

Echocardiography Killip Classification (eKillip Class) as a Predictor of Cardiovascular Rehospitalization and Mortality in Patients with Acute Myocardial Infarction

Ayu Putu Harina Ferdiyanti*, Ida Bagus Rangga Wibhuti,
I Kadek Susila Surya Darma

Department of Cardiology and Vascular Medicine, Faculty of Medicine Udayana University
Prof. dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali, Indonesia

E-mail: harinadian@gmail.com; rangga.w@gmail.com; kadek.susila@yahoo.co.id

*Corresponding author: Ayu Putu Harina Ferdiyanti; harinadian@gmail.com

ABSTRACT

Background: Patients with acute myocardial infarction (AMI) are at risk of experiencing cardiovascular events such as rehospitalization and mortality. The Echocardiography Killip Classification (eKillip Class) is a combined echocardiography hemodynamic assessment of stroke volume index (SVI) and diastolic function as indicators of systemic perfusion and pulmonary congestion, to assess the prognosis of AMI patients. This study aims to assess the eKillip Class as a predictor of cardiovascular rehospitalization and mortality in AMI patients. **Methods:** This is a prospective cohort study of 114 AMI patients who were obtained using a consecutive sampling technique that met the inclusion and exclusion criteria, then categorized into one of eKillip class I-IV. The follow-up duration was 30 days. The study outcomes were cardiovascular rehospitalization and mortality. Survival analysis was done using Kaplan-Meier test, and hazard ratio was estimated using a Cox proportional hazards model. **Results:** eKillip Class IV was present in 39 patients (34.3%), while 25 (21.9%), 20 (17.5%), and 30 (26.3%) patients were in eKillip Classes I to III, respectively. During 30 days of follow-up, a total of 22 patients (19.3%) with cardiovascular rehospitalization and 13 patients (13.2%) with cardiovascular mortality occurred. Multivariate cox regression analysis using the backward stepwise LR method showed that eKillip Class IV is independently associated with cardiovascular rehospitalization and mortality (adjusted HR 3.7; 95%CI 1.6–8.6; $p = 0.003$; and adjusted HR 3.5; 95%CI 1.2–9.9; $p = 0.018$, respectively). eKillip Class IV had a significantly lower mean survival time and 30-day survival rate than non-eKillip Class IV in terms of cardiovascular rehospitalization (24.7 days [95%CI 21.9-27.6] and 66.7% vs. 27.9 days [95%CI 26.4-29.4] and 88%; $p = 0.001$) and cardiovascular mortality (23.7 days [95%CI 19.9-27.3] and 76.9% vs. 27.8 days [95%CI 26.2-29.5] and 92%; $p = 0.019$). **Conclusions:** The eKillip Class was an independent predictor of cardiovascular rehospitalization and mortality in AMI patients. AMI patients with eKillip Class IV had lower survival rates for cardiovascular rehospitalization and mortality compared to patients with non-eKillip Class IV.

Keywords: eKillip Class; acute myocardial infarction; cardiovascular rehospitalization cardiovascular mortality

INTRODUCTION

Acute myocardial infarction (AMI) has varying degrees of clinical severity in the acute phase, ranging from stable hemodynamic status to cardiogenic shock [1]. Cardiogenic shock and the pre-shock state of acute decompensated heart failure represent a spectrum of hemodynamic deficits in patients with cardiovascular disease. Both conditions describe situations where cardiac output is insufficient to provide adequate tissue perfusion or may be sufficient but requires compensatory hemodynamic changes. Currently, the incidence of decompensated heart failure with cardiogenic shock resulting from MI is increasing [2, 3].

The prevention of complications from AMI also depends on the ability to identify high-risk individuals.

Risk stratification methods include clinical, laboratory, imaging, and non-invasive examinations [4]. Non-invasive support such as echocardiography has been proven to provide an overview of the prognosis in patients with AMI. Echocardiography can assess the systolic and diastolic functions of the heart, which are the basis of the patient's hemodynamic condition [5].

The Killip classification is a simple clinical classification of heart failure severity in patients with acute coronary syndrome. According to the Killip and Kimball criteria, patients are classified into four classes based on findings on physical examination (class I, with no evidence of heart failure; class II, with physical findings consistent with mildly elevated filling

pressure; class III, with overt pulmonary edema; and class IV, with cardiogenic shock) [6]. The Killip classification hierarchy is a combined assessment of the two main functions of the left heart to draw blood from the peripheral and pulmonic circulation and to eject it forward, referred to as diastolic and systolic functions. [6]. This system effectively stratifies short-term and long-term outcomes in patients with acute myocardial infarction [7]. However, the determination of Killip classification is quite subjective because the main basis is physical examination. Apart from that, the clinical features and predictors of high Killip class on admission and its prognostic impact in patients with STEMI as the first clinical cardiovascular event are still poorly known [8].

Echocardiographic evaluation is highly specific for the diagnosis of AMI (95% to 97%) but not sensitive (approximately 30%) [9]. Using the same logic as the Killip classification, echocardiography, which is the main examination of CVD patients in hospitals, should be used to evaluate a combination of systolic and diastolic function to provide objective hemodynamic assessment in patients with AMI [10-13].

Echocardiography based on the Killip classification can provide a combined hemodynamic assessment, which will be used to objectively assess the patient's hemodynamics. This is because the assessment results are based on parameters that can be measured and standardized. An echocardiographic assessment of the diastolic function is used as an indicator of pulmonary congestion, and the stroke volume index (SVI) is used as an indicator of systemic perfusion.

The aims of the present study were to establish the Echocardiography Killip Classification (eKillip Class), and investigate its prognostic value in patients with AMI. The eKillip Class would be a useful risk stratification modality in predicting rehospitalization and cardiovascular mortality in AMI patients.

METHODS

This is an analytical observational study with a prospective cohort design. This study began with the echocardiography assessment in AMI patients by several experienced cardiovascular residents and was reviewed by a single senior cardiology specialist in echocardiography. Each patient categorized into four groups according to the eKillip class category (eKillip class I, normal SVI [≥ 35 mL/m²] with normal or grade I diastolic patterns; eKillip class II, normal SVI with grade 2/indeterminate diastolic dysfunction; eKillip class III, normal SVI with grade 3 diastolic dysfunction or decreased SVI [< 35 mL/m²] with normal/grade 1/indeterminate diastolic patterns); and eKillip class IV, decreased SVI [< 35 mL/m²] with grade 2 or grade 3 diastolic dysfunction) [6].

Each group was followed for 30 days after the eKillip Class assessment to see whether one or both cardiovascular rehospitalization and/or cardiovascular mortality occurred.

This study was conducted from October 2023 to January 2024, located at the Cardiovascular Installation of Prof. dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali. An echocardiography examination to assess the eKillip Class in AMI patients is carried out in the cardiovascular emergency room of Prof. dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali. The target population in this study was all patients with acute myocardial infarction who came to the Cardiovascular Installation of Prof. dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali.

Inclusion criteria are patients aged 18 and over who had their first MI incident in the period October to December 2023 at the Cardiovascular Installation of Prof. dr. I.G.N.G. Ngoerah Hospital. Exclusion criteria include: incomplete stroke volume index (SVI) assessment; inability to accurately assess diastolic grade (patients with mitral valve stenosis or significant mitral valve regurgitation, aortic valve stenosis or significant aortic valve regurgitation, mitral or aortic valve prosthesis, presence of shunt in congenital heart disease, on pacemaker, or during echocardiography examination there were arrhythmias such as atrial fibrillation or atrial flutter, supraventricular tachycardia, and/or ventricular tachycardia; AMI patients who have received revascularization or hemodynamic therapy before echocardiography is performed; patients with other hemodynamic disorders or high output states such as sepsis; patients who are not willing to participate or are not willing to sign the informed consent. All patients were obtained using a consecutive sampling technique.

All data collected in each group were analyzed using the SPSS version 26, which includes descriptive analysis, survival analysis using the Kaplan-Meier test, and a Cox proportional hazards model. The confidence level in this study is 95%. H_0 is rejected, and H_1 is accepted if the p -value is < 0.05 . The study endpoints were cardiovascular rehospitalization and/or mortality.

RESULTS

The mean age of the study population was 58 ± 10.4 years, 93 (81.6%) were a man; 25 patients (21.9%) were in eKillip class I, 20 (17.5%) in class II, 30 (26.3%) in class III, and 39 (34.3%) in class IV. There were significant differences in baseline clinical such as PCI, and echocardiographic characteristics among the four eKillip classes, as presented in Tables 1 and 2.

