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Clinical Profile of Acute Coronary Syndrome Patients in Kupang: a Result from 1–Year iSTEMI Registry

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Abstract

Background: Cardiovascular diseases (CVDs) have been the leading cause of global deaths over the years. In Indonesia, coronary heart disease (CHD) is the most common CVDs, responsible for 29% of all deaths in 2017. East Nusa Tenggara is one of the provinces in Indonesia with the highest prevalence of CHD, which corresponded with growing cases of acute coronary syndromes (ACS). Therefore, we develop a registry to obtain patients' profiles as a basis for strategy development in ACS management.

Methods: A retrospectively cross-sectional study was conducted on all patients who presented with ACS between January 2019 and September 2020 at a general hospital in Kupang, East Nusa Tenggara. Data collected include demography, patient awareness and transfer history, risk factors, physical findings, diagnosis, workup, treatment, and mortality.

Results: A total of 282 patients with ACS (STEMI, 41.2%; NSTEACS, 58.8%) were included in this study. Most patients were male with a mean age of 58.2 ± 12.2 years and normal BMI (32.6%). Nearly 50% of all ACS patients have one or more comorbidities, followed by relatively low adherence to therapy. Half of the patients were referred, but only 16.9% of patients arrived at the first medical facility less than 1 hour after onset. Patients with NSTEACS had more risk factors than patients with STEMI. The median LOS was five days (range, 1-17 days) with 2.8% in-hospital death. The presence of patient and system delay might contribute to the low number of STEMI patients who received reperfusion therapy.

Conclusion: This research serves as the primary data for the improvement of acute coronary syndrome management in Kupang and East Nusa Tenggara.

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Keywords: acute coronary syndrome; myocardial infarction; registry; Kupang.

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Introduction

Cardiovascular diseases cause one-third of global mortality, with acute coronary syndrome (ACS) alone contributes to more than 8.1 million deaths per year.[1] Death from coronary heart diseases (CHD) ranked second among all-cause mortalities in Indonesia in 2019.[2] Prevalence of ACS with ST-elevation in Indonesia also has increased 15% in recent years.[3] Aside from mortality, ACS episode also contributes to a high rate of hospital stay and even 30% of discharged patients are readmitted within six months.[4] It is projected that this burden will inflict a significant economic loss of US$ 177 billion.[5]

Occlusion of coronary artery followed by vasoconstriction in ACS leads to ischemia and even progresses to myocardial infarction (MI). The first hours are a critical period that determines patient's prognosis.[6] Unless an appropriate and timely treatment are commenced, the adverse outcome such as hemodynamic instability and cardiac complications may occur.[7] Therefore, it is crucial to identify and eliminate any factors that prolong the interval between onset and medical contact.

It is not uncommon in ACS patients to find concurring morbidities that are interrelated as risk factors and independent prognostic factors.[8] Hence, the long-term strategy on ACS management should also consider how these diseases are associated and can be prevented.

East Nusa Tenggara is amongst the provinces with high CHD prevalence (4.4%), which face challenges in implementing management as per guidelines due to constrained resources, poorly distributed health personnel, and limited geographical access.[3] There is a limited publication about the patient's demographic and clinical profile of patients with ACS in East Nusa Tenggara. Without a factual basis, it is difficult to address the most suitable approach to a distinct population. Thus, to improve the current health strategies, we develop a registry to provide reliable and accurate information regarding the ACS patient's profile in Kupang, East Nusa Tenggara

Methods

Patient recruitment and data collection

We conducted a retrospective cross-sectional study on ACS patients admitted to the emergency department and Intensive Cardiovascular Critical Care Unit (ICCU) at Prof. W.Z. Johannes Hospital in Kupang, East Nusa Tenggara. All confirmed ACS cases between January 2019 to September 2020 were consecutively recruited. Patients had to present with symptoms consistent with ACS whose diagnosis was further confirmed by cardiologists based on 1 of the following items: electrocardiographic (ECG) findings specific to ACS, initial/serial elevation of cardiac biomarkers, and/or documentary of coronary heart disease. Study investigators received approval from the Ethical Committee of Faculty of Medicine Nusa Cendana University (37/UN15.16/KEPK/2020). Demographic characteristics, medical history, presenting symptoms, Killip class, GRACE- and TIMI-scoring system, prehospital transfer, ECG and serum marker results, treatment practices, and hospital-related outcome were obtained.

