomes for ST-elevation myocardial infarction (STEMI) patients undergoing PCI in the ASPECT registry.

Methods Seven (7) ASPECT members were approached to provide a harmonised anonymised dataset from their local registry. Patient characteristics were summarised and associations between the characteristics and in-hospital outcomes for STEMI patients were analysed.

Results Six (6) participating sites (86%) provided governance approvals for the collation of individual anonymised patient data from 2015 to 2017. Five (5) sites (83%) provided >90% of agreed data elements and 68% of the collated elements had <10% missingness. From the registry (n=12,620), 84% were male. The mean age was 59.2±12.3 years. The Malaysian cohort had a high prevalence of previous myocardial infarction (34%), almost twice that of any other sites ($p<0.001$). Adverse in-hospital outcomes were the lowest in Hong Kong whilst in-hospital mortality varied from 2.7% in Vietnam to 7.9% in Singapore.

Conclusions Governance approvals for the collation of individual patient anonymised data was achieved with a high level of data alignment. Secure data transfer process and repository were established. Patient characteristics and presentation varied significantly across the Asia-Pacific region with this likely to be a major predictor of variations in the clinical outcomes observed across the region.

Keywords Cardiovascular outcome • STEMI • Registry • Asia-Pacific

Introduction

Cardiovascular disease (CVD), particularly coronary artery disease, has been the major cause of death and disability across the globe for the past two decades [1,2]. In the low- to middle- and high-income countries of the Asia-Pacific region, the CVD epidemic is in full swing as these countries see a rapid transition into modern industrial societies [3,4]. Not only are they experiencing changes to traditional diet and physical activity patterns that were cardio-protective, but Asia is also seeing an unprecedented change in population demographics with dramatic increases in the number of people entering their sixth, seventh and eighth decades of life in virtually all countries around the region [5]. As part of this rapid development, Asia has also seen major advances in treatments of acute coronary artery disease, and percutaneous coronary intervention (PCI) is now becoming more available across the Asia-Pacific region [6,7]. First conducted in the region in 1981, PCI was limited to specialist centres until the mid-to-late 1990s but the last 15–20 years has seen an explosive growth in annual numbers of PCI cases across the regions [8]. It was recently estimated that approximately one million PCI cases were performed in Asia in 2016, close to the North America and European experience, and this figure is likely to rapidly expand [8].

In recent years, we have seen a major recognition in the value of "real-world data" or data collected as part of the routine clinical practice of performing coronary interventions with endeavours to monitor PCI at national and international levels, and efforts in Europe and North America are world leading in this field [9,10]. Countries in Asia are rapidly catching up in terms of establishing registries across the region, led initially by efforts in Korea and Japan, which have well established national registries [11,12]. In Australia, despite the efforts of many, there is still no national registry, however there are some state-based registries [13–15]. Some countries, like Malaysia, have developed national registries, and major advances in technology have led to Big Data approaches in countries like Singapore to gather key information on the management of cardiac disease, including PCI [16,17]. However, the extent of the development of individual registries varies across the region and the Asia Pacific Evaluation of Cardiovascular Therapies (ASPECT) initiative was established and endorsed through the Asia Pacific Society of Cardiology, with the aim to foster collaboration on PCI registry-based activities across the region.

A feasibility project was designed to validate the methods, identify governance and analysis issues for a merged data registry analysis. The focus was to describe the regional characteristics and outcomes for patients presenting with ST-elevation myocardial infarction (STEMI) undergoing PCI. This paper describes the findings from the feasibility project and presents the initial individual patient data analysis from the ASPECT registry.

Materials and Methods

Study Setting

At the 2018 European Society of Cardiology Scientific Sessions representatives from PCI clinical quality registry initiatives across the region met and agreed to progress with a

demonstration project regarding harmonisation of data for pooled individual data analysis. All volunteer registries were accepted as participants irrespective of level of maturity and representativeness from a country. Registries included single-hospital registries in Singapore, Hong Kong and Vietnam, state-based registries from Australia (Victoria and South Australia), and a national registry from Malaysia [18]. Briefly, data from Singapore were based on a single public tertiary care hospital that contributes to a national registry, whereas data from Australia's Melbourne Interventional Group were from six public tertiary care hospitals. Whilst the collaboration is opportunistic and with the exception of Malaysia does not reflect populations data, these registries assist to identify trends in variation in patient and procedural details and monitor the quality of activity and changes in clinical practice [19]. The participating clinical quality registries collect data from all patients admitted to the hospital between 2015 and 2017 with the exception of Vietnam, for which the data collection was restricted to all patients over a few typical days according to a pre-specified protocol to manage workload and feasibility [20].

Ethics Approval

Protocol was developed and submitted to the Alfred Hospital in Melbourne as the lead Ethics Committee (Ethics Committee No. 586/18). Following approval, each participating registry satisfies the ethical review requirements for the collection of confidential data within the local jurisdiction. All STEMI patients who had undergone PCI at the participating registries during the period were included in the analyses. All participating registries then extracted the agreed set of data elements (Supplementary file) between 2015 and 2017 and prepared anonymised individual patient data sets for merging.