TABLE 1: Sociodemographic Characteristics of Research Subjects Based on the eKillip Class.

Variable	Total	eKillip Class				p
		I	II	III	IV	
Number of subjects	114	25 (21.9)	20 (17.5)	30 (26.3)	39 (34.3)	
Age, mean±SD (years)	58±10.4	57±8.7	58±10.4	58±11.2	58±11.1	
Young adults, n (%)	4 (3.5)	0 (0)	0 (0)	1 (3.3)	3 (7.7)	0.975 ^c
Old adults, n (%)	65 (57)	17 (68)	12 (60)	15 (50)	21 (53.8)	0.900#
Elderly, n (%)	45 (39.5)	8 (32)	8 (40)	14 (46.7)	15 (38.5)	
Gender						
Man, n (%)	93 (81.6)	21 (84)	17 (85)	27 (90)	28 (81.6)	0.232#
Woman, n (%)	21 (18.4)	4 (16)	3 (15)	3 (10)	11 (18.4)	
Smoke						
Yes, n (%)	60 (52.6)	11 (44)	8 (40)	18 (60)	23 (59)	0.130#
No, n (%)	54 (47.4)	14 (56)	12 (60)	12 (40)	16 (41)	
BMI, median (kg/m²)	24.7 (16.6-41.6)	24.8 (18.4-32.8)	25.3 (18.7-39.2)	24.2 (18.1-36.8)	24.0 (16.6-41.6)	
Normal, n (%)	56 (49.1)	13 (52)	8 (40)	14 (46.7)	21 (53.8)	0.968 ^p
Underweight, n (%)	4 (3.5)	1 (4)	0 (0)	2 (6.7)	1 (2.6)	0.755#
Overweight, n (%)	39 (34.2)	8 (32)	9 (45)	10 (33.3)	12 (30.8)	
Obese, n (%)	15 (13.2)	3 (12)	3 (15)	4 (13.3)	5 (12.8)	
Hypertension						
Yes, n (%)	65 (57)	15 (60)	11 (55)	14 (46.7)	25 (64.1)	0.784#
No, n (%)	49 (43)	10 (40)	9 (45)	16 (53.3)	14 (35.9)	
Diabetes mellitus						
Yes, n (%)	42 (36.8)	8 (32)	6 (30)	7 (23.3)	21 (53.8)	0.080#
No, n (%)	72 (63.2)	17 (68)	14 (70)	23 (76.7)	18 (46.2)	
Hyperuricemia						
Yes, n (%)	31 (28.2)	5 (20)	8 (42.1)	7 (24.1)	11 (29.7)	0.712#
No, n (%)	79 (71.8)	20 (80)	11 (57.9)	22 (75.9)	26 (70.3)	
Dyslipidemia						
Yes, n (%)	106 (96.4)	24 (96)	17 (89.5)	29 (100)	36 (97.3)	0.420#
No, n (%)	4 (3.6)	1 (4)	2 (10.5)	0 (0)	1 (2.7)	
AMI						
STEMI, n (%)	88 (77.2)	18 (72)	15 (75)	21 (70)	34 (38.6)	0.180#
NSTEMI, n (%)	26 (22.8)	7 (28)	5 (25)	9 (30)	5 (19.2)	
PCI						
Yes, n (%)	80 (70.2)	21 (84)	16 (80)	19 (63.3)	24 (61.5)	0.030#*
No, n (%)	34 (29.8)	4 (16)	4 (20)	11 (36.7)	15 (38.5)	

^cOne Way Anova Test, ^pKruskal-Wallis test, #Linear-by-Linear Association Test, *Statistically significant.

BMI, body mass index; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention.

p values refer to the difference between one and any of the remaining three groups.

TABLE 2: Echocardiographic Characteristics of Research Subjects Based on the eKillip Class.

Variable	Total	eKillip Class				p
		I	II	III	IV	
SV, mean±SD (mL)	54.4±18.7	72.5±13.6	62.0±13.1	51.7±19.1	40.9±11.3	<0.001 ^{σ*}
Low, n (%)	43 (37.7)	0 (0)	3 (15)	15 (50)	25 (64.1)	<0.001#*
Normal, n (%)	71 (62.3)	25 (100)	17 (85)	15 (50)	14 (35.9)	
SVI, mean±SD (mL/m²)	30.8±10.3	40.6±7.5	35.9±8.3	29.2±9.8	23.3±5.9	<0.001 ^{σ*}
Low, n (%)	66 (57.9)	0 (0)	4 (20)	25 (83.3)	37 (94.9)	<0.001#*
Normal, n (%)	48 (42.1)	25 (100)	16 (80)	5 (16.7)	2 (5.1)	
CO, median (L/min)	4.1 (1.6-11.1)	5.9 (3.6-8.1)	4.9 (2.5-6.5)	3.7 (2.3-11.1)	3.5 (1.6-8.1)	<0.001 ^{ρ*}
Low, n (%)	53 (46.5)	2 (8)	5 (25)	18 (60)	28 (71.8)	<0.001#*
Normal, n (%)	61 (53.5)	23 (92)	15 (75)	12 (40)	11 (28.3)	
LAVI, median (mL/m²)	26.7 (6.5-63.9)	22.4 (6.5-38.9)	32.9 (13-56.4)	23.3 (12.7-51.4)	38.7 (11.8-63.9)	<0.001 ^{ρ*}
Increased, n (%)	39 (34.2)	1 (4)	10 (50)	4 (13.3)	24 (61.5)	<0.001#*
Normal, n (%)	75 (65.8)	24 (96)	10 (50)	26 (86.7)	15 (38.5)	
LVVI, median (mL/m²)	52.0 (17.3-259.7)	51.3 (27.4-108.2)	65.8 (34.8-259.7)	47.7 (19.7-135)	48.9 (17.3-164)	0.058 ^ρ
Increased, n (%)	27 (23.7)	4 (16)	9 (45)	4 (13.3)	10 (25.6)	0.984 [#]
Normal, n (%)	87 (76.3)	21 (84)	11 (55)	26 (86.7)	29 (74.4)	
ePCWP, median (mmHg)	20.3 (8.5-46.8)	14.8 (8.5-38.4)	23.3 (13.2-32.3)	19.4 (8.8-35.7)	23.9 (12.4-46.8)	<0.001 ^{ρ*}
High, n (%)	92 (80.7)	12 (48)	19 (95)	25 (83.3)	36 (92.3)	<0.001#*
Normal, n (%)	22 (19.3)	13 (52)	1 (5)	5 (16.7)	3 (7.7)	
EF, mean±SD (%)	43.3±10.7	48.8±10.5	43.9±12.8	42.1±8.9	40.3±10.1	0.018 ^{σ*}
Normal, n (%)	32 (28.1)	11 (44)	7 (35)	6 (20)	8 (20.5)	0.007#*
Mildly reduced, n (%)	42 (36.8)	10 (40)	6 (30)	13 (43.3)	13 (33.3)	
Reduced, n (%)	40 (35.1)	4 (16)	7 (35)	11 (36.7)	18 (46.2)	
Degree of diastolic function						
Normal, n (%)	14 (12.3)	9 (36)	0 (0)	5 (16.7)		<0.001#*
Decreased grade I, n (%)	35 (30.7)	16 (64)	0 (0)	18 (60)	0 (0)	
Decreased grade II, n (%)	45 (39.5)	0 (0)	17 (85)	0 (0)	1 (2.6)	
Decreased grade III, n (%)	14 (12.3)	0 (0)	0 (0)	5 (16.7)	28 (71.7)	
Indeterminate, n (%)	6 (5.2)	0 (0)	3 (15)	2 (6.6)	9(23.1)1 (2.6)	
E/e' average, median	14.8 (5.3-36.2)	10.4 (5.3-29.5)	17.3 (9.1-34.5)	14.1 (5.6-27.2)	17.7 (8.4-36.2)	<0.001 ^{ρ*}
High, n (%)	71 (62.3)	3 (12)	18 (90)	16 (53.3)	34 (87.2)	<0.001#*
Normal, n (%)	43 (37.7)	22 (88)	2 (10)	14 (46.7)	5 (12.8)	
E/A Ratio, median	1.1 (0.4-4.3)	0.9 (0.5-1.6)	1.1 (0.5-1.5)	1.1 (0.5-3.1)	1.3 (0.4-4.3)	0.063 ^ρ
Normal, n (%)	74 (64.9)	19 (76)	16 (80)	20 (66.7)	19 (48.7)	0.002#*
Low, n (%)	26 (22.8)	6 (24)	4 (20)	4 (13.3)	12 (30.8)	
High, n (%)	14 (12.3)	0 (0)	0 (0)	6 (20)	8 (20.5)	

^σOne Way Anova Test, ^ρKruskal-Wallis test, [#]Linear-by-Linear Association Test, ^{*}Statistically significant.

