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Characteristics and the average 30-day and 6-month clinical outcomes of patients hospitalised with coronary artery disease in a poor South-East Asian setting: the first cohort from Makassar Cardiac Center, Indonesia

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ABSTRACT

Objective To provide a detailed description of characteristics at hospital admission and clinical outcomes at 30-day and 6-month follow-up in patients hospitalised with coronary artery disease (CAD) in a poor South-East Asian setting.

Design Prospective observational cohort study.

Setting From February 2013 to December 2014, in Makassar Cardiac Center, Indonesia.

Participants 477 patients with CAD (acute coronary syndrome and stable CAD).

Outcome measures All-cause mortality and major adverse cardiovascular events (MACE).

Results Out of 477 patients with CAD, the proportion of young age (<60 years) was 53.9% and 72.7% were male. At admission, 44.2% of patients were diagnosed with ST-segment elevation myocardial infarction (STEMI), 38.6% with diagnosis or signs of heart failure and 75.1% had previous hypertension. Out of 211 patients with STEMI, only 4.7% had been treated with primary percutaneous coronary intervention (PCI) and 6.2% received thrombolysis. The time lapse from symptom onset to hospital admission was 26.8 (IQR 10.0–48.0) hours, and 19.1% of all patients had undergone either PCI or coronary artery bypass graft. The survival rate at 6 months was 78.9%. The rates of all-cause mortality at 30 days and 6 months were 13.4% and 7.3%, respectively; the rate of composite MACE at 30 days was 26.2% and 18.0% at 6 months.

Conclusions Patients with CAD from a poor South-East Asian setting present themselves with predominantly unstable conditions of premature CAD. These patients show relatively severe illness, have significant time delay from symptom onset to admission or intervention, and most do not receive the guidelines-recommended treatment. Awareness of symptoms, prompt initial management of acute CVD, well-established infrastructures and resources both in primary and secondary hospital for CVD should be improved to reduce the high rates of 30-day and 6-month mortality and adverse outcomes in this population.

Strengths and limitations of this study

- This is the first study that fully reports on characteristics at admission as well as the short-term and mid-term outcomes of patients with coronary artery disease (CAD) in Indonesia.
- We completed, to the best of our ability, the follow-up of this study by actively visiting patients' houses or contacting their family members to obtain outcomes data.
- Diversity on places of origin in our cohort represents the population in Indonesia, and generally represents a population in South-East Asia with limited resources.
- Due to geographical and distance constraints, follow-up was completed by telephone in half of this cohort.
- We excluded all patients with normal coronary angiography, and therefore our study might overlook the minor group of non-obstructive CAD.

INTRODUCTION

The South-East Asia region, which accounts for one-quarter of the world's population and 40% of the global poor, is facing a rapid epidemiological transition.[1] This leads to the high rates of premature death from non-communicable diseases (NCD), primarily from cardiovascular disease (CVD).[2] Of the 7.9 million annual NCD in this region, 34% occur before the age of 60 years compared with 16% in the European region and 23% in the rest of the world.[2] Half of the world's cardiovascular burden is estimated to occur in Asia,[3] and the prevalence of symptomatic heart failure appears to be higher in South-East Asia countries compared with the rest of

the world.[4] Despite the high burden of CVD in South-East Asia, little is known about characteristics at admission and clinical outcomes in patients with coronary artery disease (CAD), especially acute coronary syndrome (ACS).

Recent studies indicate the insufficient access to evidence-based interventions for combating CVD in low-income and middle-income countries.[5 6] Particularly in Indonesia, the population of 260 million and a unique demographic situation (consisting of 17 508 islands, over 6000 are inhabited) aggravate the inequity in the access to healthcare services, not only between the the rich and the poor, but also between rural and urban population within the country. Logistics and financial shortcomings,[7] as well as the low awareness of the symptoms[6] associated with CVD in these populations—resulted in delayed diagnosis and a younger age of death from CVD compared with the Western world.[8] In Indonesia, there were approximately 760 cardiologists[9] and only 70 certified interventional cardiologists[10] available to serve 883 447 patients diagnosed with CAD and approximately 2 650 340 patients suspected with CAD in 2013.[11] However, half of these cardiologists work on Java island and in the big cities, leaving other regions even less well served.[9]

Besides the centralisation of healthcare facilities and the lack of healthcare professionals, 94.1% of households in 18 provinces in Indonesia are located more than 5 km from any primary healthcare centre or hospital[12] with very minimal means of transportation and infrastructure. In addition, 28.6 million people (11.2% of total population) are living at poor socioeconomic levels,[13] and the majority were insufficiently health insured until 2013.[7] Despite the fact that CVD ranks as the top cause of mortality in Indonesia, any follow-up studies of hospitalised patients with CAD (ACS and stable CAD (SCAD)) are rare.

Thus, in Indonesia there is clearly a general problem with access to care, but possibly also with the quality of care. It is suspected that many hospitalised patients who should be considered for early invasive strategy actually encounter delayed or overly conservative approaches. We studied the characteristics and clinical profiles of patients with CAD presenting at the Makassar Cardiac Center, Indonesia. These patient outcomes were evaluated in hospital, at 30 days and at 6 months.

METHODS

Study population

This was an observational cohort study of 477 consecutive patients who presented between February 2013 and December 2014 with a diagnosis of CAD at the Makassar Cardiac Center, Wahidin Sudirohusodo Hospital, one of the two public cardiac referral centres in East Indonesia. The cardiac centre with seven cardiologists mainly serves the 9.5 million South Sulawesi population, and also other regions inside and outside Sulawesi island.

