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RELATIONSHIP BETWEEN LEFT VENTRICULAR EJECTION FRACTION AND AGE WITH MAJOR CARDIOVASCULAR INCIDENCE IN NSTE-ACS PATIENTS

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Abstract
Cardiovascular diseases (CVDs) are the leading cause of mortality worldwide, with non-ST-elevation acute coronary syndrome (NSTE-ACS) significantly contributing to morbidity and mortality. Left ventricular ejection fraction (LVEF) and age are critical factors influencing major adverse cardiovascular events (MACE). However, limited research has examined their combined impact on NSTE-ACS patients. This study aims to analyze the relationship between LVEF and age with the incidence of MACE in NSTE-ACS patients at Prof. Dr. R. D. Kandou General Hospital, Manado, from January to December 2023. A retrospective cohort study was conducted using medical record data from NSTE-ACS patients. The study examined LVEF, age, and MACE incidence over six months using Chi-Square and Fisher's Exact tests. Among 85 patients meeting inclusion criteria, 42.35% experienced MACE. Patients with reduced LVEF had a significantly higher incidence of MACE than those with preserved LVEF. Older patients, particularly those in the 75–84 age group, exhibited a higher tendency for MACE. Statistical analysis confirmed a significant relationship between LVEF and MACE (p=0.006), while age showed a non-significant correlation (p>0.05). The findings highlight the importance of early LVEF assessment in NSTE-ACS patients to improve risk stratification and optimize management strategies. Future studies should explore interventions to mitigate age-related cardiovascular risks.

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INTRODUCTION

Cardiovascular diseases (CVDs) continue to be the leading cause of mortality worldwide, with ischemic heart disease (IHD) being one of the most significant contributors (WHO, 2024). The World Health Organization (WHO) estimates that CVDs are responsible for approximately 17.9 million deaths annually, accounting for 31% of all global deaths (Di Cesare et al., 2024). A significant portion of these deaths results from acute coronary syndromes (ACS), particularly myocardial infarctions, both ST-elevation myocardial infarctions (STEMI) and non-ST-elevation acute coronary syndromes (NSTE-ACS) (Khan et al., 2020).

The Global Burden of Disease study in 2021 further highlights that ischemic heart disease remains a primary contributor to mortality, with an estimated 9 million deaths per year

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(Naghavi et al., 2024). This burden is not evenly distributed across the globe, as socio-economic status, healthcare infrastructure, and access to preventive care significantly impact outcomes. In Indonesia, ischemic heart disease ranks as the second leading cause of death (IHME, 2021). Additionally, urban populations are disproportionately affected, with lifestyle changes and increasing prevalence of risk factors such as hypertension, diabetes, and obesity contributing to the growing incidence of CVD (Rokom, 2021).

Among various types of ischemic heart disease, non-ST-elevation acute coronary syndrome (NSTE-ACS) is a predominant concern due to its high morbidity and mortality. The American College of Cardiology (ACC) notes that NSTE-ACS comprises approximately 70% of all acute myocardial infarctions in the United States (ACC, 2024). In the United Kingdom, the Myocardial Ischaemia National Audit Project (MINAP) recorded that out of 81,735 heart attack patients in 2023, 52,470 had NSTE-ACS (MINAP, 2024). The British Journal of Cardiology also reports a rising prevalence of NSTE-ACS in older adults, demonstrating a direct correlation between aging and the incidence of this syndrome (Gale, 2017).

One of the most critical determinants of cardiovascular prognosis is the left ventricular ejection fraction (LVEF), a measure of the heart's pumping ability. Patients with reduced LVEF are at a significantly higher risk of developing major adverse cardiovascular events (MACE), including recurrent myocardial infarction, stroke, heart failure, and cardiovascular death (Gupta et al., 2018; García-Blas et al., 2021). Studies suggest that aging exacerbates the decline in LVEF, further increasing the risk of adverse outcomes (Houghton et al., 2016; NIH, 2024). However, while age and LVEF are independently associated with MACE, their combined impact on NSTE-ACS patients remains inadequately studied.