Data Dictionary

The collaborators established definitions and a data dictionary for relevant fields to minimise misclassification bias. For instance, STEMI was defined according the Third Universal Definition of Myocardial Infarction (MI) [21]. Peri-procedural MI was defined as response to the following question [22]: Was a peri-/postoperative myocardial infarction (MI) diagnosed by finding at least two of the following criteria:

a. Enzyme level elevation either:
   i. CK-MB >30 units; OR
   ii. Troponin > 20.0 micrograms/L; OR
   iii. Troponin level equivalent documented at your instruction, provided operation does not involve myocardial incision
b. New wall motion abnormalities
c. Serial ECG (at least two) showing Q waves, duration ≥0.03 ms in two contiguous leads. Major bleeding was defined according to the Bleeding Academic Research Consortium (BARC) consensus [23], specifically, BARC 3 and 5 types of bleeding. New renal impairment was defined as a Yes/No response by asking; "Was there acute post-operative renal insufficiency" characterised by one of the following:
   i. Increased serum creatinine to >0.2 mmol/L (>200 μmol/L) AND a doubling or greater increase in creatinine over the baseline preoperative value AND the patient did not require preoperative dialysis/haemofiltration, OR
   ii. A new postoperative requirement for dialysis/haemofiltration (when the patient did not require this preoperatively).

The definitions and a data dictionary as well as a data extract schema defining the attributes for each field required were provided to each registry. Whilst the process of data collection varied at each site, data were checked and reviewed locally at each site prior to entry in the registry. No formal data validation procedures were undertaken as part of the registry data collection.

Data Management

Each registry dataset was transferred by Secure Unified File Exchange (SUFEX) provided by the Centre for Clinical Research and Education (CCRE) at Curtin University. The data were initially checked for completeness and queries were generated and sent back to the individual registry for confirmation to clarify whether any data marked as "missing" meant that the data were not supplied, and not due to some oversight or conversion error. Clean data were then resubmitted to the CCRE for compilation into an integrated ASPECT STEMI dataset for analysis. The ASPECT STEMI dataset was housed in a SafeHaven at Curtin University using secure ISO27001 compliant technology deployed via a mutual collaboration with Swansea Universities Secure Anonymous Information Linkage (SAIL) Gateway in the United Kingdom [24]. Access to the data may be requested via the SeRP@Curtin platform from this link: https://research.curtin.edu.au/healthsciences/health-sciences-research/research-institutes-centres/centre-for-data-linkage/serp/.

Feasibility Assessment

Feasibility was determined through the following measures:

- The number of ASPECT members able to gain governance approvals within the allocated time frame to provide data. The allocated time frame was within 6 months of project ethical approval;
- The number of sites able to provide >90% of agreed data elements; and
- The number of sites with missing data <10% for all variables included.

Statistical Analyses of Patient Characteristics and In-Hospital Outcomes

Demographics, medical conditions, presentation details, procedural characteristics and in-hospital clinical outcomes of patients admitted with STEMI at each of the PCI registries

(the relatively small South Australia registry was combined with the Victoria registry) were described in mean and standard deviation (or median and interquartile range) or number of observations and percentage. Comparison of these variables by sites were performed using one-way analysis of variance, Kruskal-Wallis, or Chi-squared tests, where appropriate. The in-hospital clinical outcomes included new renal impairment, major bleeding, peri-procedural recurrent myocardial infarction, stent thrombosis, emergency coronary artery bypass graft (CABG), target vessel revascularisation (TVR), cerebrovascular events (CVE)/stroke, death and any major adverse cardiovascular and cerebrovascular events (MACCE) in hospital. In-hospital MACCE was defined as having experienced peri-procedural recurrent myocardial infarction, stent thrombosis, emergency CABG, CVE/stroke, or death.

Predictors of in-hospital MACCE on univariate logistic regression models were included in the corresponding multiple logistic regression models with registry sites as an additional covariate. Stepwise approach was then applied until the final models contained only the predictors associated significantly ($p<0.05$) with in-hospital MACCE. The adjusted odds ratios (OR) and 95% confidence intervals (CI) were reported. It is acknowledged that residual confounding is unavoidable in this analysis due to lack of data, such as data on marker of use of statin and marker of frailty. Complete case analyses were performed as the missing data were likely to be missing completely at random. Significance was set as <0.05. All statistical analyses were performed using Stata MP version 16 (StataCorp, College Station, TX, USA).

Results

Feasibility—Governance Approval

Six (6) of seven ASPECT registries (86%) gained governance approvals for the project and were able to provide data in the time frame for analysis; South Australia, Melbourne (combined into one "Australia" due to the relatively small number from South Australia), Vietnam, Hong Kong, Malaysia and Singapore. Governance requirements from a single non-participating registry (Indonesia) were not in place for inclusion in this analysis.

Feasibility—Data Quality

Across the six registries, five (83%) were able to provide >90% of the agreed data elements (Tables 1 and 2). About 68% (21/31) of the collated elements had <10% of missingness. The patient characteristic variables with missingness over 40% were family history of coronary artery disease (CAD) and lung disease (none from Malaysia and Vietnam), estimated ejection fraction data (none from Hong Kong, 68% missing from Malaysia) and door to balloon time (none from Vietnam, 79% missing from Hong Kong and Malaysia). None of the key variables (age, gender, treatments given prior to procedure, major bleeding and deceased status) had any missingness.