Clinical definition and endpoints

"STEMI" was defined as ACS with persistent ST-segment elevation on ECG. "NSTEACS" was defined as ACS without persistent ST-segment elevation on ECG, which further classified into "NSTEMI" if the patient had elevated cardiac enzyme level or "UA" if myocardial ischemia occurred in the absence of cardiac necrosis. In-hospital death was defined as all-cause mortality during hospitalization, and rehospitalization was defined as all-cause readmission to the hospital after a previous ACS episode.

Statistical analysis

Distributions of continuous variables are described using means or median, whereas discrete variables are presented as frequencies and percentages. T-test was used to compare means or medians in STEMI vs. NSTEACS group. Comparison of proportions in the respective group was analyzed with Chi-squared test or Fisher exact's test when the requirements were not met. The relationship between Killip class and length of

stay were evaluated using Spearman's rank correlation coefficient.

Results

Study population

A total of 282 patients with ACS (STEMI, 41.2%; NSTEACS, 58.8%) were included in this study (Table 1). The mean age of patients was 58.2 ± 12.2 years with slightly older patients in NSTEACS compared to their STEMI counterparts. Men predominated both in NSTEACS and STEMI cases. The majority of patients had normal BMI (32.6%); however, the STEMI arm had higher proportions of patients who were overweight and obese (50.8%).

Patients in the NSTEACS group had a somewhat higher prevalence of several medical histories such as angina (39.2%), hyperlipidemia (15.1%), myocardial infarction (31.9%), and hypertension (57.8%) compared to the STEMI group, implying that patients with NTSEACS had a more complex medical history. Overall, 47.2% of patients never smoked, but the STEMI group had more patients who were actively smoking (38.8%) or had smoked before (6%).

Out of 68 patients who had a history of Diabetes Mellitus (DM) type 2, only 28 (41.2%) had regulated blood glucose levels and or taking antidiabetics—most of them (21/28) were in the NSTEACS group. Only 48 (32.4%) hypertensive patients had controlled blood pressure, and most were (36/48) diagnosed with NSTEACS.

Table 2 shows an equal proportion between the patients who were referred to the hospital and those who came directly to the hospital. Despite the absence of several timestamp records, the data demonstrated that 49 out of 142 patients first went to the primary healthcare center or other lower-tier hospitals 1 to 3 hours after symptoms onset. Nevertheless, transferred patients tended to miss the first hour since their onset upon arriving at the hospital, as one-third of them came more than 12 hours after their worst symptoms.

Clinical presentations and diagnosis

Although chest discomfort is a common presentation in ACS, we found that 30% of patients did not complain of chest pain upon admission. Slightly more patients with STEMI reported dull chest pain compared to NSTEACS group (73.3% vs 67.5%, p = 0.290). A higher prevalence of Killip class I (76.6%) indicates that the patients in the present study had a less severe clinical presentation (Table 1).

Initial ECG time was only available in 247 cases; however, from this data, we found that patients presented with chest pain were more likely (OR 3.184 ; 95%CI 1.605-6.314) to undergone ECG examinations in 10 minutes after admission (Table 3). Out of all patients who complained of typical chest pain, more than half did not have ST-elevation on their ECG. From 49 subjects without typical chest pain but had ECG time less than 10 minutes, 19 patients came to health care with chief complaints dyspnea and epigastric pain, 12 patients had sharp chest pain, 10 patients only had dyspnea, 3 patients only had epigastric pain, 2 patients had cephalgia, 2 patients had general weakness/syncope, and 1 patient had palpitation.