Patients were included if they had confirmed CAD, defined as ACS and SCAD. ACS was defined as a spectrum of clinical presentations consistent with acute cardiac ischaemia within 24 hours of hospital presentation, including unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and STEMI.[14 15] SCAD was defined as at least one of the following criteria: stable angina, history of UA, prior MI, prior coronary revascularisation (percutaneous coronary intervention (PCI) and/or coronary artery bypass graft (CABG)), or multivessel CAD without revascularisation.[16] All eligible patients signed written informed consent before the first interview. We excluded all fatal patients who immediately died at the emergency department or cardiovascular intensive care unit before being able to give informed consent, and all suspected patients with normal coronary angiography (CAG) (defined as 0% lumen stenosis in all coronary vessels).[17] The flow chart of the study population is presented in figure 1.

Data collection and follow-up

At hospital admission, we obtained baseline data from medical records and questionnaire interviews. Data on sociodemographic characteristics included age, gender, occupation, living area, monthly income and educational level; lifestyle included smoking status, dietary pattern and physical activity; family history of CVD included family history of premature sudden death at age <60 years[18]; clinical profiles included characteristics and onset of chest pain, previous medications, as well as history of previous diseases (ie, hypertension, type 2 diabetes mellitus, MI, stroke and kidney disease). Detailed methods were presented as online supplementary material.

Clinical data were collected prospectively at the time of hospital admission based on physical examination including vital signs, anthropometric measurements (ie, height, weight and waist circumference), electrocardiography, echocardiography including left ventricular ejection fraction (LVEF), CAG, laboratory tests including cardiac enzymes and estimated glomerular filtration rate. In-hospital managements and at-discharge medications were also recorded. Plasma glucose, lipid profiles, uric acid, renal and liver functions were measured within 24 hours of hospital admission following a minimum 8 hours fast for all patients hospitalised at Wahidin Sudirohusodo Hospital. While, for patients who were referred from other hospitals or clinics (n=70), we obtained baseline and laboratory data from their medical records. All blood samples analyses were generated with standardised methods at the hospital laboratory.

Furthermore, data on mortality and major adverse cardiovascular events (MACE) were obtained during hospitalisation, at 30 days and at 6 months after hospital admission. For referred patients, we obtained data on in-hospital mortality from their family members and this was confirmed with hospital medical records from where the patients were admitted (n=1). We actively performed the follow-up by visiting patient's houses or by an interview via telephone. The nurses asked a detailed questionnaire about patient's current condition, cardiovascular complaints, rehospitalisation, deaths and other

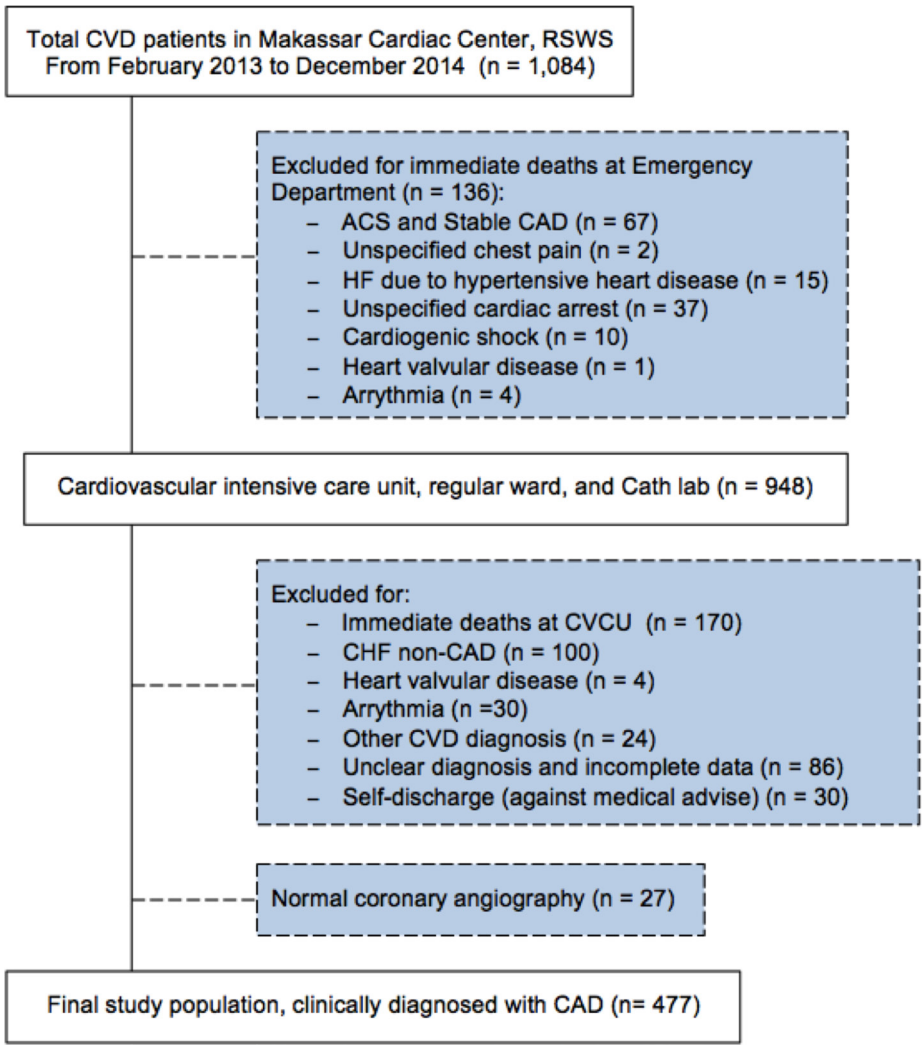


Figure 1 Flow chart of the study population. ACS, acute coronary syndrome; CAD, coronary artery disease; CHF, congestive heart failure; CVD, cardiovascular disease; HF, heart failure; RSWS: Rumah Sakit Wahidin Sudirohusodo (Wahidin Sudirohusodo hospital).

