Heart Sci J 2022; 3(1): 37-42

Contents list available at www.heartscience.ub.ac.id

Heart Science Journal

Journal Homepage : www.heartscience.ub.ac.id

Original Article

Factors Associated with In-hospital Mortality in Patients with Acute Coronary Syndrome

Hiradipta Ardining[1*], Nisa Amnifolia Niazta[1], Muchammad Dzikrul Haq Karimullah[2]

[1] *General Practitioner, Kediri District Hospital, Kediri, Indonesia.*
[2] *Department of Cardiology and Vascular Medicine, Kediri District Hospital, Kediri, Indonesia.*

ARTICLE INFO

Keywords:
In-Hospital Mortality;
Acute Coronary Syndrome;
Killip Class;
Decreased Consciousness.

ABSTRACT

Background : Acute coronary syndrome (ACS) remains the primary cause of death worldwide. Therefore, it is essential to determine factors associated with worse outcomes to elucidate better which patients deserve a more aggressive approach for management.
Objectives : To describe the characteristics of patients admitted with ACS to Kediri General Hospital and factors associated with in-hospital mortality in ACS patients.
Methods : In this cross-sectional study, 117 patients admitted with ACS to Kediri General Hospital between January and June 2020 were included. Data were collected retrospectively from medical records and analyzed using SPSS software v25.
Results : During hospitalization, 18 (15.4%) died. The bivariate analysis showed the patients who died were predominantly female, had a higher prevalence of Killip IV, higher prevalence of clinical signs of heart failure, lower admission systolic and diastolic blood pressure, and higher heart rate. From multivariable analysis, variables significantly associated with in-hospital mortality were decreased consciousness (OR = 11; 95%CI = 1.327-92.4; p = 0.026) and Killip class IV (OR = 9.558; 95%CI = 2.016-45.317; p = 0.004).
Conclusion : Decreased consciousness and Killip class IV were associated with increased in-hospital mortality in ACS.

1. Introduction

Acute coronary syndrome (ACS) continues to be a leading cause of death around the world. The incidence of ACS was 141/100,000 people per year in 2006, with a 7% death rate. One out of every three patients with ST-segment elevation acute coronary syndrome (STE-ACS) died within 24 hours of the beginning of ischemia, while 15% of patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) died or had a reinfarction within 30 days after diagnosis.[1,2]

Considering the high mortality rate, it is necessary to determine factors associated with worse outcomes to elucidate better which patients deserve a more aggressive approach for management. Several established risk scores for quantitative risk stratification, such as GRACE scores, did not systematically include Asian countries, so these scores may underestimate or overestimate actual risk when applied to these countries.[1,2] In this study, we described the characteristics of patients hospitalized with ACS to Kediri General Hospital and factors associated with in-hospital mortality in ACS patients.

2. Methods

2.1 Study Design

Between January and June 2020, a cross-sectional study was undertaken at Kediri General Hospital in East Java to determine the characteristics of patients hospitalized with ACS and factors associated with in-hospital mortality in ACS patients. Our research has been approved by Kediri General Hospital's local ethics committee.

2.2 Participants and eligibility criteria

All patients hospitalized with symptoms of acute, persistent chest pain more than 20 minutes or acute chest discomfort, with or without ischaemic ECG changes to Kediri General Hospital between January and June 2020 were included. Exclusion criteria for this study were samples that had incomplete data. The diagnosis of ACS was made according to the recent guideline. Demographic, clinical, ECG, laboratory, and follow-up echocardiography data were obtained from the medical record. The endpoint was all-cause mortality during hospitalization.

*Corresponding author at: Kediri District Hospital, Kediri, Indonesia.
E-mail address: hiradipta.ardining@gmail.com (H. Ardining).

https://doi.org/10.21776/ub.hsj.2022.003.01.6
Received 9 August 2021; Received in revised form 30 November 2021; Accepted 15 December 2021
Available online 1 January 2022