The troponin concentration of 109 of the 116 STEMI patients was measured, and 90.5% of them were positive. To distinguish between NSTEMI and unstable angina, troponin levels were also measured in NSTEACS patients. There were 62 patients who had elevated troponin levels at initial or after serial measurement and classified into NSTEMI (table 4). On the other hand, one patient who had positive troponin after serial measurement was eventually categorized as having UA. As many as 32.5% of patients with low initial troponin levels were not followed by further measurement, so they were discharged as UA/NSTEACS (table 4). In this study, there were a total 4.3% of patients who did not have Troponin I data, and half of them were diagnosed as STEMI.

ACS management

All patients received standard therapy with dual antiplatelet acetylsalicylic acid-clopidogrel, subcutaneous anticoagulant fondaparinux/enoxaparin, and statin. Nitrate, antidiabetic drugs and/or antihypertensive drugs were given based on every patient's condition and comorbidity. Of all STEMI patients, only 31% of patients underwent fibrinolytic therapy. Door-to-needle time was only available in 31 out of 36 patients, with a median of 1 hour 50 minutes (range, 10 min – 4 hours 30 minutes).

Table 1. Patient demographics and clinical characteristics.

Variables	STEMI (n = 116)	NSTEACS (n =166)	All cases (n = 282)	P value
Demographics				
Age, y	56.9 ±11.7	59.0 ±12.4	58.2 ±12.2	
Sex, n (%)				0.043
Male	91 (78.4)	112 (67.5)	203 (72)	
Female	25 (21.6)	54 (32.5)	79 (28)	
BMI, n (%)				0.003
Normal	24 (20.7)	68 (41.0)	92 (32.6)	
Overweight	33 (28.4)	26 (15.7)	59 (20.9)	
Obesity	26 (22.4)	38 (22.9)	64 (22.7)	
No data	29 (25)	31 (18.7)	60 (21.3)	
Medical History*, n(%)				
Angina	25 (21.6)	65(39.2)	90 (31.9)	<0.001
Hyperlipidemia	14 (12.1)	25 (15.1)	39 (13.8)	0.002
Myocardial infarction	12 (10.3)	53 (31.9)	65 (23)	<0.001
Family history of premature CHD	3 (2.6)	8 (4.8)	11(3.9)	0.597
Peripheral vascular disease	4 (3.4)	3 (1.8)	7 (2.5)	0.330
Stroke	6 (5.2)	7 (4.2)	13 (4.6)	0.027
Congestive heart failure	6 (5.2)	9 (5.4)	15 (5.3)	0.682
Asthma/COPDs	3 (2.6)	3 (1.8)	6 (2.1)	0.126
Hypertension	52 (44.8)	96 (57.8)	148(52.5)	0.048
Diabetes Mellitus	25 (21.6)	43 (25.9)	68 (24.1)	0.162
Smoking habit, n (%)				0.004
Active smoker	45 (38.8)	32 (21.1)	80 (28.4)	
Past smoker	7 (6.0)	5 (3.0)	12 (4.3)	
Never smoke	44 (37.9)	89 (53.6)	133 (47.2)	
No data	20 (17.2)	37 (22.3)	57 (20.2)	
Clinical presentation, n (%)				
Chest pain*	85 (73.2)	113 (68.1)	198 (70.2s)	
Killip class I	90 (77.6)	126 (75.9)	216 (76.6)	0.490
Killip class II	8 (6.9)	18 (10.8)	26 (9.2)	
Killip class III	7 (6.0)	12 (7.2)	19 (6.7)	
Killip class IV	11 (9.5)	10 (6.0)	21 (7.4)	
Rehospitalization	8(6.9)	13(7.8)	21(7.4)	0.769
Mortality				
In-hospital death	7 (6.0)	1 (0.6)	8(2.8)	0.009

BMI: body mass index; COPD: chronic obstructive pulmonary disease, *missing data
also accounted in the percentage, in each group and overall population <5% data were not available

Table 2. Interval from worst symptoms onset to first medical contact (FMC) and secondary hospital.