CVD-related events from the patients, family members or their relatives. Subsequently, we verified their answers with the medical records in hospital, or with the patient's documentation at home.

Study outcomes

The primary endpoints of our study were the rates of in-hospital, 30-day and 6-month all-cause mortality and composite MACE. The composite MACE counting for cardiac and non-cardiac death, MI rehospitalisation, heart failure requiring hospitalisation, rehospitalisation due to stroke, (emergency) CABG, stent thrombosis, repeat PCI, repeat CAG, first PCI and first CAG.

Statistical analysis

Continuous variables were presented as mean±SD, and categorical variables as number (percentage). Skewed data were provided as median (Q1–Q3). Baseline characteristics, clinical profiles and managements during hospitalisation were divided into acute (ACS) and non-acute (SCAD) groups. The rates of mortality and composite MACE in hospital, at 30 days and at 6 months after hospital admission were calculated. Kaplan-Meier curves were used to describe the cumulative survival during 6-month follow-up. Log rank statistics were used to assess the difference between guideline-treated and non-guideline-treated groups. A 95% CI not including one, corresponding to a two-sided $p<0.05$ was considered statistically significant. All statistical analyses were performed using SPSS V.23.0.

Patient involvement

Patients were not involved in the design and development of the research questions. The results of this study are used to provide information for the stakeholders and health-policy makers to improve healthcare services in Indonesia. Therefore, the findings of our study were not disseminated directly to all participants.

RESULTS

Among 477 patients hospitalised with CAD, 257 (53.9%) were at young age (<60 years),[19] and 347 (72.7%) were male.

Table 1 Baseline characteristics at hospital admission

Variables	ACS (n=364)	SCAD (n=113)	Total (n=477)	P values
Age (years)	57.5±11.2	60.6±8.8	58.2±10.8	0.007
Male	260 (71.4)	87 (77.0)	347 (72.7)	0.246
Systolic BP (mm Hg)	130.0±27.6	127.3±20.4	129.4±26.1	0.336
Diastolic BP (mm Hg)	82.7±16.1	80.8±10.3	82.2±14.9	0.228
Fasting plasma glucose (mmol/L)*	7.3 (5.8–9.6)	5.9 (5.1–8.2)	7.0 (5.7–9.1)	<0.001
Total cholesterol (mmol/L)*	5.0 (4.2–5.7)	5.1 (3.7–5.6)	5.0 (4.1–5.7)	0.233
Triglycerides (mmol/L)*	1.4 (1.1–1.9)	1.5 (1.0–1.9)	1.5 (1.1–1.9)	0.654
HDL-chol (mmol/L)	0.95±0.31	0.92±0.35	0.94±0.32	0.456
LDL-chol (mmol/L)*	3.3 (2.6–4.0)	3.2 (2.3–3.7)	3.3 (2.6–3.9)	0.032
Waist circumference (cm)	84.6±7.4	84.9±6.1	84.6±7.1	0.666
Obese (BMI ≥25 kg/m^2)	119 (32.7)	46 (40.7)	165 (34.6)	0.118
Metabolic syndrome†	208 (57.1)	56 (49.6)	264 (55.3)	0.157
Parental history of CVD‡	95 (26.1)	27 (23.9)	122 (25.6)	0.639
Monthly income ≥Rp1 810 000§	155 (42.6)	74 (65.5)	229 (48.0)	<0.001
College education	134 (36.8)	55 (48.7)	189 (39.6)	0.024
Living >20 km from hospital (rural)	193 (53.0)	54 (47.8)	247 (51.8)	0.331
Funding/insurance				
Private fund (high income)	30 (8.2)	6 (5.3)	36 (7.5)	0.303
Jamsostek (company)¶	10 (2.7)	0 (0.0)	10 (2.1)	0.127
Askes (middle income)	144 (39.6)	97 (85.8)	241 (50.5)	<0.001
Jamkesmas/Jamkesda (low income)	107 (29.4)	8 (7.1)	115 (24.1)	<0.001
BPJS (national)**	73 (20.1)	2 (1.8)	75 (15.7)	<0.001
Current smoker	103 (28.3)	20 (17.7)	123 (25.8)	0.024
Former smoker	118 (32.4)	56 (49.6)	174 (36.5)	0.001
Physical inactivity	218 (59.9)	59 (52.2)	277 (58.1)	0.148
High-sugar intake	202 (55.5)	46 (40.7)	248 (52.0)	0.006
High-salty food and MSG intake	148 (40.7)	33 (29.2)	181 (37.9)	0.028
High-fried food intake	221 (60.7)	68 (60.2)	289 (60.6)	0.919
Often reuse cooking oil	190 (52.2)	29 (25.7)	219 (45.9)	<0.001

Values are n (%) or means±SD, unless otherwise stated. Comparison of baseline characteristics was performed using independent-samples t-test for continuous variables and Pearson χ^2 test for categorical variables.
*Values are medians (Q1–Q3). Comparison was performed using Mann-Whitney U test.
†Metabolic syndrome was defined using National Cholesterol Education Program Adult Treatment Panel III classification.
‡Parental history of CVD was positive, if patients have had either mother with CVD at the age under 65 years, or father with CVD at the age under 55 years, or second degree of family with history of premature sudden cardiac death.
§US$1=Rp13 500 (Indonesian Rupiah). The cut-point based on the national average of decent-living minimum income in 2015.
¶Comparison was done using Fisher's exact test.
**As a national health insurance, BPJS has been started since 1 January 2014.
ACS, acute coronary syndrome; Askes, asuransi kesehatan (civil servant insurance); BMI, body mass index; BP, blood pressure; BPJS, badan penyelanggara jaminan sosial (national insurance); CVD, cardiovascular disease; HDL-chol, high-density lipoprotein cholesterol; Jamkesda, jaminan kesehatan daerah (local insurance for poor people); Jamkesmas, jaminan kesehatan masyarakat (national insurance for poor people); Jamsostek, jaminan sosial tenaga kerja (company insurance); LDL-chol, low-density lipoprotein cholesterol; MSG, mono-sodium glutamate; SCAD, stable coronary artery disease.