Patient Characteristics

The combined ASPECT STEMI dataset comprised a total of 12,620 cases (Table 1) with the number varying from each participating registry due to a differing number and size of contributing sites. Most of the patients were from Malaysia (39%), followed by Hong Kong (27%), Melbourne and South Australia combined (24%), Singapore (9%) and Vietnam (1%).

There were more male patients admitted for STEMI across all sites ($p<0.001$; Table 1). On average, the Vietnamese patients were the oldest across all sites ($p<0.001$). Forty-four per cent (44%) of the Malaysian patients were current smokers while 59% of the Singaporean patients never smoked. Whilst 29% of the Australian patients had family history of CAD, the majority of patients from Hong Kong and Singapore had no family history of CAD. Diabetes was more prevalent in Singapore (30%), Hong Kong (34%) and Malaysia (38%) than in Australia (18%) and Vietnam (14%). Of note, 98% and 88% of the patients from Hong Kong had dyslipidaemia and hypertension respectively. Most of the patients across all registries did not have a history of congestive heart failure, cerebrovascular disease, peripheral vascular disease, previous PCI or previous CABG. About 34% of the Malaysian patients had previous myocardial infarction (MI), which was at least two times the rate observed in the other registries ($p<0.001$).

Presentation Details and Treatment

The percutaneous entry location was primarily radial or brachial across all sites whilst Singapore reported similar percentage for radial or brachial (49%) and femoral (51%) (Table 1). The median door to balloon time was the longest in Malaysia (101 mins) and shortest in Vietnam (65 mins). Treatments provided were similar across the region with high use of aspirin and any P2Y12 inhibitors. Majority of stents used were drug eluting (87% of cases). Bare-metal stent use ranged from 19.4% in Australia to no bare metal stents used in Vietnam.

The majority of lesions (95%) were *de novo*. The lesion type, as defined by the American College of Cardiology/American Heart Association (ACC/AHA) guidelines [25], differed across the registries. With respect to Type C lesions, Vietnam reported a rate of 87% whereas Malaysia reported 43% and Hong Kong reported just 12% (Figure 1). Data related to lesion types, lesion length >20 mm, lesion success and complications are presented in Figure 1. Lesion success was high across all sites. The lesion complication rate ranged from 0.3 to 8.2%.

Table 2 illustrates in-hospital outcomes, with low rates of major bleeding, peri-procedural recurrent MI, stent thrombosis, emergency CABG, TVR or stroke. New renal impairment was reported in 6% of the patients in Vietnam, 5% in Australia and 3% in Singapore ($p<0.001$). The in-hospital mortality ranged from 3% in Vietnam to 8% in Singapore ($p=0.012$) whilst the prevalence of MACCE ranged from 3% in Vietnam to 10% in Singapore ($p<0.001$).

Table 1 Characteristics and presentation details of ASPECT STEMI patients, and treatment provided, by sites (n=12,620)*