	Transferred patient (n=142)		Non-transferred patients (n=140)
Interval from onset…	**To FMC**	**To hospital**	**To hospital**
<1 hour	24 (16.9)	2 (1.4)	29 (20.7)
1-3 hours	25 (17.6)	12 (8.5)	34 (24.3)
3-6 hours	11 (7.7)	27 (19.0)	21(15.0)
6-12 hours	18 (12.7)	29 (20.4)	8(5.7)
>12 hours	20 (14.1)	43 (30.3)	21(15.0)
No data	44 (31.0)	29 (20.4)	27 (19.3)

Table 3. Relationship between chest pain and first 12-lead ECG after hospital arrival.

	ECG ≤ 10 minutes (n= 205)	**ECG > 10 minutes (n=42)**	**P value**	**OR 95%CI**
Chest pain	156	21	0.001	3.184 (1.605-6.314)
No chest pain	49	21		

Table 4. Serial troponin assays and final diagnoses in NSTEACS group (n=166).

		Final Diagnosis		
		NSTEMI (n= 64)	**UA (n=80)**	**NSTEACS (n=22)**
Troponin level after serial assay, n (%)	No change/low	1 (1.6)	33 (41.3)	4 (18.2)
	Elevated after serial measurement	25 (39.0)	1 (1.2)	5 (22.7)
	Single measurement	37 (57.8)[a]	44 (55)[b]	10 (45.5)[b]
	No data	1 (1.6)	2 (2.5)	3 (13.6)

[a]Increased troponin I level on initial measurement, blow troponin level on initial measurement

Table 5. GRACE and TIMI risk score vs mortality.

All deaths (n=8)	**Risk stratification**	**Events/subjects**
STEMI + NSTEACS based on GRACE	Low	0/104
	Intermediate	4/61
	High	2/54
	No data	2/63
STEMI (n=7) based on TIMIa	Low	3/23
	Intermediate	1/9
	High	0/2
	No data	3/82
NSTEACS (n=1) based on TIMI	Low	0/40
	Intermediate	0/16
	High	1/2
	No data	0/108

[a]low:0-4 pts, intermediate:5-8 pts, high:>8

Patient outcome

The median LOS was five days from 205 length-of-stay (LOS) data available (range, 1-17 days). For overall population, there were low but significant correlation between Killip class and length of stay (r = 0.158, p = 0.023). There were also 7.4% of readmission cases that were not exclusively associated with cardiac problems.

The distribution of GRACE and TIMI risk score for in-hospital death events is shown in table 5. There were 6 out of 8 deceased patients who had intermediate to high risk of in-hospital mortality based on GRACE score. According to the TIMI risk score, only one death in the NSTEACS group was considered high 30-day mortality risk, whereas, in the STEMI group, four deaths were classified into low-intermediate risk.

Discussion

Kupang is the capital city of East Nusa Tenggara province, located in the Timor Island. At the time of study, there are 4 cardiologist serving 442.758 people in Kupang, made the ratio of cardiologist and the citizen about 1:110.000.[9] In this study, we found that 41% of ACS were STEMI and 59% were NSTEACS. These proportions are consistent with the finding from the ACCESS group who reported that in developing countries, ACS tend to be predominated by NSTEACS compared to STEMI (46% vs. 54%).[10] The same trend has also been observed in the Asian and Western studies, which showed a reduction in STEMI patients and an increase in NSTEMI patients—implying more effective preventive measures among STEMI patients and better diagnostic tools to recognize STEMI.[11–13]

Individuals hospitalized for ACS in Kupang mainly were male and almost a decade younger than those in the more developed countries (mean age for STEMI vs. NSTEMI, 67 years old vs. 73 years old). The earlier age for the first episode of ACS is likely due to earlier adoption of unfavourable health behaviours as well as CVD risk factors.[13] The male patients in Malaysia and even South Asian countries like Sri Lanka also showed earlier age on first ACS while their female counterparts were affected 7-10 years later owing to the premenopausal estrogen exposure that presumably delays atherosclerotic process.[1,12,14]