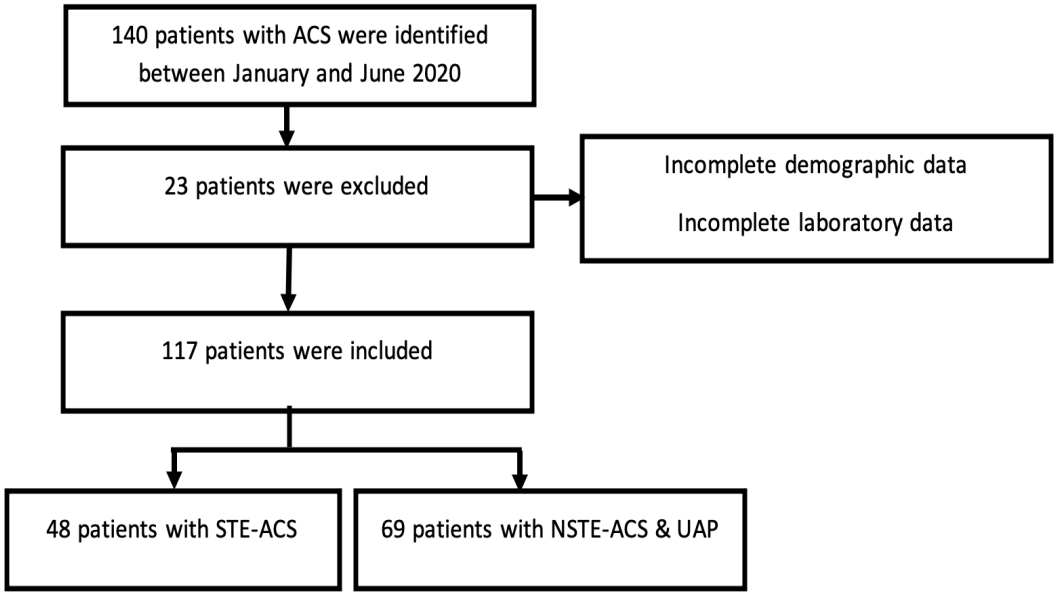

Figure 1. Flowchart eligibility criteria of participant in this study.
ACS = acute coronary syndrome; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; STE-ACS = ST-segment elevation acute coronary syndrome; UAP = unstable angina pectoris.

2.3 Measure

Demographic data collected were gender and age. Clinical data collected were history of coronary artery disease, onset and quality of chest pain, consciousness, blood pressure (mmHg), heart rate (beat per minute), and Killip class. Decreased consciousness was defined as a patient with Glasgow Coma Scale (GCS) less than 14 without any metabolic or intracranial abnormality. Killip class I was categorized as no sign of congestive heart failure, Killip class II if there were rales or increased jugular venous pressure, Killip class III if there was pulmonary edema, while Killip class IV if there was a cardiogenic shock. Laboratory data collected were hemoglobin (g/dL), white blood cell (cells/mL), thrombocyte (cells/mL), ureum (mg/dL), and creatinine (mg/dL). Electrocardiograms were recorded and read by a trained doctor to identify ischaemic ECG changes. Electrocardiogram changes may include ST-segment elevation > 0.2 mV in leads V1-V3 or ST-elevation > 1 mV in other adjacent leads; new LBBB; ST-segment depression > 0.05 mV in leads V1-V3 or ST-segment depression > 0.1 mV in the other leads, with or without symmetrical T inversion more than 0.2 mV; or normal ECG picture.

2.4 Statistical analysis

SPSS software v25 was used to analyze the data. For baseline characteristics, a univariate analysis was used. The Kolmogorov Smirnov test was used to determine the distribution of quantitative data. The mean standard deviation (SD) was used to describe data with a normal distribution, while the median was used to describe data that did not have a normal distribution (minimum-maximum). Counts and proportions (%) were used to present categorical variables. The link between each variable and in-hospital mortality was ruled out by bivariate analysis. The results were presented as odds ratios (ORs) and 95 percent confidence intervals (CIs). Multivariate analysis was used on variables with a p value of < 0.25. The connection between variables that fit the ACS patient's criteria and in-hospital mortality was investigated using a logistic regression backward model. The final model comprised variables with a significance level of 0.05. The Hosmer and Lemeshow test were used to determine the regression's goodness of fit. Under the receiver operating characteristic (ROC) curve, the area estimated the final model's discriminative power.

3. Results

3.1 Patient selection

Between January and June 2020, there were 140 patients with ACS in Kediri General Hospital. Twenty-three patients were excluded due to incomplete data. A flowchart displaying eligibility is shown in figure 1.

3.2 Baseline characteristics

Of 117 subjects, the median age was 60 (36-93) years old, 64 (54.7%) were male. They were presented either with STE-ACS (41%) or NSTE-ACS (59%). About 74.3% of the patients presented with the chief complaint of chest pain, 16.2% with epigastric pain, 5% with palpitation, and 33% with shortness of breath. Other baseline characteristics of the ACS patient are described in table 1.