Table 1 shows the baseline characteristics of patients with CAD. As presented, patients with CAD in Indonesia had high levels of systolic blood pressures, fasting plasma glucose and low-density lipoprotein (LDL) cholesterol, and low level of high-density lipoprotein cholesterol. More than half of these patients had metabolic syndrome but did not have central obesity. Most came from rural areas and from low and middle socioeconomic status, more often were current or former smokers, had poor dietary habits with high consumption of sugar and deep

Table 2 Clinical presentation at hospital admission[1]

Variables	ACS (n=364)	SCAD (n=113)	Total (n=477)	P values
Prehospital				
Previous hypertension	268 (73.6)	90 (79.6)	358 (75.1)	0.196
On medication of hypertension	156 (42.9)	55 (48.7)	211 (44.2)	0.277
Previous MI	126 (34.6)	38 (33.6)	164 (34.4)	0.847
Previous stroke	27 (7.4)	9 (8.0)	36 (7.5)	0.848
Previous CAG	48 (13.2)	21 (18.6)	69 (14.5)	0.154
Previous PCI	14 (3.8)	13 (11.5)	27 (5.7)	0.002
In hospital				
STEMI	211 (58.0)	NA	211 (44.2)	NA
NSTE-ACS	153 (42.0)	NA	153 (32.1)	NA
Diabetes mellitus	112 (30.8)	35 (31.0)	147 (30.8)	0.967
With HF diagnosis/signs	150 (41.2)	34 (30.1)	184 (38.6)	0.034
Atrial fibrillation*	9 (2.5)	3 (2.7)	12 (2.5)	1.000
Left ventricle hypertrophy	124 (34.1)	21 (18.6)	145 (30.4)	0.002
Echocardiography assessed	210 (57.7)	52 (46.0)	262 (54.9)	0.029
LVEF (%)	45±13.2	49.3±17.4	45.8±14.2	0.049
Troponin T (µg/L)†	0.42 (0.10-1.58)	0.00 (0.00-0.02)	0.20 (0.02–1.00)	<0.001
Haemoglobin (g/dL)	13.6±2.1	13.5±2.1	13.6±2.1	0.61
Haematocrit	0.40±0.06	0.41±0.14	0.40±0.09	0.296
Creatinine (µmol/L)†	88.4 (79.6–114.9)	88.4 (77.8–114.9)	88.4 (79.6–114.9)	0.869
eGFR < 60 mL/min	108 (29.7)	41 (36.3)	149 (31.2)	0.185
Comorbidities				
Concomitant stroke*	18 (4.9)	3 (2.7)	21 (4.4)	0.3
With cardiogenic shock*	17 (4.7)	0 (0.0)	17 (3.6)	0.017
Concomitant pneumonia	37 (10.2)	5 (4.4)	42 (8.8)	0.06
VD				
Non-significant 1 - 2 VD‡	27 (7.4)	12 (10.6)	39 (8.2)	0.666
1 VD	45 (12.4)	20 (17.7)	65 (13.6)	0.738
2 VD	30 (8.2)	15 (13.3)	45 (9.4)	0.954
3 VD	53 (14.6)	41 (36.3)	94 (19.7)	0.007
> 3 VD*	28 (7.7)	2 (1.8)	30 (6.3)	0.001

Values are n (%) or means ±SD, unless otherwise stated. Comparison was performed using independent-samples t-test for continuous variables and Pearson χ^2 test for categorical variables.
*Comparison was done using Fisher's exact test.
†Values are medians (Q1–Q3). Comparison was done using Mann-Whitney U test.
‡Defined as 1%–49% lumen stenosis in at least one coronary vessel.[17]
ACS, acute coronary syndrome; CAG, coronary angiography; eGFR, estimated glomerular filtration rate; HF, heart failure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NA, not applicable; NSTE, non-ST-elevation; PCI, percutaneous coronary intervention; SCAD, stable coronary artery disease; STEMI, ST-segment elevation myocardial infarction; VD, vessel disease.

fried food, and had low physical activity. The clinical profiles at hospital admission are presented in table 2. Of all patients, 75.1% had previous hypertension, 34.4% had previous MI and 7.5% had a previous stroke. Patients diagnosed with STEMI, NSTEMI, UA and SCAD were 44.2%, 17.8%, 14.3% and 23.7%, respectively. At hospital admission, 30.8% of patients had diabetes mellitus, 38.6% were diagnosed or presented with heart failure signs and 31.2% had reduced renal function. Out of 273 patients with CAG, 169 (61.9%) had multivessel disease. Among 262 (54.9%) patients who underwent echocardiography, 24.0% had an LVEF ≤35%.

Table 3 summarises invasive and pharmacotherapy managements during hospitalisation. Of 211 patients with STEMI, only 10 (4.7%) underwent primary PCI and 13 (6.2%) received thrombolysis for early reperfusion.