SV, stroke volume; SVI, stroke volume index; CO, cardiac output; LAVI, left atrial volume index; LVVI, left ventricular volume index; ePCWP, estimated pulmonary capillary wedge pressure.

p values refer to the difference between one and any of the remaining three groups.

During the study period, 22 patients (19.3%) had cardiovascular rehospitalization and 13 patients (13.2%) had cardiovascular mortality. Distribution analysis results in cardiovascular rehospitalization based on the sociodemographic and echocardiographic characteristics can be seen in Tables 3 and 4. Variables that were significant for cardiovascular rehospitalization, including the eKillip Class, gender, hyperuricemia, LVVI, and degree of diastolic function, with $p < 0.05$. Whereas, variables that were significant for cardiovascular mortality, including the eKillip Class, age, diabetes mellitus, degree of diastolic function, E/e' average, and E/A ratio with $p < 0.05$. Variables with $p < 0.25$ and theoretically related to the outcome will then be

entered into a multivariate analysis to see whether there is an independent relationship with the outcome. However, variables that represent hemodynamics or are the main assessment component of the eKillip Class itself, even though they have a significant p -value, are not included in the multivariate analysis. The variables that will be controlled through multivariate analysis are gender, smoking, hyperuricemia, hypertension, diabetes mellitus, PCI, and LVVI for cardiovascular rehospitalization, and the variables that will be controlled through multivariate analysis for cardiovascular mortality are age, smoking, diabetes mellitus, and PCI.

TABLE 3: Distribution of Cardiovascular Rehospitalization Based on Sociodemographic Characteristics of Research Subjects.

Variable	Cardiovascular Rehospitalization		p
	Yes	No	
Number of subjects	22 (19.3)	92 (80.7)	
Age, mean±SD (years)	57±11.6	58±10.2	0.651 μ
Young adults, n (%)	1 (25)	3 (75)	0.410#
Old adults, n (%)	14 (21.5)	51 (78.5)	
Elderly, n (%)	7 (15.6)	38 (84.4)	
Gender			
Man, n (%)	14 (15.1)	79 (84.9)	0.028 $^{\wedge}$ * ϕ
Woman, n (%)	8 (38.1)	13 (61.9)	
Smoke			
Yes, n (%)	9 (15)	51 (85)	0.220 $^{\Omega}$ ϕ
No, n (%)	13 (24.1)	41 (75.9)	
BMI, median (kg/m²)	24.6 (16.6-37.5)	24.7 (18.1-41.6)	0.954 \ddagger
Normal, n (%)	10 (17.9)	46 (82.1)	0.447#
Underweight, n (%)	1 (25)	3 (75)	
Overweight, n (%)	6 (15.4)	33 (84.6)	
Obese, n (%)	5 (33.3)	10 (66.7)	
Hypertension			
Yes, n (%)	15 (23.1)	50 (76.9)	0.239 $^{\Omega}$ ϕ
No, n (%)	7 (14.3)	42 (85.7)	
Diabetes mellitus			
Yes, n (%)	11 (26.2)	31 (73.8)	0.154 $^{\Omega}$ ϕ
No, n (%)	11 (15.3)	61 (84.7)	
Hyperuricemia			
Yes, n (%)	10 (32.3)	21 (67.7)	0.044 $^{\Omega}$ * ϕ
No, n (%)	12 (15.2)	67 (84.8)	
Dyslipidemia			
Yes, n (%)	21 (19.8)	85 (80.2)	1,000 $^{\wedge}$
No, n (%)	1 (25)	3 (75)	
AMI			
STEMI, n (%)	15 (17)	73 (83)	0.262 $^{\Omega}$
NSTEMI, n (%)	7 (26.9)	19 (73.1)	
PCI			
Yes, n (%)	13 (16.2)	67 (83.8)	0.206 $^{\Omega}$ ϕ
No, n (%)	9 (26.5)	25 (73.5)	

μ Independent T Test, \ddagger Mann Witney Test, #Linear-by-Linear Association Test, $^{\wedge}$ Fisher's Exact Test, $^{\Omega}$ Pearson Chi-Square Test, *Statistically significant, ϕ Enter the multivariate test. BMI, body mass index; AMI, acute myocardial infarction; PCI, percutaneous coronary intervention. p values refer to the difference between one and any of the remaining three groups.

TABLE 4: Distribution of Cardiovascular Rehospitalization Based on Echocardiographic Characteristics of Research Subjects.

Variable	Cardiovascular Rehospitalization		p
	Yes	No	
eKillip Class			
I, n (%)	1 (4)	24 (96)	0.004#* ^φ
II, n (%)	3 (15)	17 (85)	
III, n (%)	5 (16.7)	25 (83.3)	
IV, n (%)	13 (33.3)	26 (66.7)	
SV, mean±SD (mL)			
Low, n (%)	49.9±23.7	55.5±17.3	0.215 ^μ
Normal, n (%)	11 (25.6)	32 (74.4)	0.186 ^Ω
SVI, mean±SD (mL/m2)			
Low, n (%)	28.4±12.1	31.4±9.8	0.210 ^μ
Normal, n (%)	16 (24.2)	50 (75.8)	0.117 ^Ω
CO, median (L/min)			
Low, n (%)	3.8 (1.6-11.1)	4.1 (1.7-8.1)	0.628 [¶]
Normal, n (%)	12 (22.6)	41 (77.4)	0.399 ^Ω
LAVI, median (mL/m2)			
Increased, n (%)	33.9 (11.8-63.9)	24.4 (6.5-60.6)	0.029 [¶] *
Normal, n (%)	11 (28.2)	28 (71.8)	0.082 ^Ω
LVVI, median (mL/m2)			
Increased, n (%)	69.0 (26.4-164)	48.1 (17.3-259.7)	0.001 [¶] * ^φ
Normal, n (%)	11 (40.7)	16 (59.3)	0.001 ^Ω * ^φ
ePCWP, median (mmHg)			
High, n (%)	22.2 (12.4-45.3)	20.2 (8.5-46.8)	0.272 [¶]
Normal, n (%)	19 (20.7)	73 (79.3)	0.560 [^]
EF, mean±SD (%)			
Normal, n (%)	40.7±11.3	43.9±10.6	0.212 ^μ
Mildly reduced, n (%)	6 (18.8)	26 (81.2)	0.302 [#]
Reduced, n (%)	5 (11.9)	37 (88.1)	
Degree of diastolic function			
Normal, n (%)	2 (14.3)	12 (85.7)	0.033 [#] *
Decreased grade I, n (%)	2 (5.7)	33 (94.3)	
Decreased grade II, n (%)	11 (24.4)	34 (75.6)	
Decreased grade III, n (%)	6 (42.9)	8 (57.1)	
Indeterminate, n (%)	1 (16.7)	5 (83.3)	
E/e' average, median			
High, n (%)	16.4 (8.4-35)	14.7 (5.3-36.2)	0.272 [¶]
Normal, n (%)	16 (22.5)	55 (77.5)	0.260 ^Ω
E/A Ratio, median			
Normal, n (%)	1.2 (0.5-4.3)	1.1 (0.4-3.3)	0.451 [¶]
Low, n (%)	11 (14.9)	63 (85.1)	0.061 [#]
High, n (%)	6 (23.1)	20 (76.9)	
	5 (35.7)	9 (64.3)	

^μIndependent T Test, [¶]Mann Whitney Test, [#]Linear-by-Linear Association Test, [^]Fisher's Exact Test, ^ΩPearson Chi-Square Test, *Statistically significant, ^φEnter the multivariate test.

SV, stroke volume; SVI, stroke volume index; CO, cardiac output; LAVI, left atrial volume index; LVVI, left ventricular volume index; ePCWP, estimated pulmonary capillary wedge pressure.

p values refer to the difference between one and any of the remaining three groups.

TABLE 5: Distribution of Cardiovascular Mortality Based on Sociodemographic Characteristics of Research Subjects.