Nearly half of all ACS patients at least have one or more cardiac or non-cardiac comorbidities.[15] This also increased the mortality risk by 26% compared to patients without comorbidity, especially in the younger patient.[16] Similar to our study, patients with STEMI in the Western and Asian populations, were less likely to present with a history of several comorbidities (i.e., angina, stroke, DM, hypertension) in comparison to patients with NSTEMI.[1,12,13] Our results are also in line with a 2013 study which found that the Indonesian population also had a long-standing burden of modifiable CVD risk factors: 30% of males had a high level of cholesterol, 23% had hypertension, 6% had diabetes, and 20% were overweight. In the female population, the percentages are higher where 40% had hypercholesterolemia, 29% had hypertension, 8% had diabetes, and 33% were overweight. The BMI of our subjects were relatively low because East Nusa Tenggara has the lowest obesity levels (6.2%) and central obesity (15.2%) among other provinces in Indonesia.3 The proportion of subjects with normal BMI in NSTEACS group are two times higher than in STEMI group, but hyperlipidemia in NSTEACS group is a bit higher than in STEMI group (Table 1). It can be inferred that hyperlipidemia could also associated with normal BMI.[9]

Current smoking is one of the strongest risk factors for acute MI based on multivariate analysis by INTERHEART study.[17] It is known from the previous research that one-third of the overall Indonesian population have ever smoke (daily, occasional, or ex-smokers), and even a staggering 65% of men smoked tobacco. This high smoking rate for men is also seen in most Asian countries ranging from 40-60%.18 This high prevalence of smokers in Indonesia was not reflected in our study apparently due to high missing data (20.2%).

More than 50% of our patients had a history of hypertension; however, ACCESS study reported an even higher prevalence of hypertension (STEMI 78%, NSTE-ACS 87%) in ACS patients in other developing countries.[10] NSTEACS arm had significantly more patients with hypertension, as seen in a study from South Asia.[1] The plausible explanation might be related to the formation of collaterals in hypertension-induced left ventricular hypertrophy. These collaterals lead to partial-thickness infarction, which results in ischemia without total occlusion hence NSTEMI/UA manifestation.[17] Diabetes was also observed in nearly 25% of overall populations with almost the same proportion in both

STEMI and NSTEACS group, consistent with the Asian studies which found the prevalence of DM in ACS patients were estimated at 20-30%.[1, 20]

Among the obstacles in intervening with these risk factors is the lack of awareness and control of the disease and comorbidities. In our study, less than 50% of patients with hypertension or DM received adequate treatment and achieved a controlled state. A study among individuals in Bintan Island, Riau Archipelago, in 2015 reported that around 50% of people with high blood pressure were unaware and untreated. Furthermore, only over 30% of people with hypertension received some medications, but only 15% were adequately treated.[21] This phenomenon also occurs in 8.5 million people with diabetes where 19% did not seem aware of their diagnosis, 41% knew their diagnosis but did not receive treatment, 39% have been treated, but only 1% take regular medication.[22]

Half of the patients in this study were referred to a hospital from the primary healthcare center or other lower tier hospitals in Kupang. However, only over 30% of this group of patients encountered medical personnel under 3 hours after onset, which led them to arrive even later at the hospital and potentially prolonged their ischemic time. Aside from patients' delays, system delay might be one of the most significant barriers to timely in-hospital management in East Nusa Tenggara. An analysis based on universal health coverage in East Nusa Tenggara found that lower-tier health facilities were burdened by high severity levels of CVDs.[23] These patients required specialistic management in higher-tier hospitals, which are primarily available in the main hospital. Establishing a communication network (i.e., telecardiology) with the cardiology treatment center might support the transition of care from remote areas in order to reduce symptoms-to-treatment time.[24,25] One of evidence came from West Jakarta, Indonesia who successfully reduced the median transfer time by 50 minutes in 3 years of implementing iSTEMI telecardiology network.[24]

Approximately 20-30% of subjects in this study did not suffer chest pain. This result is similar to a Korean and Western study which reported the absence of chest pain in 23% ACS patients and 20-30% of patients with STEMI, respectively.[26,27] Individuals without chest pain were more likely to have delayed ECG examination, which led to prolonged contact-to-treatment time and increased risk for adverse events by 3-fold, particularly in STEMI patients.[26,28] The presenting severity level in our study is similar to studies in other provinces like Bandung and Jakarta. Even in a tertiary hospital, most patients (70%) are in the Killip I class, reflecting that most patients had a better prognosis.[25,29]