	Total (n=12,620)	Australia (n=3,068)	Hong Kong (n=3,408)	Malaysia (n=4,888)	Singapore (n=1,108)	Vietnam (n=148)	P-value
Patient Characteristics							
Age (mean±SD), years	59.3±12.3	62.4±12.5	61.8±11.9	55.0±11.1	60.1±12.8	67.7±12.2	*p<0.001*
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	
Gender							
Male	10,657 (84.4)	2,429 (79.2)	2,903 (85.2)	4,316 (88.3)	899 (81.1)	110 (74.3)	*p<0.001*
Female	1,963 (15.6)	639 (20.8)	505 (14.8)	572 (11.7)	209 (18.9)	38 (25.7)	
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	
Smoking history							
Current smoker	5,005 (39.7)	1,122 (36.6)	1,247 (36.6)	2,151 (44.0)	454 (41.0)	31 (20.9)	*p<0.001*
Never or ex-smoker	6,559 (52.0)	1,771 (57.7)	1,878 (55.1)	2,139 (43.8)	654 (59.0)	117 (79.1)	
Missing (% of total)	*1,056 (8.4)*	*175 (5.7)*	*283 (8.3)*	*598 (12.2)*	*0*	*0*	
Family history of CAD	1,067 (8.5)	886 (28.9)	39 (1.2)	*(missing)*	142 (12.8)	*(missing)*	*p<0.001*
Missing (% of total)	*5,702 (45.2)*	*401 (13.1)*	*265 (7.8)*	*4,888 (100.0)*	*0*	*148 (100.0)*	
History of diabetes	3,912 (31.0)	539 (17.6)	1,173 (34.4)	1,844 (37.7)	335 (30.2)	21 (14.2)	*p<0.001*
Missing (% of total)	*476 (3.8)*	*17 (0.6)*	*0*	*459 (9.4)*	*0*	*0*	
History of dyslipidaemia	7,335 (58.1)	1,461 (47.6)	3,349 (98.3)	1,922 (39.3)	586 (52.9)	17 (11.5)	*p<0.001*
Missing (% of total)	*748 (5.9)*	*21 (0.7)*	*0*	*727 (14.9)*	*0*	*0*	
History of hypertension	8,005 (63.4)	1,648 (53.7)	2,995 (87.9)	2,639 (54.0)	635 (57.3)	88 (59.5)	*p<0.001*
Missing (% of total)	*459 (3.6)*	*22 (0.7)*	*0*	*437 (8.9)*	*0*	*0*	
History of heart failure	315 (2.5)	52 (1.7)	92 (2.7)	110 (2.3)	61 (5.5)	*(missing)*	*p<0.001*
Missing (% of total)	*379 (3.0)*	*34 (1.1)*	*0*	*197 (4.0)*	*0*	*148 (100.0)*	
History of stroke	509 (4.0)	134 (4.4)	177 (5.2)	115 (2.4)	60 (5.4)	23 (15.5)	*p<0.001*
Missing (% of total)	*244 (1.9)*	*37 (1.2)*	*0*	*207 (4.2)*	*0*	*0*	
History of PVD	194 (1.5)	94 (3.1)	57 (1.7)	13 (0.3)	29 (2.6)	1 (0.7)	*p<0.001*
Missing (% of total)	*316 (2.5)*	*40 (1.3)*	*0*	*276 (5.7)*	*0*	*0*	
History of lung disease	362 (2.9)	296 (9.6)	45 (1.3)	*(missing)*	21 (1.9)	*(missing)*	*p<0.001*
Missing (% of total)	*5,075 (40.2)*	*39 (1.3)*	*0*	*4,888 (100.0)*	*0*	*148 (100.0)*	
Previous MI >7 days	2,794 (22.1)	374 (12.2)	609 (17.9)	1,667 (34.1)	144 (13.0)	*(missing)*	*p<0.001*
Missing (% of total)	*545 (4.3)*	*29 (1.0)*	*0*	*368 (7.5)*	*0*	*148 (100.0)*	
Previous PCI	1,253 (9.9)	362 (11.8)	277 (8.1)	434 (8.9)	160 (14.4)	20 (13.5)	*p<0.001*
Missing (% of total)	*26 (0.2)*	*26 (0.9)*	*0*	*0*	*0*	*0*	
Previous CABG	140 (1.1)	76 (2.5)	16 (0.5)	20 (0.4)	27 (2.4)	1 (0.7)	*p<0.001*
Missing (% of total)	*20 (0.2)*	*20 (0.7)*	*0*	*0*	*0*	*0*	
eGFR median (IQR), µmol/L	88.0 (32.4)	86.1 (42.4)	88.0 (29.0)	88.0 (31.0)	89.0 (34.0)	85.0 (31.0)	*p<0.001*
eGFR or creatinine, µmol/L							
<30	79 (0.6)	76 (2.5)	1 (0.0)	0	2 (0.2)	0	*p<0.001*
30-60	810 (6.4)	419 (13.7)	145 (4.3)	169 (3.5)	65 (5.9)	12 (8.1)	
>60	10,190 (80.7)	2,097 (68.4)	3,251 (95.4)	3,720 (76.1)	987 (89.1)	135 (91.2)	
Missing (% of total)	*1,541 (12.2)*	*476 (15.5)*	*11 (0.3)*	*999 (20.4)*	*54 (4.9)*	*1 (0.7)*	
Presentation Details							
Cardiogenic shock at PCI	1,189 (9.4)	254 (8.3)	316 (9.3)	509 (10.4)	100 (9.0)	10 (6.8)	*0.020*
Missing (% of total)	*6 (0.1)*	*6 (0.2)*	*0*	*0*	*0*	*0*	
PCI vascular access – radial/brachial	7,370 (58.4)	1,782 (58.1)	1,924 (56.5)	3,004 (61.5)	542 (48.9)	118 (79.7)	*p<0.001*
Missing (% of total)	*179 (1.4)*	*0*	*179 (5.3)*	*0*	*0*	*0*	
est EF†							
Severe (<35%)	841 (6.7)	202 (6.6)	*(missing)*	194 (12.4)	432 (39.6)	13 (12.5)	*p<0.001*
Moderate (35-44%)	1,275 (10.1)	541 (17.6)	*(missing)*	485 (30.9)	215 (19.7)	34 (32.7)	
Mild (45-50%)	1,532 (12.1)	887 (28.9)	*(missing)*	465 (29.7)	157 (14.4)	23 (22.1)	
Normal (>50%)	1,954 (15.5)	1,210 (39.4)	*(missing)*	424 (27.0)	286 (26.2)	34 (32.7)	

Table 1. (continued).