Table 3 Managements in hospital from admission to 6 months

Variables	ACS (n=364)	SCAD (n=113)	Total (n=477)	P values
Onset to admission (hours)	24 (9–48)	36 (16.3–72)	26.8 (10–48)	0.002
Length of hospitalisation (days)	7 (5–10)	1 (0–7)	6 (4–9)	<0.001
Admission to intervention (hours)	120 (8–168)	8 (4–149.6)	96 (8–149.6)	<0.001
Invasive treatment				
Thrombolysis	13 (3.6)	NA	13 (2.7)	NA
Primary PCI	10 (2.7)	NA	10 (2.1)	NA
Elective PCI	47 (12.9)	32 (28.3)	79 (16.6)	0.003
CABG+PCI*	2 (0.5)	0 (0.0)	2 (0.4)	1
CAG only	124 (34.1)	58 (51.3)	182 (38.2)	0.001
No exploration	181 (49.7)	23 (20.4)	204 (42.8)	<0.001
Pharmacotherapy				
Anticoagulant	168 (46.2)	16 (14.2)	184 (38.6)	<0.001
ASA	320 (87.9)	74 (65.5)	394 (82.6)	<0.001
Clopidogrel	308 (84.6)	58 (51.3)	366 (76.7)	<0.001
Statin	271 (74.5)	54 (47.8)	325 (68.1)	<0.001
Hypertension medication	263 (72.3)	80 (70.8)	343 (71.9)	0.123

Values are n (%) and medians (Q1–Q3). Comparison was done using Mann-Whitney U test for continuous variables and Pearson χ^2 test for categorical variables.
*Comparison was done using Fisher's exact test.
ACS, acute coronary syndrome; ASA, acetylsalicylic acid; CABG, coronary artery bypass graft surgery; CAG, coronary angiography; NA, not applicable; PCI, percutaneous coronary intervention; SCAD, stable coronary artery disease.

Meanwhile, of 477 patients, 42.8% had no exploration of CAG, and 19.1% underwent either PCI or CABG for revascularisation. Overall, there was a 24–36 hours time lapse between angina onset and hospital admission in ACS and SCAD groups, respectively (p=0.002). Patients with stable disease (SCAD) stayed shorter in hospital compared with patients with ACS (p<0.001).

Figure 2 describes the clinical outcomes at 30-day and 6-month follow-up. More patients with ACS died during hospitalisation compared with SCAD (12.6% vs 5.3%, p=0.029). However, these SCAD group experienced 6-month adverse cardiovascular events more frequently compared with ACS group (25.7% vs 15.7%, p=0.043). The rates of all-cause mortality in hospital, at 30 days and at 6 months were 10.9%, 2.5%, and 7.3%, respectively. In total, 189 (39.6%) participants experienced at least one adverse event during the study period. A detailed description of MACE at 30 days and 6 months of these CAD patients is presented in table 4.

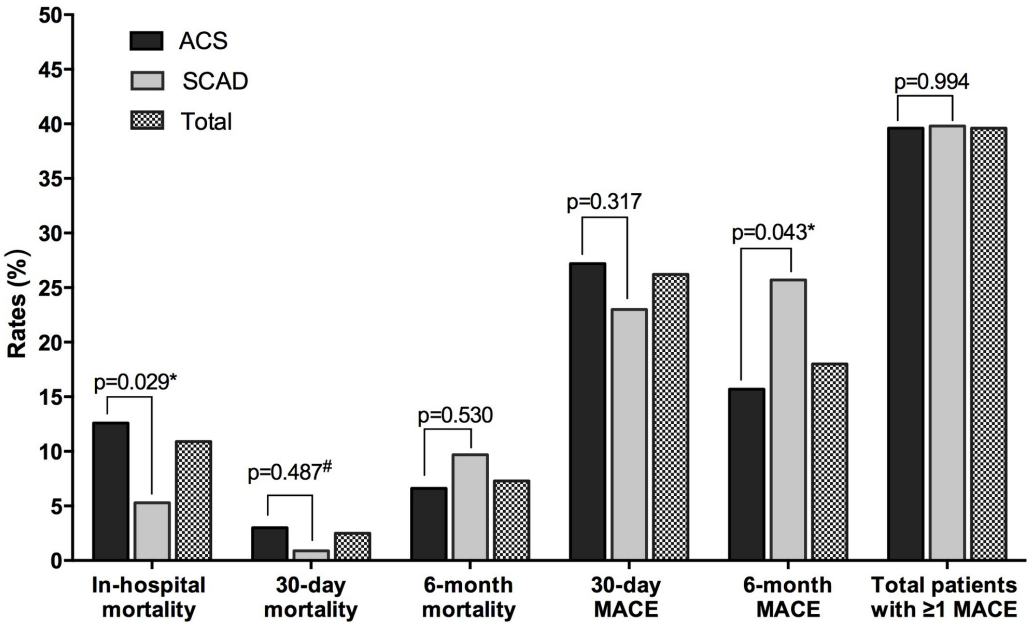
Seven (1.5%) participants were lost to follow-up. At 6 months, the survival rate was 78.9%. The Kaplan-Meier curves showed significantly better survival in patients with statin (p=0.002), clopidogrel (p<0.001) and revascularisation (PCI/CABG) groups (p=0.001) compared with the respective counterparts. In subgroup analysis, patients with ACS and SCAD without PCI/CABG had the worst survival rates compared with those with revascularisation (p=0.002) (figure 3). Description of the most notable complaints or symptoms reported by all survivors is provided as online supplementary material.

DISCUSSION

The present study shows that patients with CAD in Indonesia are predominantly young males with high prevalence of cardiovascular risk factors. More than half of this cohort had metabolic syndrome and prior hypertension; and approximately one-third had prior MI and diabetes mellitus. The majority came from rural areas with a low or middle socioeconomic status, and had a history of smoking. These patients with CAD showed relatively severe illness, had significant time delay from angina onset to admission or intervention, and rarely received the guidelines-recommended treatment.