3.3 Main findings

During hospitalization, 18 (15.4%) patients died. The bivariate analysis showed (table 2) the patients who died were predominantly female (22.6% vs 9.4%; p = 0.048); higher prevalence of Killip class IV (38.9% vs. 61.1%; p=0.003); higher prevalence of patients with clinical signs of heart failure (23.7% vs. 6.9%; p = 0.012); had lower admission blood systolic blood pressure (117 ± 26.0 vs. 137 ± 37.0; p= 0.036); lower admission diastolic blood pressure (70.6 ± 20.6 vs. 81.5 ± 20.5; p = 0.04); higher heart rate (104 ± 24 vs. 91 ± 22; p = 0,026). Other difference between groups may be seen in Table 2 and Table 3.

We ran multivariate analysis logistic regression, including variables with a p-value <0.25. Variables entered in multivariate analysis were gender, time to treatment, consciousness, mean arterial pressure category, hypertension status, presence of tachycardia, shock,

Table 1. Baseline characteristics.

Variables	In-hospital mortality (n=18)	Survivor (n=99)
Age (year)	61.5 (36 - 87)	60 (36 - 93)
>60	9 (17.6%)	42 (82.4%)
50-59	5 (10%)	45 (90%)
40-49	2 (20%)	8 (80%)
<40	2 (33.3%)	4 (66.7%)
Gender		
Male	6 (9.4%)	58 (90.6%)
Female	12 (22.6%)	41 (77.4%)
History of CAD		
Yes	6 (15.4%)	33 (84.6%)
No	12 (15.4%)	66 (84.6%)
Type of ACS		
STE-ACS	8 (16.7%)	40 (83.3%)
NSTE-ACS & UAP	10 (14.5%)	59 (85.5%)
Killip Score		
Killip IV	7 (38.9%)	11 (61.1%)
Killip III	3 (18.8%)	13 (81.3%)
Killip II	4 (16.0%)	21 (84%)
Killip I	4 (6.9%)	54 (93.1%)
Signs of heart failure		
Yes	14 (23.7%)	45 (76.3%)
No	4 (6.9%)	54 (93.1%)
Consciousness		
Decreased consciousness	3 (50%)	3 (50%)
Compos mentis	15 (13.5%)	96 (86.5%)
Hemodynamic		
Systolic blood pressure (mmHg)	117 ± 26.0	137 ± 37.0
Diastolic blood pressure (mmHg)	70.6 ± 20.6	81.5 ± 20.5
Mean arterial pressure (mmHg)	86.0 ± 21.9	100 ± 25.5
Laboratory parameter		
Haemoglobin (g/dL)	12 ± 2.2	13 (4-18)
Leukocytes (/ml)	13.394 ± 6.531	10.000 (3.500 - 26.900)
Thrombocytes (/ml)	292.500 (107.000 - 558.000)	279.000 (32.500 - 591.000)
Ureum (mg/dL)	40 (17 - 296)	32.5 (8 - 501)
Creatinine (mg/dL)	1.13 (0.49 - 18)	0.89 (0.42 - 15)
Electrocardiographic pattern		
ST segment elevation	9 (20.5%)	35 (79.5%)
ST segment depression	2 (25%)	6 (75%)
T inversion	5 (17.2%)	24 (82.8%)
Pathological Q wave	0 (0%)	3 (100%)
LBBB	0 (0%)	3 (100%)
RBBB	5 (23.8%)	16 (76.2%)

Note. ACS = acute coronary syndrome; CAD = coronary artery disease; LBBB = left bundle branch block; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; RBBB = right bundle branch block; STE-ACS = ST-segment elevation acute coronary syndrome; UAP = unstable angina