	Total (n=12,620)	Australia (n=3,068)	Hong Kong (n=3,408)	Malaysia (n=4,888)	Singapore (n=1,108)	Vietnam (n=148)	P-value
Missing (% of total)	*7,018 (55.6)*	*228 (7.4)*	*3,408 (100.0)*	*3,320 (67.9)*	*18 (1.6)*	*44 (29.7)*	
Multi-vessel disease	5,705 (45.2)	1,633 (53.2)	1,831 (53.7)	1,456 (29.8)	761 (68.7)	24 (16.2)	*p<0.001*
Missing (% of total)	*3,432 (27.2)*	*0*	*3,432 (70.2)*	*0*	*0*	*0*	
Door to balloon time, median (IQR), minutes	77 (72)	71 (74)	90 (54)	101 (90)	65 (36)	*(missing)*	*p<0.001*
Missing (% of total)	*7,306 (57.9)*	*158 (5.1)*	*2,701 (79.3)*	*3,865 (79.1)*	*434 (39.2)*	*148 (100.0)*	
Treatment Given Prior to the Procedure							
Aspirin	12,108 (95.9)	2,989 (97.4)	3,362 (98.7)	4,528 (92.6)	1,083 (97.7)	146 (98.6)	*p<0.001*
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	
P2Y12 inhibitors (any of thienopyridine/clopidogrel/ticagrelor/prasugrel)	11,714 (92.8)	2,957 (96.4)	3,366 (98.8)	4,142 (84.7)	1,101 (99.4)	148 (100)	*p<0.001*
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	

*Data presented are n (%) unless otherwise stated.

†Percentages were calculated based on the available EF data instead of the total cohort within each registry.

Abbreviations: STEMI, ST-elevation myocardial infarction; SD, standard deviation; CAD, coronary artery disease; PVD, peripheral vascular disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; IQR, interquartile range; PCI, percutaneous coronary intervention; est EF, estimated ejection fraction.

Potential Predictors of In-Hospital MACCE and Mortality

Predictors associated with odds of any MACCE in hospital varied while adjusted for sites (Figure 2). Having had cardiogenic shock at PCI, experienced complications with lesion and had bare-metal stent were associated with higher odds of in-hospital MACCE. However, the estimation for cardiogenic shock is imprecise (95% CI of aOR 6.5–15.3). Lower odds of in-hospital MACCE were associated with history of dyslipidaemia, having eGFR of >30, having ejection fraction of >35% (Figure 2).

Discussion

The ASPECT collaboration has successfully merged individual anonymised patient data from six independent registries across the Asia-Pacific region. The registries have been independently established and collected data for varying time periods, however a high degree of alignment of data definitions was observed with the standard definitions of variables being used and there was no issue with translation being documented because English is commonly spoken across the six sites. Nevertheless, missingness was observed. Majority of the high level of missingness (>40%) was contributed by missing data from the entire registries and hence routine data check at individual registry site and where possible, multiple imputation are recommended to further improve data harmonising. It is worth noting that some of the variables with high level of missingness (such as history of lung disease and target vessel revascularisation) are not influential of the main clinical outcomes (death or MACE) whilst the main predictors (age, gender, treatments given prior to procedure, major bleeding) had no missingness. To our knowledge, our study is the first demonstration of the prospects of pooling of anonymised individual patient data from independent registries across the Asia-Pacific region.

Risk factors, in particular smoking, diabetes and hypertension varied widely across the region which could impact on management decisions and clinical outcomes. High rates of diabetes in Hong Kong, Malaysia and Singapore in comparison to the Australian and the Vietnamese registries is consistent with other population-based cohort studies of cardiovascular risk factors across the region [26]. The relatively low rate of current smoking amongst patients from Vietnam is unusual, given the high population rates of smoking, particularly in males. This could be due to following medical advice to quit smoking. The quality of self-reported family and personal medical history also varied across the registries, however did reflect previously reported higher rates of family history of CAD in predominantly Caucasian populations and lower rates amongst Chinese [27].

Multi-vessel coronary disease (MVD) was highly prevalent across the region with Vietnam being the exception (range 16.2% to 68.7%). It is unclear why the rate of MVD reported was so low in Vietnam. This may reflect the level of background cardiovascular risk factors including diabetes and hyperlipidaemia, as Vietnam might be considered as the least

Table 2 **In-hospital clinical outcomes by sites (n=12,620).***

	Total (n=12,620)	Australia (n=3,068)	Hong Kong (n=3,408)	Malaysia (n=4,888)	Singapore (n=1,108)	Vietnam (n=148)	P-value
New renal impairment (post procedure rise in creatinine)	224 (1.8)	159 (5.2)	*(missing)*	24 (0.5)	32 (2.9)	9 (6.1)	*p<0.001*
Missing (% of total)	*3,455 (27.4)*	*0*	*3,408 (100.0)*	*46 (0.9)*	*0*	*1 (0.7)*	
Major bleeding	132 (1.0)	79 (2.6)	3 (0.1)	1 (0.0)	43 (3.9)	6 (4.1)	*p<0.001*
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	
Peri-procedural recurrent myocardial infarction	106 (0.8)	34 (1.1)	12 (0.3)	46 (0.9)	14 (1.3)	0	*0.002*
Missing (% of total)	*55 (0.4)*	*0*	*0*	*55 (1.1)*	*0*	*0*	
Stent thrombosis	37 (0.3)	30 (1.0)	0	7 (0.1)	0	0	*p<0.001*
Missing (% of total)	*4,864 (38.5)*	*0*	*0*	*4,864 (99.5)*	*0*	*0*	
Emergency CABG	45 (0.4)	40 (1.3)	0	1 (0.0)	4 (0.4)	0	*p<0.001*
Missing (% of total)	*30 (0.2)*	*0*	*0*	*30 (0.6)*	*0*	*0*	
TVR	33 (0.3)	25 (0.8)	5 (0.1)	*(missing)*	3 (0.3)	0	*p<0.001*
Missing (% of total)	*7,817 (61.9)*	*2,929 (95.5)*	*0*	*4,888 (100.0)*	*0*	*0*	
CVE or stroke	46 (0.4)	21 (0.7)	3 (0.1)	3 (0.1)	17 (1.5)	2 (1.4)	*p<0.001*
Missing (% of total)	*31 (0.3)*	*0*	*0*	*31 (0.6)*	*0*	*0*	
Vital status (deceased)	729 (5.8)	176 (5.7)	188 (5.4)	273 (5.6)	88 (7.9)	4 (2.7)	*0.012*
Missing (% of total)	*0*	*0*	*0*	*0*	*0*	*0*	
MACCE	895 (7.1)	265 (8.6)	199 (5.8)	315 (6.4)	111 (10.0)	5 (3.4)	*p<0.001*
Missing (% of total)	*4,567 (36.2)*	*0*	*0*	*4,567 (93.4)*	*0*	*0*	