At baseline, compared with SCAD, patients with ACS were younger, had higher plasma glucose and LDL cholesterol, had lower income and educational level, were more often current smoker, and had poorer dietary habits. Further, we observed considerably more patients with ACS with diagnosis/signs of heart failure, with left ventricle hypertrophy and with lower LVEF than patients with SCAD. Likely as a result, those with ACS had poorer clinical outcomes mainly during hospitalisation and at 30-day follow-up compared with those with SCAD.

In contrast, at 6-month follow-up, more patients with SCAD had adverse cardiac events compared with ACS (p=



Clinical Outcomes	ACS (n = 364)	SCAD (n = 113)	Total (n = 477)
All-cause mortality			
In-hospital	46 (12.6)	6 (5.3)	52 (10.9)
30-day#	11 (3.0)	1 (0.9)	12 (2.5)
6-month	24 (6.6)	11 (9.7)	35 (7.3)
Total	**81 (22.3)**	**18 (15.9)**	**99 (20.8)**
Composite MACE			
30-day	99 (27.2)	26 (23.0)	125 (26.2)
6-month	57 (15.7)	29 (25.7)	86 (18.0)
Total	**156 (42.9)**	**55 (48.7)**	**211 (44.2)**
Patients with ≥1 MACE (including mortality)	**144 (39.6)**	**45 (39.8)**	**189 (39.6)**

Values are n (%). Comparison was performed using Pearson Chi-square test.
#Comparison was performed using Fisher's Exact test.
*p<0.05

Figure 2 Clinical outcomes at 30-day and 6-month follow-up. ACS, acute coronary syndrome; MACE, major adverse cardiovascular events; SCAD, stable coronary artery disease.

0.043). The most likely explanation is that these patients with SCAD were undertreated for secondary prevention and aftercare management. Out of 113 patients with SCAD, 34 (30.1%) were admitted for congestive heart failure (CHF); and of 90 patients with SCAD with cardiac catheterisation, 58 (64.4%) had multivessel CAD. Of those, only 32 (55.2%) underwent elective PCI. Therefore, the lack access or adherence to the guidelines-recommended treatment (ie, elective PCI or CABG) and the lack of engagement to the long-term cardiovascular medications might largely contribute to these poorer outcomes. Meanwhile, in ACS, low access to an early invasive strategy was more likely to be associated with the high incidence of short-term death, chiefly in the first 30 days since admission.

In this study, we found that patients with ACS in Indonesia (mean age 57.5 years) were younger than patients with ACS in Japan (66.4 years)[20] and in the Global Registry of Acute Coronary Events (GRACE) from 14 countries (65 years),[21] but equally young with patients with ACS in Malaysia (58.1 years).[22] In these previous studies, the majority of patients were male (>65%).[20–22]

Hypertension, diabetes and smoking are the top three risk factors responsible for 3.5 million deaths in South-East Asia every year, and particularly afflicting the young population.[2 4] In our ACS group, the proportions of

Table 4 MACE during follow-up

Composite MACE	At 30 days (n=477)	At 6 months (n=477)	Total (n=477)
All-cause mortality	64 (13.4)	35 (7.3)	99 (20.8)
MI rehospitalisation	14 (2.9)	23 (4.8)	37 (7.8)
HF rehospitalisation	1 (0.2)	6 (1.3)	7 (1.5)
Stroke	2 (0.4)	4 (0.8)	6 (1.3)
Emergency CABG	1 (0.2)	1 (0.2)	2 (0.4)
Repeat PCI	5 (1.0)	3 (0.6)	8 (1.7)
Repeat CAG	3 (0.6)	5 (1.0)	8 (1.7)
First PCI postdischarge	23 (4.8)	3 (0.6)	26 (5.5)
First CAG postdischarge	11 (2.3)	6 (1.3)	17 (3.6)
Stent thrombosis	1 (0.2)	0 (0.0)	1 (0.2)
Total MACE	125 (26.2)	86 (18.0)	211 (44.2)

Values are n (%).
CABG, coronary artery bypass graft surgery; CAG, coronary angiography; HF, heart failure; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

hypertension (73.6% vs 47.1%) and diabetes mellitus (30.8% vs 15.6%) were higher than in a similar multicentre study of patients with acute MI in France.[23] The smoking-experience rate of patients with CAD in Indonesia (62.3%) was strikingly higher than in Japan (57.0%),[20] UK (53.4%)[19] and Malaysia (47.0%).[22] This finding is compatible with WHO Global Status Report in 2014.[4]

Asian populations are less obese than Western populations.[4 24] Despite a much lower prevalence of overweight or obesity (22%–26% in South-East Asia vs 67% in UK and 70% in USA), raised blood glucose/diabetes mellitus is a pivotal risk factor in South-East Asia, reaching similarly high prevalence with the UK and USA.[4] In contrast to the Western populations where diabetes is strongly associated with obesity, South-East Asia populations have a unique 'lean diabetic' phenotype.[4] In terms of lifestyles, patients with CAD in Indonesia have a poor dietary pattern as reflected by high intakes of sugar and deep-fried foods. Our cohort showed physical inactivity levels (58.1%) higher than the open population reported in Malaysia (51.6%), UK (40.0%) and USA (35.0%).[4]

Overall at hospital admission, these patients with CAD showed relatively severe clinical features, with more renal insufficiency and heart failure. Our findings are in line with a previous report that, compared with the Netherlands, patients with STEMI in Indonesia more often presented with severe illness with heart failure signs and had a longer time delay between symptom onset and hospital admission.[7] We found that the time lapse between symptom onset and admission was 24 (IQR 9–48) hours in patients with ACS. This was much longer compared with the GRACE study from 95 hospitals of 14 countries for patients with STEMI (139 (73–313) min), NSTEMI (190 (90–510) min) or for UA (180 (90–435) min).[21]

The time lapse from admission to intervention and length of stays were remarkably shorter in SCAD than in ACS group, because in our study the majority of referred patients (n=50, 71.4%) were classified as SCAD. These patients underwent an elective cardiac catheterisation and/or PCI and were then immediately returned to the referring hospitals. We did not track and record the duration of stay in the original hospitals. However, we assumed hospital stay duration in the referring hospitals to be relatively short because these patients usually underwent elective interventions for SCAD.