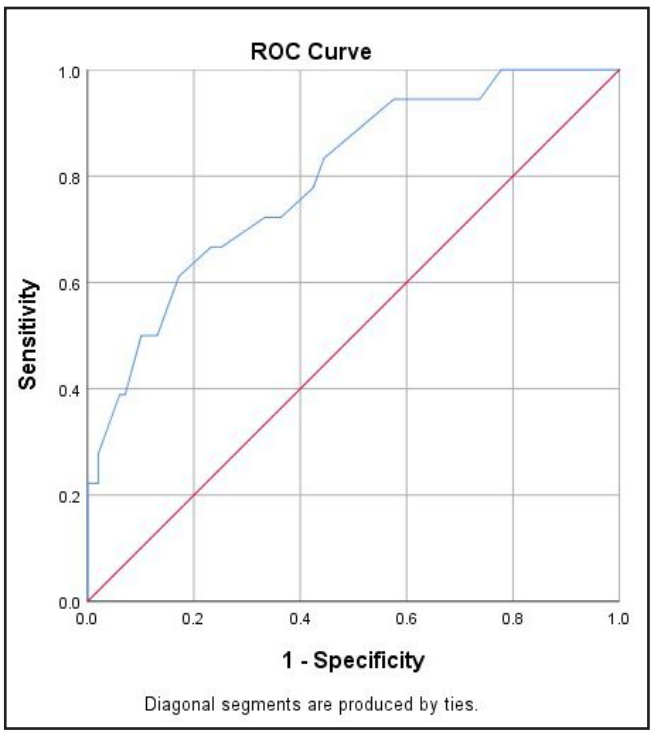

Figure 2. Receiver operating characteristics curve of final model including gender, decrease of consciousness, Killip score, and leucocytosis for in-hospital mortality ACS patient. ACS = acute coronary syndrome.

anemia, leucocytosis, ureum/creatinine category, and Killip class. Only consciousness and Killip class IV maintain statistical significance. We summarize the multivariate analysis in table 4. The C-statistic of the final model, including gender, a decrease of consciousness, Killip score, and leucocytosis for in-hospital mortality ACS patients, was 0.796 with 95%CI 0.685 – 0.907, shown in figure 2.

4.Discussion

Mortality in ACS, especially in STEMI, can be caused by several things, including old age, time delay to treatment, availability of STEMI-emergency medical system network, history of ACS, diabetes mellitus, renal failure, and left ventricular ejection fraction.[2] Our study revealed that decrease of consciousness and Killip class IV were associated with a higher risk of in-hospital mortality in patients with ACS.

Our study found that decreased consciousness (altered mental status) was associated with in-hospital mortality (OR = 11; 95%CI = 1.327 - 92.4; p = 0.026). Our present finding was consistent with some previous studies. Kataja et al. found significantly higher ninety-day mortality in patients with altered mental status (51% vs. 22%; p <0.001).[3] Altered mental status could indicate a state of hypoperfusion in ACS and has been associated with poor outcomes in several studies. In patients with ACS, myocardial infarction may cause sudden onset of hemodynamic derangement, causing hypotension and impairing cerebral blood flow, manifesting as altered mental status.

Compared to patients with Killip Class I, patients with Killip Class IV had worse outcomes. Class IV was related to increased in-hospital mortality in acute coronary syndrome (OR = 9.558, 95%CI = 2.016 - 45.317; p = 0.004). These findings were also consistent with previous studies. In a study by El-Menyar et al., higher Killip class was an independent predictor of mortality in ACS; Killip classes II, class III, and class IV were associated with increased mortality.[4]

Leucocytosis had been associated with in-hospital mortality in previous studies. Shah et al. found that leukocyte count was independently associated with MACE (hazard ratio [HR] = 1.05; 95%CI = 1.02 - 1.09; P = 0.001) and cardiac death (HR = 1.10; 95%CI = 1.05 - 1.17; P <0.001).5 Several mechanisms can explain this association: hypercoagulable state, resistance to thrombolytic therapy due to alterations in the microcirculation, and marker of reparative response that indicate a more significant amount of necrosis.6 However, in our study, leucocytosis was not shown to be statistically significant with in-hospital mortality in our multivariate analysis (OR = 2,22, 95%CI = 0.79 – 6.2; p = 0.12). The reason might be that there were other

Table 2. Bivariate analysis of categoric variables associated with higher mortality.

Variable	p-value	OR (95% CI)
Gender. female	0.048	2.83 (0.98 - 8.15)
Killip Score		
Killip IV	0.003	8.59 (2.14 - 34.46)
Killip III	0.168	3.11 (0.62 - 15.66)
Killip II	0.234	2.57 (0.59 - 11.24)
Killip I	reference	
Sign of heart failure	0.012	4.20 (1.29 - 13.66)
Decrease of consciousness	0.046	6.40 (1.18 - 34.70)
Mean arterial pressure <60 mmHg	0.105	3.76 (0.81 - 17.39)
Tachycardia	0.148	2.09 (0.76 - 5.78)
Cardiogenic shock	0.054	3.40 (1.01 - 11.61)
Anemia	0.087	2.41 (0.86 - 6.8)
Leukocytosis	0.122	2.22 (0.79 - 6.2)
Elevated ureum	0.260	1.86 (0.65 - 5.32)
Elevated creatinine	0.090	2.5 (0.89 - 7.05)

Table 3. Bivariate analysis of numeric variables associated with higher mortality.