*Data presented are n (%).

Abbreviations: TVR, target vessel revascularisation; CVE, cerebrovascular event; CABG, coronary artery bypass graft; MACCE, major adverse cardiovascular event was defined as having experienced peri-procedural recurrent myocardial infarction, stent thrombosis, emergency CABG, CVE/stroke, or death.

'westernised society' of the countries involved in the collaboration. Collecting data over a longer period instead of a few typical days from registries may be useful to explain the differences.

Previous research into comparative studies of clinical outcomes in patients with STEMI undergoing interventional procedures across the region have used a meta-analytical approach from individual registry reporting [28]. The

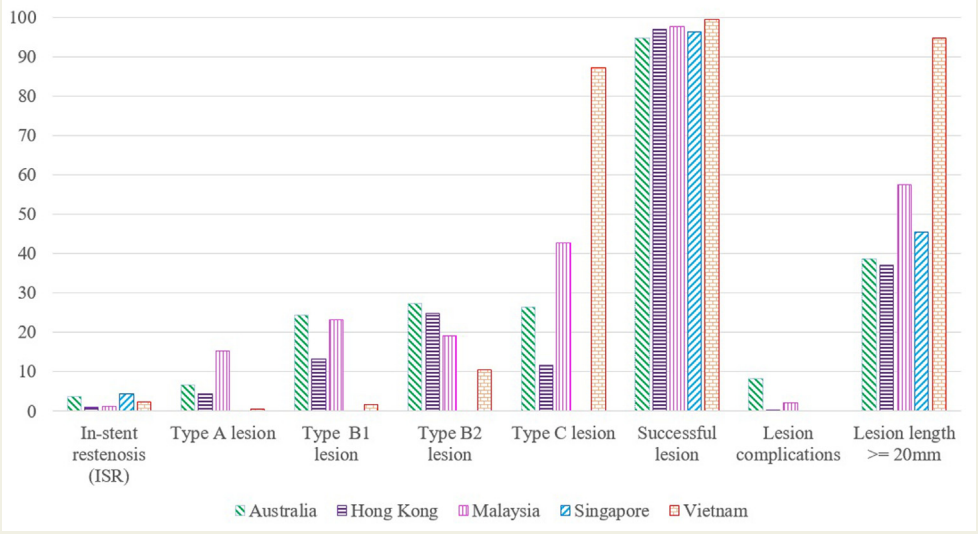

Figure 1 STEMI lesion details across the ASPECT registry.

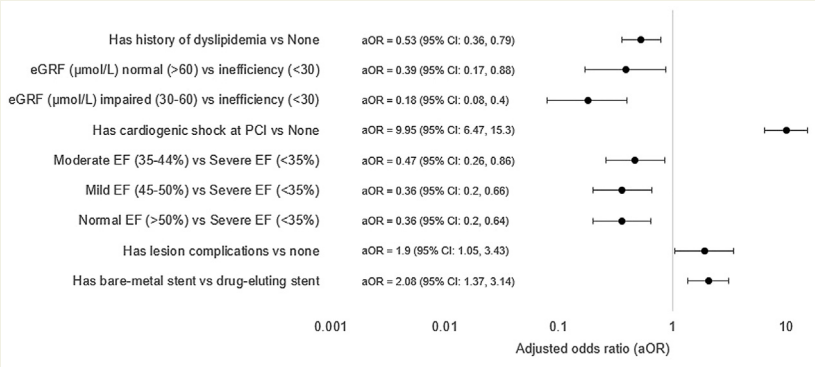

Figure 2 In-hospital major adverse cardiovascular event (MACCE).
Abbreviations: PCI, percutaneous coronary intervention.

current analysis sees Singapore and Malaysian in-hospital mortality rates similar to those reported in Australia, Hong Kong and Vietnam, with the overall mortality approximately 5%. This compares favourably with that reported in the UK, Europe and the United States [29–32]. Other non-fatal outcomes, including major bleeding and peri-procedural recurrent myocardial infarction were low [32].