Longer time delay from the symptom onset to hospital admission remains one of the most crucial issues in cardiovascular services in the low-income and middle-income countries,[25] particularly in Indonesia. The prominent problems appeared from the patients side were the lack of awareness of precursor symptoms,[25 26] the negative perception and apprehension to the hospital, and financial problems.[26] On the other hand, clinicians delay in making an early diagnosis and treatment in primary hospital or clinic, lack of collaboration between hospitals and doctors, administrative barriers, transportation problems and lack of ambulance organisation[26] were also the influential factors for this extensive delay. Those who live in very remote areas, tend to manage their complaints with a visit to the local/traditional healer or non-traditional healthcare provider. As a result, there was a very low frequency of primary PCI and thrombolysis procedures conducted in our centre considering the 'golden time' period for effective reperfusion. A previous study reported that in the real-world practice, primary PCI as recommended by the guidelines is very difficult to perform in patients with STEMI in Indonesia; time delay is a critical issue for decision-making in choosing reperfusion strategy (primary PCI, fibrinolytic or the combination).[26]

We believed there are many unrecorded deaths due to CVD in this population because patients with more severe disease are likely to die before reaching the hospital and are not reported. This indicated that those with more stable and stronger physical endurance will have a chance to turn up alive in the hospital. We conclude that in general, haemodynamically unstable patients—for logistic reasons (ie, the lack of transportation, interventional cardiologist and cath lab capacity)—first had to be stabilised prior to a rather planned intervention. Evidently, the infrastructure and resources were not sufficient to deal with emergency CAG followed by rescue PCI to treat the patients with acute CVD.

From hospital admission to 6 months, 59 (16.2%) patients with ACS underwent primary or elective PCI. This is comparable with PCI following ACS in Malaysia (13%–17%),[27] but much lower than Japan (74%) and USA (71%–87%).[27] The total mortality rate at 30 days was