Variable	Cardiovascular Mortality		p
	Yes	No	
Number of subjects	15 (13.2)	99 (86.8)	
Age, mean±SD (years)			
Young adults, n (%)	62±11.1	57±10.2	0.049 [¶] *
Old adults, n (%)	0 (0)	4 (100)	0.005 [#] * ^φ
Elderly, n (%)	4 (6.2)	61 (93.8)	
Gender			
Man, n (%)	11 (24.4)	34 (75.6)	
Woman, n (%)	14 (15.1)	79 (84.9)	0.298 [^]
	1 (4.8)	20 (95.2)	

Variable	Cardiovascular Mortality		p
	Yes	No	
Smoke			
Yes, n (%)	5 (8.3)	55 (91.7)	0.108 ^{Ωϕ}
No, n (%)	10 (18.5)	44 (81.5)	
BMI, median (kg/m²)			
Normal, n (%)	9 (16.1)	47 (83.9)	0.263 [#]
Underweight, n (%)	1 (2.5)	3 (7.5)	
Overweight, n (%)	4 (10.3)	35 (89.7)	
Obese, n (%)	1 (6.7)	14 (93.3)	
Hypertension			
Yes, n (%)	7 (10.8)	58 (89.2)	0.385 ^Ω
No, n (%)	8 (16.3)	41 (83.7)	
Diabetes mellitus			
Yes, n (%)	9 (21.4)	33 (78.6)	0.046 ^{Ω*ϕ}
No, n (%)	6 (8.3)	66 (91.7)	
Hyperuricemia			
Yes, n (%)	4 (12.9)	27 (87.1)	1,000 [^]
No, n (%)	9 (11.4)	70 (88.6)	
Dyslipidemia			
Yes, n (%)	13 (12.3)	93 (87.8)	1,000 [^]
No, n (%)	0 (0)	4 (100)	
AMI			
STEMI, n (%)	10 (11.4)	78 (88.6)	0.327 [^]
NSTEMI, n (%)	5 (19.2)	21 (80.8)	
PCI			
Yes, n (%)	7 (8.8)	73 (91.3)	0.065 ^{^ϕ}
No, n (%)	8 (23.5)	26 (76.5)	

^ΩIndependent T Test, [¶]Mann Witney Test, [#]Linear-by-Linear Association Test, [^]Fisher's Exact Test, ^ϕPearson Chi-Square Test, *Statistically significant, ^ϕEnter the multivariate test.

SV, stroke volume; SVI, stroke volume index; CO, cardiac output; LAVI, left atrial volume index; LVVI, left ventricular volume index; ePCWP, estimated pulmonary capillary wedge pressure. p values refer to the difference between one and any of the remaining three groups

TABLE 6: Distribution of Cardiovascular Mortality Based on Echocardiographic Characteristics of Research Subjects.

Variable	Cardiovascular Mortality		p
	Yes	No	
eKillip Class			
I, n (%)	0 (0)	25 (100)	0.004 ^{#*ϕ}
II, n (%)	1 (5)	19 (95)	
III, n (%)	5 (16.7)	25 (83.3)	
IV, n (%)	9 (23.1)	30 (76.9)	
SV, mean±SD (mL)			
Low, n (%)	47.9±14.9	55.4±19.1	0.151 ^μ
Normal, n (%)	7 (16.3)	36 (83.7)	
SVI, mean±SD (mL/m²)			
Low, n (%)	27.7±8.9	31.3±10.4	0.207 ^μ
Normal, n (%)	10 (15.2)	56 (84.8)	
CO, median (L/min)			
Low, n (%)	4.2 (1.7-8.1)	4.1 (1.6-11.1)	0.980 [¶]
Normal, n (%)	6 (11.3)	47 (88.7)	
LAVI, median (mL/m²)			
Increased, n (%)	4.2 (1.7-8.1)	4.1 (1.6-11.1)	0.927 [¶]
Normal, n (%)	5 (12.8)	34 (87.2)	
LVVI, median (mL/m²)			
Increased, n (%)	23.9 (12-52.8)	26.7 (6.5-63.9)	0.939 ^Ω
Normal, n (%)	5 (12.8)	34 (87.2)	
LVVI, median (mL/m²)			
Increased, n (%)	53 (26.2-87)	51.3 (17.3-259.7)	0.438 [¶]
Normal, n (%)	5 (18.5)	22 (81.5)	
ePCWP, median (mmHg)			
High, n (%)	27.2 (15.5-46.8)	19.8 (8.5-45.3)	0.002 ^{¶*}
Normal, n (%)	15 (16.3)	77 (83.7)	
ePCWP, median (mmHg)			
High, n (%)	15 (16.3)	77 (83.7)	0.072 [^]
Normal, n (%)	0 (0)	22 (100)	

Variable	Cardiovascular Mortality		p
	Yes	No	
EF, mean±SD (%)	38.1±11.1	44.1±10.5	0.045 ^{u*}
Normal, n (%)	4 (12.5)	28 (87.5)	0.304 [#]
Mildly reduced, n (%)	3 (7.1)	39 (92.9)	
Reduced, n (%)	8 (20)	32 (80)	
Degree of diastolic function			
Normal, n (%)	1 (7.1)	13 (92.9)	0.007 ^{#*}
Decreased grade I, n (%)	1 (2.9)	34 (97.1)	
Decreased grade II, n (%)	6 (13.3)	39 (86.7)	
Decreased grade III, n (%)	6 (42.9)	8 (57.1)	
Indeterminate, n (%)	1 (16.7)	5 (83.3)	
E/e' average, median	20.4 (10.9-36.2)	14.3 (5.3-35)	0.002 ^{†*}
High, n (%)	13 (18.3)	58 (81.7)	0.037 ^{Ω*}
Normal, n (%)	2 (4.7)	41 (95.3)	
E/A Ratio, median	1.8 (0.8-3.3)	1.1 (0.4-4.3)	0.001 ^{†*}
Normal, n (%)	8 (10.8)	66 (89.2)	0.007 ^{#*}
Low, n (%)	0 (0)	26 (100)	
High, n (%)	7 (50)	7 (50)	

^uIndependent T Test, [†]Mann Witney Test, [#]Linear-by-Linear Association Test, [^]Fisher's Exact Test, ^ΩPearson Chi-Square Test, *Statistically significant, ^φEnter the multivariate test.

SV, stroke volume; SVI, stroke volume index; CO, cardiac output; LAVI, left atrial volume index; LVVI, left ventricular volume index; ePCWP, estimated pulmonary capillary wedge pressure.

p values refer to the difference between one and any of the remaining three groups.

Of the 114 patients, 39 patients were in the eKillip Class IV category and 75 patients were in the non-eKillip Class IV (eKillip Class I-III) category. Among the patients who experienced cardiovascular rehospitalization, there were 13 patients with eKillip Class IV and 9 patients with non-eKillip Class IV. The descriptive Kaplan-Meier curve depicted in Figure 1 shows that AMI patients with eKillip class IV had a higher risk of cardiovascular rehospitalization event. Based on Table 7, the 30 days survival rate for

cardiovascular rehospitalization in eKillip Class IV patients was 66.7% and the mean survival time was 24.7 days (95% CI = 21.9–27.6), while the 30 days survival rate in patients with non-eKillip Class IV was 88% and the mean survival time was 27.9 days (95% CI = 26.4–29.4). Log-rank test showed that there was a significant difference in the cardiovascular rehospitalization survival rate of eKillip Class IV than non-eKillip Class IV patients, with a value of p = 0.001.