Whilst this study demonstrated the prospects of pooling anonymised individual patient data from independent registries across the Asia-Pacific region, and the potential to identify predictors of the outcomes using the current state of pooled data, there is room for improvements in relation to the feasibility of data quality. For instance, formal data validation routine (especially of variables that are prone to missing) may need to be integrated in registry data collection in order to harmonise the data for robust statistical modelling. Additional variables such as use of statin or marker for statin use, marker of frailty could also be included in the data elements to minimise the impact of residual confounding. The predictors identified from this preliminary feasibility study need to be interpreted with caution.

Whilst the co-authors across different countries noted that the findings were comparable to observations at their clinical practices, this study has some limitations. For instance, lack of data to minimise impact of missingness and residual confounding in the modelling. In addition, with the exception of Malaysia, which collects data from all PCI hospitals in the country through the National Cardiac Databank, the data presented represent one or more PCI capable centres in the region and may not provide a true representation of all patients undergoing PCI in the country or region. We learnt that it may also be useful to collect data over a longer period instead of across a few typical days. In addition, a number of the registries across the region link the respective National Death data sets and incorporate 12-month follow-up into their registry outcomes ascertainment. Future studies may aim to look at harmonising longer-term outcomes data for robust statistical modelling in order to identify influential factors on quality of care and outcomes for patients across the Asia-Pacific region.

Conclusions

It is possible to identify variation across the region in terms of patient characteristics and procedural details, and to monitor the quality of activity in terms of time for treatment, contemporary clinical practice and patient outcomes at the regional level using the ASPECT registry data. The process of individual patient data merging has been validated and has the potential to provide a platform for research, education and training on the delivery of cardiac interventions at a national and international level. As appropriate ethics and governance procedures have been established, and more registries are established through ASPECT, broader participation from sites across the Asia-Pacific region is possible to facilitate further pooled data analyses addressing questions related to the quality of care and outcomes for patients across the Asia-Pacific region. The collaboration will inform clinicians of patient outcomes from cardiac interventions in the region and provide opportunity to compare longitudinal data with the North American and European data to predict (long-term) patient outcomes.

Funding

The ASPECT Collaboration activities are supported by an Australian National Health and Medical Research Council (NHMRC) Program Grant [grant number: GNT 546272]. The first author is supported by a NHMRC Principal Research Fellowship [grant number: GNT 1136372].

Conflict of Interest

All authors declare no competing interest.

Acknowledgement

We acknowledge the contribution of all data managers and clinicians participating in country specific registries.

Appendices

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2022.08.012

References

[1] Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997;349(9061):1269–76.

[2] Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. J Am Coll Cardiol. 2017;70(1):1–25.

[3] Yuyun MF, Sliwa K, Kengne AP, Mocumbi AO, Bukhman G. Cardiovascular diseases in sub-Saharan Africa compared to high-income countries: an epidemiological perspective. Glob Heart. 2020;15(1):15.

[4] Zhang G, Yu C, Zhou M, Wang L, Zhang Y, Luo L. Burden of ischaemic heart disease and attributable risk factors in China from 1990 to 2015: findings from the global burden of disease 2015 study. BMC Cardiovasc Disord. 2018;18(1):18–31.

[5] Hayes A. Population dynamics and sustainable development in Asia and the Pacific. Asia Pac Popul J. 2014;28.

[6] Chan MY, Du X, Eccleston D, Ma C, Mohanan PP, Ogita M, et al. Acute coronary syndrome in the Asia-Pacific region. Intl J Cardiol. 2016;202:861–9.

[7] Ohira T, Iso H. Cardiovascular disease epidemiology in Asia: an overview. Circ J. 2013;77(7):1646–52.

[8] Gao R. The evolution of percutaneous coronary intervention in Asia: in celebration of the 40th anniversary of percutaneous transluminal coronary angioplasty. AsiaIntervention. 2017;3:95–6.

[9] Moussa I, Hermann A, Messenger JC, Dehmer GJ, Weaver WD, Rumsfeld JS, et al. The NCDR CathPCI Registry: a US national perspective on care and outcomes for percutaneous coronary intervention. Heart. 2013;99(5):297.

[10] Szummer K, Wallentin L, Lindhagen L, Alfredsson J, Erlinge D, Held C, et al. Improved outcomes in patients with ST-elevation myocardial infarction during the last 20 years are related to implementation of evidence-based treatments: experiences from the SWEDEHEART registry 1995-2014. Eur Heart J. 2017;38(41):3056–65.

[11] Inohara T, Kohsaka S, Yamaji K, Amano T, Fujii K, Oda H, et al. Impact of institutional and operator volume on short-term outcomes of percutaneous coronary intervention: a report from the Japanese Nationwide Registry. JACC Cardiovasc Interv. 2017;10(9):918–27.

[12] Jang J-S, Han K-R, Moon K-W, Jeon DW, Shin D-H, Kim J-S, et al. The current status of percutaneous coronary intervention in Korea: based on year 2014 cohort of Korean Percutaneous Coronary Intervention (K-PCI) Registry. Korean Circ J. 2017;47(3):328–40.

[13] Ajani AE, Reid CM, Duffy SJ, Andrianopoulos N, Lefkovits J, Black A, et al. Outcomes after percutaneous coronary intervention in contemporary Australian practice: insights from a large multicentre registry. Med J Aust. 2008;189:423–8.