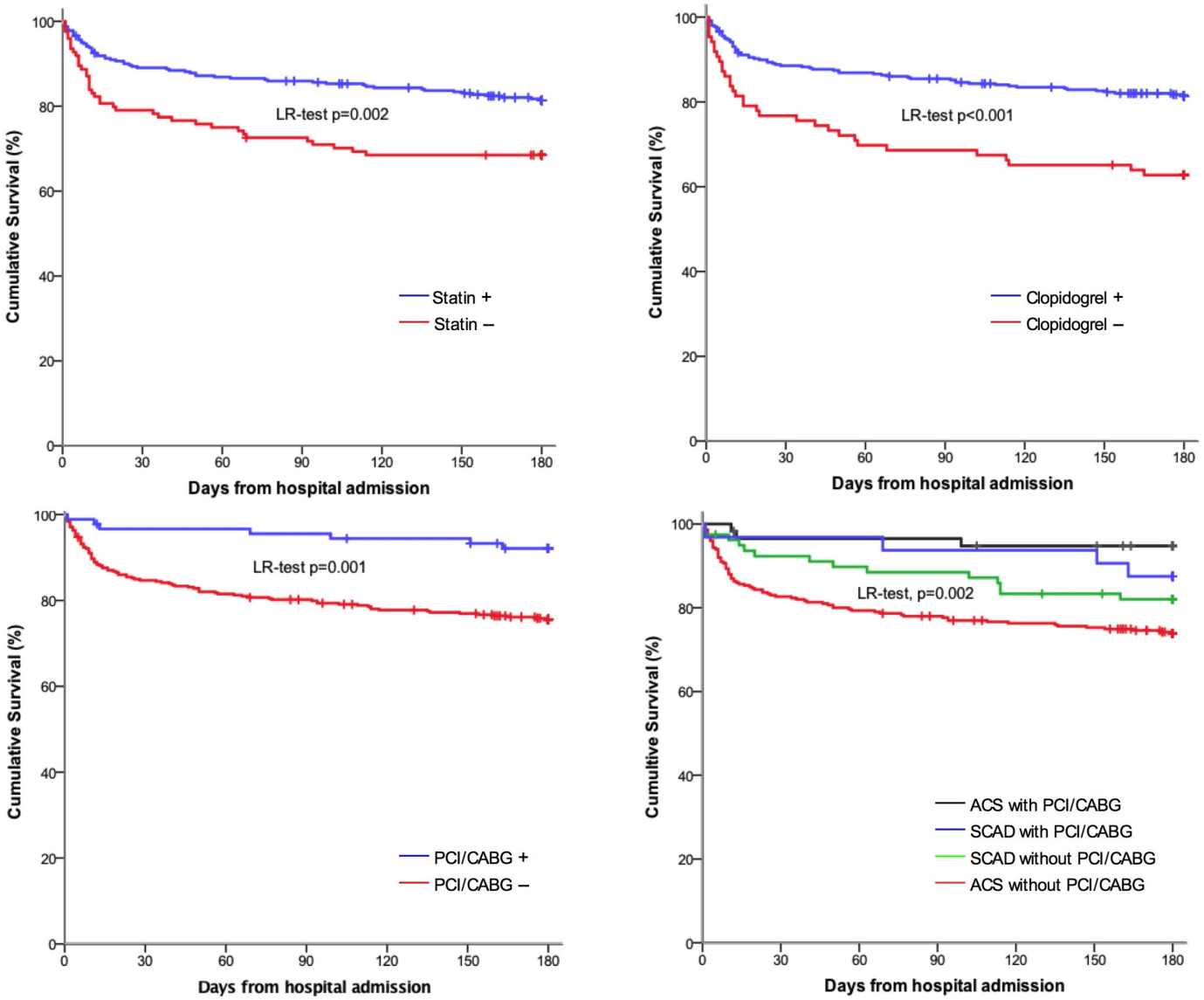


Figure 3 Kaplan-Meier curves for cumulative 6-month survival, comparing the guideline-treated versus non-guideline-treated groups in all participants and between diagnosis groups. Comparison was performed using LR (Mantel-Cox) test. ACS, acute coronary syndrome; CABG, coronary artery bypass graft surgery; LR, log rank; PCI, percutaneous coronary intervention; SCAD, stable coronary artery disease.

15.7% in patients with ACS (figure 2), which is incredibly higher compared with patients in Japan (3.4%),[20] and in the US patients after PCI intervention (1.0%).[28] Meanwhile, 24 (6.6%) patients with ACS died between discharge and 6-month follow-up, and therefore higher than in the GRACE registry study (4.7%).[29]

Previous studies suggested that optimal revascularisation could prevent ~32% of deaths by 6 months,[27 29] and better 6-month survival was associated with the use of clopidogrel, statin and timely PCI or CABG.[27 30] Our data showed similar findings: the survival was significantly better in patients with statin, clopidogrel and revascularisation (PCI/CABG) compared with the non-guidelines-treated groups (see figure 3).

Patients undergoing PCI for ACS have higher short-term and long-term mortality rates compared with those with SCAD undergoing elective PCI.[31] In our study, patients with revascularisation (PCI or CABG) in ACS and SCAD groups were not significantly different in terms of survival (p=0.236). However, when we compared the 6-month survival between patients with versus without revascularisation, there was an explicitly lower survival in those who did not undergo a revascularisation, both in ACS and SCAD groups (p=0.002) (figure 3).

Despite the fact that over 80% of mortality from CVD occurs in low-income and middle-income countries,[32] these countries often do not have integrated primary healthcare programmes for early detection and treatments for cardiovascular risk factors to meet that challenge. In Indonesia, the poorest and very remote people are affected the most. Before the national health insurance era started in 2014, 80% of Indonesian people were uncovered by a sufficient health insurance.[7] Although the existing insurance schemes (Askes, Jamsostek, Jamkesmas

and Jamkesda) conferred a large positive impact on access to healthcare facilities—notably for people from the low and middle socioeconomic level[33]—still, the provided access to specific 'elitary treatments' were limited.[34]

Moreover, people who already suffered from CVD have also less access to an effective secondary prevention.[8] Geographical and regional distances, low awareness and support from family members, and financial constraints were most likely responsible for the lack of access to this aftercare rehabilitation. According to the guidelines also adopted in Indonesia, most of these patients were not appropriately treated. Therefore, the stakeholders in Indonesia should focus on the improvement of primary and secondary prevention. Promotion of healthy lifestyles should be well established in order to reduce the prevalence of cardiovascular risk factors. The dissemination of first aid management for acute CVD as well as a rapid and standardised in-hospital response has to be established.

Strengths and limitations

There are some strengths and limitations in the present study:

- We had to exclude all patients who immediately died at emergency department and cardiovascular intensive care unit because we could not obtain a written informed consent from this group with the most critically ill conditions.
- The majority of our patients (51.8%) were living in rural, often very remote areas. Hence, it was not possible to interview all patients by means of a face-to-face interview for follow-up. In 239 (50.1%) patients, phone calls were used, which may have led to less accurate data than obtained by direct questionnaire interview. However, we always verified the answers at the next visits or phone calls with a different interviewer to reduce inaccuracies.
- We excluded all patients with normal CAG, which were mostly females. Thus, our study may have overlooked the minor group of MI with no obstructive coronary atherosclerosis.
- Our study is, to our knowledge, the first in Indonesia with regard to clinical outcomes of hospitalised patients with CAD. Thus, we consider our study a quite unique effort to properly report on characteristics at admission and on short-term and mid-term outcomes in an attempt to identify opportunities to improve care.

CONCLUSIONS

Patients with CAD from a poor South-East Asian setting present themselves with predominantly unstable conditions of premature CAD. These patients show relatively severe illness, have significant time delay from symptom onset to admission or intervention, and most do not receive the guidelines-recommended treatment. Awareness of symptoms, prompt initial management of acute CVD, well-established infrastructures and resources both in primary and secondary hospital for CVD should be improved to reduce the high rates of 30-day and 6-month mortality and adverse outcomes in this population.

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Contributors CSPMU, BAJMdM and AQ conceived the idea of the study and were responsible for the design of the study. AQ, AHA, IM, AAM and IP were responsible for the data collection and follow-up. AQ was responsible for undertaking the data analysis and produced the tables and graphs. CSPMU, BAJMdM and JPSH provided input to the data analysis and interpretation. The initial draft of the manuscript was prepared by AQ, and was then circulated repeatedly to CSPMU, BAJMdM and JPSH for critical revision. All authors approved the final version of the manuscript.

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