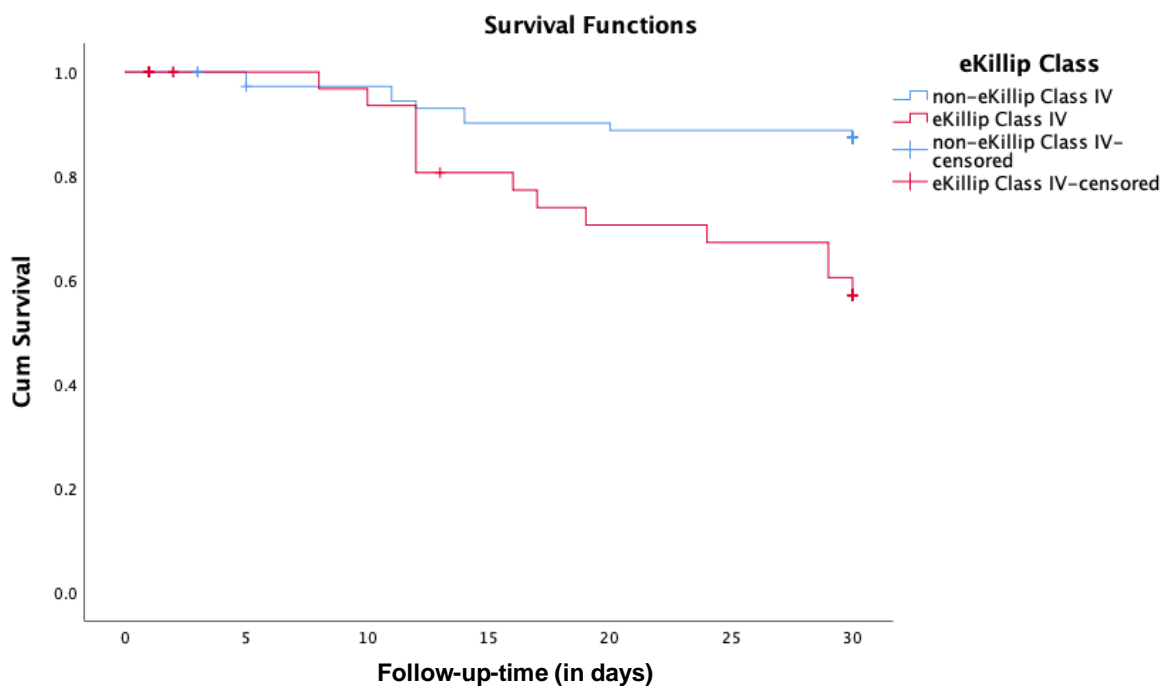


FIGURE 1: Kaplan Meier Survival Estimation Curve of Cardiovascular Rehospitalization based on the eKillip Class Category.

TABLE 7: Mean Survival Time and 30 Days Survival Rate for Cardiovascular Rehospitalization based on the eKillip Class Category.

Variable	Mean Time Survival (day)	CI (95%)	30 Days Survival Rate (%)	p
eKillip Class IV	24.7	21.9-27.6	66.7	0.001*
non-eKillip Class IV	27.9	26.4-29.4	88.0	

*Statistically significant.

Whereas, among the patients who underwent cardiovascular mortality, there were 9 patients with eKillip Class IV and 6 patients with non-eKillip Class IV. The descriptive Kaplan-Meier curve depicted in Figure 2 shows that AMI patients with eKillip class IV had a higher risk of cardiovascular mortality event. Based on Table 8, the 30 days survival rate for cardiovascular mortality in eKillip Class IV patients

was 76.9% and the mean survival time was 23.7 days (95% CI = 19.9–27.3), while the 30 days survival rate of patients with non-eKillip Class IV is 92% and the mean survival time is 27.8 days (95% CI =26.2-29.5). Log-rank test showed that there was a significant difference in the survival rate of cardiovascular mortality in eKillip Class IV than non-eKillip Class IV, with a value of $p = 0.019$.

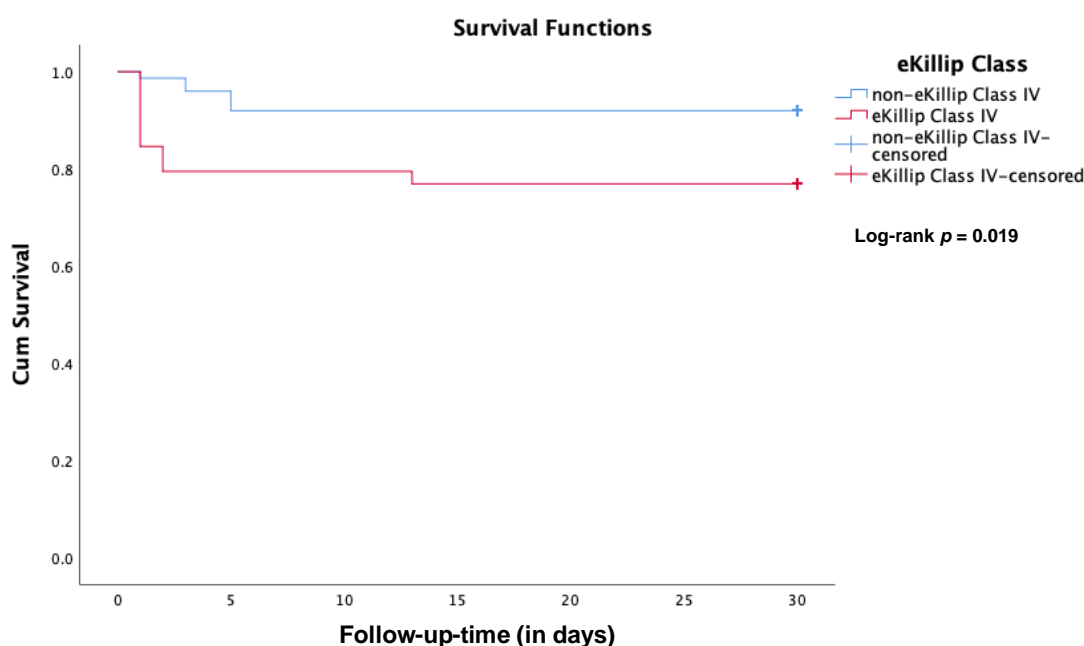


FIGURE 2: Kaplan Meier Survival Estimation Curve of Cardiovascular Mortality based on the eKillip Class Category.

TABLE 8: Mean Survival Time and 30 Days Survival Rate for Cardiovascular Mortality based on the eKillip Class Category.

Variable	Mean Time Survival (day)	CI (95%)	30 Days Survival Rate (%)	p
eKillip Class IV	23.7	19.9-27.3	76.9	0.019*
non-eKillip Class IV	27.8	26.2-29.5	92.0	

* Statistically significant.

The incidence of cardiovascular rehospitalization in AMI patients with eKillip Class IV was significantly higher compared with AMI patients with non-eKillip Class IV (unadjusted HR 3.8; 95% CI 1.6–8.9; $p = 0.002$). After adjusting with confounding factors, eKillip class IV remained significant compared with non-eKillip Class IV for cardiovascular rehospitalization within 30 days (adjusted HR 3.7; 95% CI 1.6–8.6; $p = 0.003$), based on Table 9.

This shows that cardiovascular rehospitalization within 30 days in AMI patients with eKillip Class IV after controlling for confounding factors is almost four times higher than in patients with non-eKillip Class IV. However, not only eKillip Class IV, high left ventricular volume index (LVVI) has also been proven to remain independently associated with the incidence of cardiovascular rehospitalization (adjusted HR 4.2; 95% CI 1.8–9.7; $p = 0.001$).

TABLE 9: Multivariate Cox Regression analysis of cardiovascular rehospitalization using the Backward LR method (7 steps).

Variable	Unadjusted HR	IK 95%	p	Adjusted HR	IK 95%	p
eKillip Class IV	3.8	1.6-8.9	0.002*	3.7	1.6-8.6	0.003*
JK (female)	2.5	1.1-6.0	0.037*	1.3	0.4-4.1	0.666
Smoke	0.5	0.2-1.2	0.135	0.6	0.2-1.6	0.347
Hyperuricemia	2,4	1.0-5.6	0.041*	1.4	0.5-3.9	0.494
Hypertension	1.6	0.6-3.9	0.314	1.5	0.6-3.9	0.367
Diabetes mellitus	2.1	0.9-4.9	0.073	1.9	0.8-4.6	0.135
PCI	2.1	0.9-4.9	0.082	1.9	0.8-4.7	0.124
LVVI (increased)	4.1	1.7-9.4	0.001*	4.2	1.8-9.7	0.001*

*Statistically significant.

Based on Table 10, eKillip Class IV was also an independent predictor of cardiovascular mortality within 30 days in AMI patients (adjusted HR 3.5; 95% CI 1.2-9.9; $p = 0.018$). This means that cardiovascular mortality in AMI patients with eKillip Class IV within 30 days after controlling for

confounding factors is 3.5 times higher than in patients with non-eKillip Class IV. However, not only eKillip Class IV, elderly age has also been proven to remain independently associated with cardiovascular mortality (adjusted HR 4.9; 95% CI 1.6-15.6; $p = 0.006$).

TABLE 10: Multivariate Cox Regression analysis of cardiovascular mortality using the Backward LR method (4 steps).

Variable	Unadjusted HR	IK 95%	p	Adjusted HR	IK 95%	p
eKillip Class IV	3,2	1.1-8.9	0.028*	3.5	1.2-9.9	0.018*
Age (elderly)	4.6	1.4-14.3	0.009*	4.9	1.6-15.6	0.006*
Smoke	0.4	0.1-1.3	0.133	0.7	0.2-2.1	0.481
Diabetes mellitus	2.7	0.9-7.6	0.060	1.6	0.5-4.9	0.435
PCI (no)	2.9	1.1-8.2	0.036*	2.1	0.7-5.8	0.171

* Statistically significant.