[14] Labrosciano C, Tavella R, Air T, Zeitz C, Worthley M, Beltrame J. Using the LACE index to predict 30-day all-cause unplanned readmission and mortality in acute myocardial infarction patients: insights from the CADOSA registry. Heart Lung Circ. 2019;28:S328.

[15] Papapostolou S, Dinh DT, Noaman S, Biswas S, Duffy SJ, Stub D, et al. Effect of age on clinical outcomes in elderly patients (>80 years) undergoing percutaneous coronary intervention: insights from a multicentre australian PCI registry. Heart Lung Circ. 2021;30(7):1002–13.

[16] Liew HB, Rosli MA, Wan Azman WA, Robaayah Z, Sim KH. The foundation of NCVD PCI registry: the Malaysia's first multi-centre interventional cardiology project. Med J Malaysia. 2008;63(Suppl C):41–4.

[17] Yeo KK, Ong H-Y, Chua T, Lim ZJ, Yap J, Ho HH, et al. Building a longitudinal national integrated cardiovascular database—lessons learnt from SingCLOUD. Circulation Reports. 2019;2(1):33–43.

[18] Reid CM, Yan B, Wan Ahmad WA, Bang LH, Hian SK, Chua T, et al. The Asia-Pacific Evaluation of Cardiovascular Therapies (ASPECT) Collaboration—improving the quality of cardiovascular care in the Asia Pacific Region. Int J Cardiol. 2014;172(1):72–5.

[19] Hoque DME, Kumari V, Hoque M, Ruseckaite R, Romero L, Evans SM. Impact of clinical registries on quality of patient care and clinical outcomes: a systematic review. PLoS ONE. 2017;12(9):e0183667.

[20] Vu HTT, Nguyen HTT, Pham HM, Do LD, Nguyen QN, Norman R, et al. Establishment of a percutaneous coronary intervention registry in Vietnam: rationale and methodology. Glob Heart. 2020;15(1):30.

[21] Thygesen K, Alpert Joseph S, Jaffe Allan S, Simoons Maarten L, Chaitman Bernard R, White Harvey D. Third universal definition of myocardial infarction. Eur Heart J. 2012;33(16):2551–67.

[22] Lansky AJ, Stone GW. Periprocedural myocardial infarction. Circ Cardiovasc Interv. 2010;3(6):602–10.

[23] Mehran R, Rao Sunil V, Bhatt Deepak L, Gibson CM, Caixeta A, Eikelboom J, et al. Standardized bleeding definitions for cardiovascular clinical trials. Circulation. 2011;123(23):2736–47.

[24] Jones KH, Ford DV, Jones C, Dsilva R, Thompson S, Brooks CJ, et al. A case study of the Secure Anonymous Information Linkage (SAIL) Gateway: a privacy-protecting remote access system for health-related research and evaluation. J Biomed Inform. 2014;50:196–204.

[25] Cannon CP, Brindis RG, Chaitman BR, Cohen DJ, Cross JT, Drozda JP, et al. 2013 ACCF/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes and coronary artery disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on clinical data standards. J Am Coll Cardiol. 2013;61:992–1025.

[26] Abdullah N, Attia J, Oldmeadow C, Scott RJ, Holliday EG. The architecture of risk for type 2 diabetes: understanding Asia in the context of global findings. Int J Endocrinol. 2014;2014:593982.

[27] Pandey AK, Blaha MJ, Sharma K, Rivera J, Budoff MJ, Blankstein R, et al. Family history of coronary heart disease and the incidence and progression of coronary artery calcification: Multi-Ethnic Study of Atherosclerosis (MESA). Atherosclerosis. 2014;232(2):369–76.

[28] Tern PJW, Ho AKH, Sultana R, Ahn Y, Almahmeed W, Brieger D, et al. Comparative overview of ST-elevation myocardial infarction epidemiology, demographics, management, and outcomes in five Asia-Pacific countries: a meta-analysis. Eur Heart J Qual Care Clin Outcomes. 2021;7:6–17.

[29] Alabas OA, Jernberg T, Pujades-Rodriguez M, Rutherford MJ, West RM, Hall M, et al. Statistics on mortality following acute myocardial infarction in 842 897 Europeans. Cardiovasc Res. 2020;116(1):149–57.

[30] Cretu DE, Udroiu CA, Stoicescu CI, Tatu-Chitoiu G, Vinereanu D. Predictors of in-hospital mortality of ST-segment elevation myocardial infarction patients undergoing interventional treatment. An analysis of data from the RO-STEMI registry. Maedica (Bucur). 2015;10(4):295–303.

[31] Goldberger Jeffrey J, Subacius H, Goldberg S. In-hospital mortality after acute myocardial infarction: time-dependent risk profile. J Am Coll Cardiol. 2014;63(12_Supplement):A146A–A.

[32] Sladojevic M, Pavlovic K, Velicki L, Cemerlic-Adjic N, Popov T, Tadic S, et al. In-hospital mortality prediction for STEMI patients submitted to primary PCI. Eur Heart J. 2013;34(suppl_1).