Troponin measurement is one of the essential diagnostic tools notably to rule out MI. in this study, over 90% of STEMI patients had positive troponin. Other patients who fell into the NSTEACS category underwent troponin assay to identify NSTEMI where 22% had elevated troponin level on initial measurement, and 15% detected through serial troponin measurement. A cohort study that included 51.8% ACS patients with only a single troponin evaluation reported low benefit on serial troponin testing for low-risk patients and those with extended duration of symptoms. The investigators also justified discharged of patients after initial low troponin measurement notably with the incorporation of HEART risk score since the are no difference in rates of 30-day cardiac mortality and acute MI.[30]

As for treatment practices, Kupang currently still does not have a percutaneous coronary intervention (PCI) facility, so a patient who needs reperfusion will receive fibrinolytic therapy. In our study, we found a low percentage of patients with STEMI who underwent reperfusion compared to other parts of Indonesia.[24,25,29] The median door-to-needle in this study was 1 hour 50 minutes, but the range was quite wide. One patient with ten minutes of door-to-needle time was a referred patient from cardiologist in other hospital. This could be achieved with a good coordination between hospitals and medical teams. The fibrinolytic treatment was given in emergency unit, instead of intensive cardiac care unit. This special case shows the potential of improvement in reperfusion therapy in Kupang. There is a possibility to improve this time interval as some patients only took under 30 minutes from arrival to starting intravenous thrombolytic. Implementation of telecardiology might increase the quality of care, especially for increasing hospital referral cases, reperfusion procedures, and door-to-needle time as seen in the West Jakarta study. They managed to reduce door-to-needle time by 15 minutes, followed by reduced ischemic time by 55 minutes, and finally reduced in-hospital mortality.[24,25]

The median LOS of patients in this study varied from 1 day to 17 days which might be caused by the severity

level (Killip class and complications) of the patients. Readmission of patients after ACS is not uncommon, as seen in the present study. However, it encompassed all rehospitalization in 1 year of observation, and it does not equal poor quality of care. In fact, it might represent good healthcare access or lower mortality. The in-hospital mortality in this study was relatively low (2.8%), and most were diagnosed with STEMI. This finding is fairly similar to in-hospital deaths in the Jakarta study, considering that most patients presented with Killip class I and a lower rate of comorbidities in comparison with the NSTEACS group.[25] Selection bias because of the Covid-19 pandemic and patient's tendency to avoid hospitalization might be correlated too with the low in-hospital mortality in this study.

Overall, incomplete medical record data and history-taking points, especially related to time elements as well as risk factors, are the limitations of this study. The results of this study can be used as a provision for educational programs related to the symptoms and risk factors of ACS. Increasing public awareness might reduce patient delays, particularly for people in Kupang whose access is relatively closer to the main hospital. On the other hand, improving prehospital care may be the key point in reducing system delays. Procurement of ECG machine and ACS first aid supplies for the community health centers as well as first responders (Brigade Kupang Sehat) can shorten the time for diagnosis and initiation of oral antiplatelet therapy. Further research is expected to help develop preventive programs, including lifestyle modification, risk factors screening, and optimizing drug treatment adherence.

Conclusion

This observational study showed unique profiles in the care of patients with ACS happened in Kupang, East Nusa Tenggara. Although in-hospital mortality was relatively low, a significant number of patients with STEMI did not receive reperfusion therapy due to the patient and system delay. Expansion of registry across networking healthcare facility in Kupang along with enhancement of prehospital role in ACS management provides the opportunity to improve ACS patient care in the future.

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Abbreviations

ACS	:	Acute Coronary Syndrome
CVD	:	Cardiovascular disease
BMI	:	Body Mass Index
GRACE	:	Global Registry of Acute Coronary Events
ICCU	:	Intensive Cardiac Care Unit
LOS	:	Length of Stay
NSTEACS	:	Non-ST-segment-elevation Acute Coronary Syndrome
STEMI	:	ST Segment Elevation Myocardial Infarction
TIMI	:	Thrombolysis in Myocardial Infarction
UA	:	Unstable Angina

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