DISCUSSION

Several AMI stratification systems have been widely applied in daily practice, one of which is the Killip classification. The rationale for this classification lies in the combined assessment of diastolic and systolic function of the left heart. However, the Killip classification is quite subjective because the main basis is a physical examination [8]. Relying on the same logic, echocardiography to assess both of these functions and combine them in the eKillip Class should provide more objective data.

This study evaluates the eKillip Class as a predictor of major cardiovascular events (MACE), especially cardiovascular rehospitalization and mortality in AMI patients. An important finding from this study is that a high eKillip class is a predictor of MACE in patients with AMI. It is hypothesized that the results of this study will be able to provide additional information to support the clinical judgment of a cardiologist.

This study involved 114 patients. eKillip Class IV was present in 39 patients (34.3%), while 25 (21.9%), 20 (17.5%), and 30 (26.3%) patients were in eKillip Classes I to III, respectively. This finding is quite different from the previous eKillip Class study, which found eKillip Class IV was only 7% of the total sample [6]. This is due to the different types of populations, which all patients

underwent echocardiography without looking at the underlying disease, whereas this study specifically uses patients with acute myocardial infarction, which essentially causes hemodynamic changes ranging from mild to threatening [14]. Thus, many AMI patients fall into the higher category.

A similar study on combined hemodynamic assessment via echocardiography conducted in 2017 by Abbas et al said that dividing patients with heart failure based solely on ejection fraction (EF) may oversimplify the hemodynamic state of these patients. They subdivided these patients into four hemodynamic groups based on echocardiographic SVI ($<$ or ≥ 35 mL/m²) and E/E' (\geq or $<$ 15), including group A (normal flow and normal filling pressure), group B (normal flow but high filling pressure), group C (low flow and low filling pressure), and group D (low flow and high filling pressure). It was found that patients with HFrEF mostly had a group D hemodynamic classification profile, whereas patients with HFpEF had varying hemodynamic classification profiles [15]. A study by Donato Mele et al in 2020 regarding combined hemodynamic echocardiography and mortality showed that the group of patients with a poor combined hemodynamic echocardiography profile (low flow with RV dysfunction) was associated with a worse heart failure profile and had a significantly lower survival rate [16].

There is also an invasive combined hemodynamic classification model, which is also an adaptation of the Killip classification model, the Diamond Forrester classification with the use of pulmonary capillary wedge pressure (PCWP) and cardiac index (CI) of 18 mmHg and 2.2 L/m², respectively. In the Diamond Forrester classification, patients are grouped into four groups: low PCWP (< 18 mmHg) with normal CI (> 2.2 L/m²), high PCWP (> 18 mmHg) with normal CI (> 2.2 L/m²), low PCWP (< 18 mmHg) with low CI (< 2.2 L/m²), and high PCWP (> 18 mmHg) with low CI (< 2.2 L/m²). Hospital mortality in these groups ranged from 3% to 51% [17].

In this study, the average age of all participants was 58 ± 10.4 years, with 81.6% male. Based on the eKillip Class category, there is no significant difference in age and gender. A study by Ramteke et al in 2023 also obtained similar data, where of the total AMI sample, the average age was 58.2 ± 10.7 years, with 82.1% male [18]. Although the number of female patients with acute myocardial infarction is lower, a French study showed that from 74,389 patients hospitalized for acute myocardial infarction, female patients had a higher in-hospital mortality rate (14.8% compared with 6.1%; $p < 0.0001$) [19]. Another study with a similar population variation found that women with AMI in France were older on average (75 years compared with 63 years; $p < 0.001$). Female gender independently increased in-hospital mortality by nearly 7% in STEMI cases but was associated with reduced mortality in NSTEMI cases [20]. However, there are also studies that do not show any differences in hospital mortality related to gender. In a nationwide cohort study of AMI patients in Poland, the female gender did not increase in-hospital mortality with an OR of 0.97 [21].

Analysis of several classic AMI comorbidities in this study showed that hypertension was the most common comorbid disease (57%), followed by diabetes mellitus (36.7%) and high LDL levels. Comorbidities are common and have a major negative impact on the prognosis of patients with acute myocardial infarction. A study by Junxing Lv et al in 2021 stated that patients with AMI tend to have a medical history of hyperlipidemia [22]. In a study conducted by Yadegarfar et al, 412,809 acute myocardial infarction patients had at least one comorbidity, including hypertension (302,388 [48.7%]), diabetes mellitus (122,228 [19.4%]), chronic obstructive pulmonary disease (89,221 [14.9%]), cerebrovascular disease (51,883 [8.6%]), chronic heart failure (33,813 [5.6%]), chronic renal failure (31,029 [5.0%]), and peripheral vessel disease (27,627 [4.6%]) [23].

In this study, during 30 days of follow-up, 19.3% experienced cardiovascular rehospitalization, and 13.2% experienced cardiovascular mortality. These two major cardiovascular events showed a significant relationship with the eKillip Class. eKillip Class IV was analyzed as an independent predictor of cardiovascular rehospitalization and mortality in

patients with AMI. The 30-day survival rate of cardiovascular rehospitalization and mortality in patients with eKillip Class IV were significantly lower than in patients with non-eKillip Class IV, with a shorter average survival time.

Theoretically, eKillip Class IV is a combination of low SVI and high diastolic pressure. This is equivalent to cardiogenic shock and significant cardiovascular dysfunction, which is the most severe condition of acute heart failure. Cardiogenic shock is caused by a severe reduction in myocardial performance, resulting in reduced cardiac output, end-organ hypoperfusion, and hypoxia [24, 25]. Vahdatpour et al from the AHA article also stated that the main cause of cardiogenic shock in AMI is a decrease in myocardial contractility, which results in reduced cardiac output, hypotension, systemic vasoconstriction, and cardiac ischemia, where the characteristic features are peripheral vasoconstriction and damage to vital end organs, which is caused by ineffective stroke volume and insufficient circulation compensation. Compensatory peripheral vasoconstriction may initially improve coronary and peripheral perfusion, but it contributes to increased cardiac afterload that overloads the damaged myocardium. So oxygenated blood flow is reduced to peripheral tissues and, ultimately, to the heart [25]. Myocardial diastolic function is also impaired in cardiogenic shock, where myocardial ischemia causes decreased compliance and increased left ventricular filling pressure. In addition, the compensatory increase in left ventricular volume to meet stroke volume ultimately increases filling pressure. Clinically, this condition will cause pulmonary edema and hypoxia [25, 26].

Patients with AMI, both STEMI and NSTEMI, are the conditions that contribute to the highest incidence of cardiogenic shock, up to 81%. However, this does not mean that patients with AMI will develop cardiogenic shock; in prevalence, the percentage of AMI patients experiencing cardiogenic shock complications is around 5% to 10%. The incidence of rehospitalization within 30 days after AMI is 18.6% with a median of 10 days, where patients with STEMI are slightly lower than those with NSTEMI [25, 27, 28].

After an acute myocardial infarction, myocardial ischemia, cell necrosis, microvascular dysfunction, and regional wall motion abnormalities occur that affect the rate of active relaxation. In addition, interstitial edema, fibrocellular infiltration, and scar tissue formation will directly influence left ventricular (LV) stiffness. Therefore, abnormalities in LV filling are common in this condition. LV pressure load will cause myocyte stretching, increased wall stress, poor subendocardial perfusion, and reduced energy production. This is then related to neurohormonal activation and ventricular remodelling. Although the remodelling process will initially restore ejection volume and systemic hemodynamics, continued dilatation will have detrimental effects on long-term LV function and survival. Ventricular remodelling and hyperactivity of the renin-angiotensin-aldosterone system (RAAS) likely contribute to excess mortality in

these patients [29]. AMI also plays a role in systemic inflammation that causes pathological vasodilation, releasing nitric oxide synthase and peroxynitrite, which have cardiotoxic inotropic effects. Interleukins and tumor necrosis factor- α (TNF- α) are additional systemic inflammatory mediators that cause vasodilation and contribute to death in AMI patients with cardiogenic shock [25].