Variable	p-value	Mean ± SD
Systolic blood pressure (mmHg)	0.036	117 ± 26.0 vs 137 ± 37.0
Diastolic blood pressure (mmHg)	0.040	70.6 ± 20.6 vs 81.5 ± 20.5
Heart rate (beat per minute)	0.026	104 ± 24 vs 91 ± 22

Table 4. Final model multivariate analysis of variables associated with higher mortality

Variable	p-value	OR (95% CI)
Gender. Female	0.091	3.14 (0.84-11.78)
Decrease of consciousness	0.026	11.08 (1.33-92.44)
Killip Score		
Killip IV	0.004	9.56 (2.02-45.31)
Killip III	0.597	1.72 (0.23-13.00)
Killip II	0.470	1.86 (0.34-10.09)
Killip I	reference	
Leukocytosis	0.122	2.22 (0.79-6.2)

causes of leucocytosis besides AMI, and our study did not exclude patients with signs of infection.

The female gender is known to have a greater mortality rate in ACS. A study by Lu et al. showed that females have a significantly higher in-hospital mortality rate than males (15.0% vs. 8.1%; p <0.000).7 Several explanations are that women with ACS tend to be older at presentation and tend to present later and with more atypical symptoms than men. However, in our study, gender was not shown to be statistically significant with in-hospital mortality in our multivariate analysis (OR 3.14; 95%CI 0.84-11.78; p=0.091).

The findings of this study have to be seen in the light of some limitations. This study was a retrospective, single-center, observational study. Therefore, the result was subject to biases and confounding that may influence the result. The sample size was also relatively small.

5. Conclusion

In conclusion, decreased consciousness and Killip class IV were associated with increased in-hospital mortality in ACS. These findings support routine assessment of these variables in patients with ACS to identify high-risk patients so that specific management could be addressed.

6. Declarations

6.1. Ethics Approval and Consent to participate
Not applicable.

6.2. Consent for publication
Not applicable.

6.3. Availability of data and materials
Data used in our study were presented in the main text.

6.4. Competing interests
Not applicable.

6.5. Funding source
Not applicable.

6.6. Authors contributions

Idea/concept: MDHQ. Design: MDHQ. Control/supervision: MDHQ. Data collection/processing: MDHQ, HA, NAN. Analysis/interpretation: MDHQ, HA, NAN. Literature review: HA, NAN. Writing the article: MDHQ, HA, NAN. Critical review: MDHQ, HA, NAN. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

6.7 *Acknowledgements*
We thank to Kediri District Hospital.

References

1. WHO. Coronavirus Disease (COVID-19) [Internet]. 2021 [cited Chan MY, Shah BR, Gao F, Sim LL, Chua T, Tan HC, et al. Recalibration of the Global Registry of Acute Coronary Events risk score in a multiethnic Asian population. Am Heart J. 2011;162(2):291–9.

2. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2018;39(2):119–77.

3. Kataja A, Tarvasmäki T, Lassus J, Køber L, Sionis A, Spinar J, et al. Altered mental status predicts mortality in cardiogenic shock - results from the CardShock study. Eur Hear journal Acute Cardiovasc care. 2018;7(1):38–44.

4. El-Menyar A, Zubaid M, Almahmeed W, Sulaiman K, Alnabti A, Singh R, et al. Killip classification in patients with acute coronary syndrome: Insight from a multicenter registry. Vol. 30, American Journal of Emergency Medicine. 2012. p. 97–103.

5. Shah B, Baber U, Pocock S, Krucoff M, Ariti C, Gibson C. White blood cell count and major adverse cardiovascular events after percutaneous coronary intervention in the contemporary era insights from the Paris study (Patterns of non-adherence to anti-platelet regimens in stented patients registry). Circ Cardiovasc Interv. 2017;10(8):1–8.

6. Núñez J, Núñez E, Bertomeu V, Fácila L, Sanchis J, Bodí V. Prognostic value of baseline white blood cell count in patients with acute

myocardial infarction and ST segment elevation. Heart. 2005;91(8):1094–5.

7. Lu H, Nordin R, Ahmad W, Lee C, Zambahari R, Ismail O, et al. Sex Differences in Acute Coronary Syndrome in a Multiethnic Asian Population. Glob Hear. 9(4):381–90.