At normal physiological pressure, the right ventricular stroke volume and the left ventricular stroke volume are the same. Right ventricular failure (RVF) occurs when ventricular diastolic and/or systolic pressures are not sufficiently compensated by normal myocardial adaptive processes to produce an appropriate stroke volume. Inadequate blood flow in the compromised right ventricle (RV) causes end-organ perfusion deficits along with increased venous pressure. The RV is less adaptive to afterload pressure and more tolerant of volume overload than the left ventricle (LV), which explains the inability of the right ventricle to tolerate very high increases in pulmonary artery pressure. When RVF results in RV dilatation, the interventricular septum migrates into the left ventricular chamber, impairing LV diastolic filling and further exacerbating systemic hypoperfusion, thereby increasing the risk of mortality [25].

In general, morbidity after acute myocardial infarction is not only expensive but can also impact the patient's quality of life. A study conducted by Arnold et al estimated the rates of rehospitalization due to AMI and revascularization after acute myocardial infarction to be 6.8% and 4.1%, respectively [30]. Based on research from Kwok CS et al in 2017 which evaluated rehospitalization within 30 days after AMI, of the total post-AMI patients, 9% of patients experienced rehospitalization, of which around 17.1% of patients experienced AMI recurrence, 11.6% of patients experienced stable angina, and 9.8% experienced failure of heart [31]. In another similar study by Kim LK et al (2018), of all STEMI patients who were hospitalized based on data from the Nationwide Readmissions Database (NRD) from 2010 to 2014, within 7 days and 30 days after hospitalization, 43.9% and 12.3% of patients experienced rehospitalization, either in the form of recurrent AMI or acute heart failure. Post-AMI rehospitalization also poses a huge economic burden to the country's health system, with rehospitalization within 30 days said to result in a 50% increase in cumulative inpatient costs. Moreover, AMI patients with cardiogenic shock will have a higher level of burden. They also reported that the incidence of mortality in patients with AMI occurs at approximately 8.7% (95% CI, 8.6–8.8), 4.6% (95% CI, 4.5–4.7), 5.4% (95% CI, 5.2–5.7), and 25.1% (95% CI, 24.9–25.3) for overall patients, patients with PCI, patients with CABG, and patients without revascularization, respectively, with a p -value < 0.001 [32].

Thus, risk stratification of AMI patients is very important as a basis for decision-making, using the eKillip Class assessment as a useful tool to identify

high risk patients and guide more intensive clinical management.

In this study, besides eKillip Class IV, high LVVI and elderly age in patients with AMI were also an independent predictor of cardiovascular rehospitalization and mortality, respectively.

The left ventricular volume index (LVVI) or left ventricular end diastolic volume index (LVEDVI), is an echocardiographic parameter to assess the size and volume of the left ventricle. According to the 2015 ASE/EACVI heart chamber quantification guidelines and standards, the normal range for left ventricular volume based on BSA is 54 ± 10 mL/m² (2-SD range: 34-74 mL/m²) in men and 45 ± 10 mL/m² (2-SD range: 29-61 mL/m²) in women [41]. High LVVI is related to the process of ventricular remodelling after myocardial infarction, which is a common cause of heart failure [33]. Left ventricular remodelling due to acute myocardial infarction is a type of pathological remodelling process [34, 35]. Adverse remodelling of the left ventricle is a maladaptive process caused by cardiac injury characterized by morphological changes in LV shape and structure, with subsequent changes to cardiac function [33]. Adverse remodelling after myocardial infarction is defined as a complex interaction between cellular and extracellular components of the myocardium, where neurohormonal and epigenetic regulation causes changes in cardiac architecture and geometry that affect both atrial and ventricular [36]. Even with revascularization, injuries caused by myocardial ischemia can still cause adverse left ventricular remodelling, which can then progress to heart failure [37]. Another previous study by Kazato Ito et al in 2021 also showed a similar result, where left ventricular dilation was an independent predictor of cardiovascular events [38].

Age is often associated with abnormalities in the body's organs, including the cardiovascular system. The physiological changes of aging are closely related to the pathophysiology of cardiovascular disease, and comorbid conditions often complicate clinical management. As a result of complex molecular and cellular aging processes over decades, cardiovascular physiology in older adults is characterized by: (1) endothelial dysfunction; (2) increased arterial stiffness; (3) increased left ventricular stiffness; (4) altered function and coupling of the left ventricle and arterial stiffness; (5) weakening of the baroreflex and autonomic reflexes; and (6) degenerative changes in the conduction system [39]. Cardiovascular aging is a complex process of adaptive structural and functional changes over time. With increasing age, the elasticity and compliance of the arteries begin to thicken and decrease, resulting in an increase in pulse wave velocity, systolic blood pressure, and left ventricular afterload. In response to these arterial changes, the myocardium remodels to maintain systolic function and diastolic filling. This adaptive mechanism is not always pathological but increases susceptibility to myocardial ischemia and heart failure [40].

Thus, advanced age is an important risk factor for cardiovascular disease and is a strong independent predictor of cardiovascular morbidity, mortality, and disability [39].

There is a limitation to the present study. This study did not analyze other confounding factors, such as mechanical complications, malignant arrhythmias, vascular disease, stroke, and psychosocial disorders, which are theoretically related to outcomes, because the data are not yet available, so they cannot be measured to be taken into analysis.

CONCLUSION

The eKillip Class defined by the combined echocardiographic assessment of left filling pressure and SVI, was an independent predictor of cardiovascular rehospitalization and mortality in patients with acute myocardial infarction. AMI patients with eKillip Class IV had a poorer prognosis and higher risk for cardiovascular rehospitalization and mortality compared with patients with non-eKillip Class IV.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest related to the publication of this research article.

FUNDING

This research did not receive funding from the government or other private sectors.

ETHICS IN RESEARCH

This research has received approval from the research ethics committee of Prof. dr. I.G.N.G. Ngoerah Hospital/Faculty of Medicine, Udayana University.

REFERENCES

- [1] Liu Y, Feng D-J, Wang L-F, Liu L-H, Ren Z-H, Hao J-Y, et al. The Impact of Cardiac Dysfunction Based on Killip Classification on Gastrointestinal Bleeding in Acute Myocardial Infarction. *Front Med (Lausanne)* 2022;9. <https://doi.org/10.3389/fmed.2022.865663>.
- [2] Brener MI, Rosenblum HR, Burkhoff D. Pathophysiology and Advanced Hemodynamic Assessment of Cardiogenic Shock. *Methodist Debakey Cardiovasc J* 2020;16:7. <https://doi.org/10.14797/mdcj-16-1-7>.
- [3] Josiassen J, Lerche Helgestad OK, Møller JE, Kjaergaard J, Hoejgaard HF, Schmidt H, et al. Hemodynamic and metabolic recovery in acute myocardial infarction-related cardiogenic shock is more rapid among patients presenting with out-of-hospital cardiac arrest. *PLoS One* 2020;15:e0244294. <https://doi.org/10.1371/journal.pone.0244294>.
- [4] Wang J, Tan GJ, Han LN, Bai YY, He M, Liu H bin. Novel biomarkers for cardiovascular risk prediction. *Journal of Geriatric Cardiology* 2017;14:135–50. <https://doi.org/10.11909/j.issn.1671-5411.2017.02.008>.
- [5] Yucel O, Gul I, Zararsiz A, Demirpence O, Yucel H, Cinar Z, et al. Association of soluble ST2 with functional capacity in outpatients with heart failure. *Herz* 2018;43:455–60. <https://doi.org/10.1007/s00059-017-4590-1>.
- [6] Milwidsky A, Greidinger D, Frydman S, Hochstadt A, Ifrach-Kashtan N, Mizrachi M, et al. Echocardiographic Killip Classification. *Journal of the American Society of Echocardiography* 2022;35:287–94. <https://doi.org/10.1016/j.echo.2021.10.012>.
- [7] Hashmi KA, Adnan F, Ahmed O, Yaqeen SR, Ali J, Irfan M, et al. Risk Assessment of Patients After ST-Segment Elevation Myocardial Infarction by Killip Classification: An Institutional Experience. *Cureus* 2020. <https://doi.org/10.7759/cureus.12209>.
- [8] Del Buono MG, Montone RA, Rinaldi R, Gurgoglione FL, Meucci MC, Camilli M, et al. Clinical predictors and prognostic role of high Killip class in patients with a first episode of anterior ST-segment elevation acute myocardial infarction. *Journal of Cardiovascular Medicine* 2021. <https://doi.org/10.2459/JCM.0000000000001168>.
- [9] Mechanic, O. J., Gavin, M., Grossman, S. A. (2022). Acute Myocardial Infarction. *StatPearls*. Available at <https://www.ncbi.nlm.nih.gov/books/NBK459269>.
- [10] Cao H, Li Y, Zhao Y, Xiong T, Liu Z, Zheng T, et al. Hemodynamic Characteristics of Patients with Suspected Coronary Heart Disease at Their Initial Visit. *Front Physiol* 2021;12. <https://doi.org/10.3389/fphys.2021.714438>.
- [11] 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;39:119–77. <https://doi.org/10.1093/eurheartj/ehx393>.
- [12] Sia YT, O'Meara E, Ducharme A. Role of echocardiography in acute myocardial infarction. *Curr Heart Fail Rep* 2008;5:189–96. <https://doi.org/10.1007/s11897-008-0029-6>.
- [13] Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, et al. 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J* 2021;42:1289–367. <https://doi.org/10.1093/eurheartj/ehaa575>.

- [14] Han M-M, Zhao W-S, Wang X, He S, Xu X-R, Dang C-J, et al. Echocardiographic Parameters Predict Short- and Long-Term Adverse Cardiovascular Events in Patients with Acute Myocardial Infarction. *Int J Gen Med* 2021;Volume 14:2297–303. <https://doi.org/10.2147/IJGM.S304449>.
- [15] Abbas AE, Khoury Abdulla R, Aggrawal A, Crile J, Lester SJ, Boura J. A novel echocardiographic hemodynamic classification of heart failure based on stroke volume index and left atrial pressure. *Echocardiography* 2017;34:1417–25. <https://doi.org/10.1111/echo.13642>.
- [16] Mele D, Pestelli G, Dini FL, Dal Molin D, Smarrazzo V, Trevisan F, et al. Novel Echocardiographic Approach to Hemodynamic Phenotypes Predicts Outcome of Patients Hospitalized with Heart Failure. *Circ Cardiovasc Imaging* 2020;13. <https://doi.org/10.1161/CIRCIMAGING.119.009939>.
- [17] Abbas AE, Khoury Abdulla R, Aggrawal A, Crile J, Lester SJ, Boura J. A novel echocardiographic hemodynamic classification of heart failure based on stroke volume index and left atrial pressure. *Echocardiography* 2017;34:1417–25. <https://doi.org/10.1111/echo.13642>.
- [18] Ramteke S, Kumar V, Kumar D, Gupta M. Echocardiography for Volume Assessment in Acute Myocardial Infarction. *Cureus* 2023. <https://doi.org/10.7759/cureus.47946>.
- [19] Milcent C, Dormont B, Durand-Zaleski I, Steg PG. Gender Differences in Hospital Mortality and Use of Percutaneous Coronary Intervention in Acute Myocardial Infarction. *Circulation* 2007;115:833–9. <https://doi.org/10.1161/CIRCULATIONAHA.106.664979>.
- [20] Kuehnemund L, Koeppe J, Feld J, Wiederhold A, Illner J, Makowski L, et al. Gender differences in acute myocardial infarction—A nationwide German real-life analysis from 2014 to 2017. *Clin Cardiol* 2021;44:890–8. <https://doi.org/10.1002/clc.23662>.
- [21] Gierlotka M, Zdrojewski T, Wojtyniak B, Poloński L, Stokwiszewski J, Gąsior M, et al. Incidence, treatment, in-hospital mortality and one-year outcomes of acute myocardial infarction in Poland in 2009–2012 — nationwide AMI-PL database. *Kardiologia i Pol* 2015;73:142–58. <https://doi.org/10.5603/KP.a2014.0213>.
- [22] Lv J, Ni L, Liu K, Gao X, Yang J, Zhang X, et al. Clinical Characteristics, Prognosis, and Gender Disparities in Young Patients with Acute Myocardial Infarction. *Front Cardiovasc Med* 2021;8:1–12. <https://doi.org/10.3389/fcvm.2021.720378>.
- [23] Yadegarfar ME, Gale CP, Dondo TB, Wilkinson CG, Cowie MR, Hall M. Association of treatments for acute myocardial infarction and survival for seven common comorbidity states: A nationwide cohort study. *BMC Med* 2020;18:1–12. <https://doi.org/10.1186/s12916-020-01689-5>.
- [24] Backer D De, Giglioli S. Echocardiographic approach to shock. *Journal of Emergency and Critical Care Medicine* 2019;3:35–35. <https://doi.org/10.21037/jeccm.2019.07.06>.
- [25] Vahdatpour C, Collins D, Goldberg S. Cardiogenic Shock. *J Am Heart Assoc* 2019;8. <https://doi.org/10.1161/JAHA.119.011991>.
- [26] Hollenberg SM, Kavinsky CJ, Parrillo JE. Cardiogenic Shock. *Ann Intern Med* 1999;131:47. <https://doi.org/10.7326/0003-4819-131-1-199907060-00010>.
- [27] Shah M, Patil S, Patel B, Agarwal M, Davila CD, Garg L, et al. Causes and Predictors of 30-Day Readmission in Patients with Acute Myocardial Infarction and Cardiogenic Shock. *Circ Heart Fail* 2018;11. <https://doi.org/10.1161/CIRCHEARTFAILURE.117.004310>.
- [28] Reynolds HR, Hochman JS. Cardiogenic Shock. *Circulation* 2008;117:686–97. <https://doi.org/10.1161/CIRCULATIONAHA.106.613596>.
- [29] Møller JE, Pellikka PA, Hillis GS, Oh JK. Prognostic importance of diastolic function and filling pressure in patients with acute myocardial infarction. *Circulation* 2006;114:438–44. <https://doi.org/10.1161/CIRCULATIONAHA.105.601005>.
- [30] Arnold S V., Smolderen KG, Kennedy KF, Li Y, Shore S, Stolker JM, et al. Risk factors for rehospitalization for acute coronary syndromes and unplanned revascularization following acute myocardial infarction. *J Am Heart Assoc* 2015;4:1–9. <https://doi.org/10.1161/JAHA.114.001352>.
- [31] Kwok AC, Agarwal JP. An analysis of free flap failure using the ACS NSQIP database. Does flap site and flap type matter? *Microsurgery* 2017;37:531–8. <https://doi.org/10.1002/micr.30121>.
- [32] Kim LK, Yeo I, Cheung JW, Swaminathan R V., Wong SC, Charitakis K, et al. Thirty-Day Readmission Rates, Timing, Causes, and Costs after ST-Segment-Elevation Myocardial Infarction in the United States: A National Readmission Database Analysis 2010–2014. *J Am Heart Assoc* 2018;7. <https://doi.org/10.1161/JAHA.118.009863>.

- [33] Leancă SA, Crișu D, Petriș AO, Afrăsânie I, Genes A, Costache AD, et al. Left Ventricular Remodeling after Myocardial Infarction: From Physiopathology to Treatment. *Life* 2022;12:1111. <https://doi.org/10.3390/life12081111>.
- [34] Fortuni F, Crimi G, Angelini F, Leonardi S, D'Ascenzo F, Ferlini M, et al. Early Complete Revascularization in Hemodynamically Stable Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease. *Canadian Journal of Cardiology* 2019;35:1047-57. <https://doi.org/10.1016/j.cjca.2019.03.006>.
- [35] Sutton MGStJ, Sharpe N. Left Ventricular Remodeling After Myocardial Infarction. *Circulation* 2000;101:2981-8. <https://doi.org/10.1161/01.CIR.101.25.2981>.
- [36] Berezin AE, Berezin AA. Adverse Cardiac Remodelling after Acute Myocardial Infarction: Old and New Biomarkers. *Dis Markers* 2020;2020:1-21. <https://doi.org/10.1155/2020/1215802>.
- [37] van der Bijl P, Abou R, Goedemans L, Gersh BJ, Holmes DR, Ajmone Marsan N, et al. Left Ventricular Post-Infarct Remodeling. *JACC Heart Fail* 2020;8:131-40. <https://doi.org/10.1016/j.jchf.2019.08.014>.
- [38] Ito K, Li S, Homma S, Thompson JLP, Buchsbaum R, Matsumoto K, et al. Left ventricular dimensions and cardiovascular outcomes in systolic heart failure: the WARCEF trial. *ESC Heart Fail* 2021;8:4997-5009. <https://doi.org/10.1002/ehf2.13560>.
- [39] Dai X, Hummel SL, Salazar JB, Taffet GE, Zieman S, Schwartz JB. Cardiovascular physiology in the older adults. *J Geriatr Cardiol* 2015;12:196-201. <https://doi.org/10.11909/j.issn.1671-5411.2015.03.015>.
- [40] Singam, N.S.V., Fine, C., Fleg, J.L. (2019). Cardiac changes associated with vascular aging. *Clinical Cardiology*. 2020;43:92-98. DOI: 10.1002/clc.23313.