Given the increasing burden of NSTE-ACS and the significant role of LVEF in predicting cardiovascular outcomes, it is imperative to explore the relationship between these factors to improve patient prognosis. The urgency of this study is further underscored by the aging global population. By 2050, it is estimated that 16% of the world’s population will be over 65 years old, leading to a concurrent rise in age-related cardiovascular conditions (NIH, 2024). Moreover, reduced LVEF is often overlooked in the management of NSTE-ACS, despite its strong prognostic implications (Furtado et al., 2023). This study aims to bridge this knowledge gap by providing insights into the interplay between age, LVEF, and major cardiovascular incidents in NSTE-ACS patients.

Previous studies have highlighted the significance of LVEF as a predictor of long-term mortality in patients with acute coronary syndromes. Rosselló et al. (2017) found that patients with reduced LVEF had a higher likelihood of post-discharge mortality. Similarly, Siddiqui and Holzmann (2019) demonstrated that among elderly patients with NSTE-ACS, those with reduced LVEF had significantly higher long-term mortality rates. Another study by Hendrickson et al. (2022) found that in STEMI patients, LVEF below 30% was associated with increased hospital readmission and one-year mortality. Ferreira et al. (2021) further emphasized the importance of mid-range ejection fraction (LVEF 40-49%), which is often overlooked but carries an intermediate risk of MACE.

Additionally, age has been recognized as a major factor influencing cardiovascular outcomes. Aging is associated with structural and functional changes in the cardiovascular system, including arterial stiffening, endothelial dysfunction, and increased myocardial fibrosis (Sherwood, 2017; Lilly, 2021). These changes contribute to a decline in cardiac efficiency, exacerbating the impact of low LVEF. Studies have shown that older patients with ACS tend to have worse outcomes due to a higher prevalence of comorbidities and reduced physiological reserves (Okkonen et al., 2021; Lei et al., 2022).

Despite extensive research on the prognostic value of LVEF and the impact of aging on cardiovascular health, limited studies have specifically examined the combined effect of these factors on MACE incidence in NSTE-ACS patients. Previous research has predominantly focused on STEMI patients, leaving a gap in the literature regarding NSTE-ACS (Toliu et al., 2024). This study aims to provide a more comprehensive understanding of how age and LVEF together influence cardiovascular outcomes in this specific population.

Understanding the relationship between age, LVEF, and cardiovascular events is essential for optimizing treatment strategies in NSTE-ACS patients. Given the aging global population and the increasing burden of ischemic heart disease, this study seeks to address an important gap in cardiovascular research. The findings will contribute to better risk assessment models and potentially influence clinical guidelines for managing NSTE-ACS patients with varying LVEF levels and age profiles.

By integrating evidence from global epidemiological studies, cardiovascular disease burden reports, and clinical research on LVEF and aging, this study will provide valuable insights into the prognosis of NSTE-ACS patients. The results will aid in the development of targeted interventions to mitigate the risk of MACE and improve patient outcomes.

RESEARCH METHODS

This study is an observational analytic study with a **retrospective cohort design**, aiming to analyze the relationship between left ventricular ejection fraction and age with the incidence of major cardiovascular events in patients with **Acute Coronary Syndrome Non-Elevation ST Segment (NSTE-ACS)** at Prof. Dr. R. D. Kandou General Hospital, Manado. A quantitative approach was employed to process and analyze secondary data obtained from patient medical records.

The population in this study includes NSTE-ACS patients who experienced major cardiovascular events at Prof. Dr. R. D. Kandou General Hospital during the period of January–December 2023. The sample was selected using the **consecutive sampling** method, where subjects were chosen based on meeting the inclusion criteria, including patients diagnosed with NSTE-ACS and having complete data. Patients with incomplete data or lost to follow-up were excluded from the study.

Data were collected from patient medical records, which included information such as initials, age, gender, clinical diagnosis, left ventricular ejection fraction values, laboratory results, therapies administered, and the occurrence of major cardiovascular events over six months of observation. Data analysis was performed using the **Chi-Square test** and **Fisher's Exact test** to determine the relationship between left ventricular ejection fraction and age with

the incidence of major cardiovascular events. This research methodology is designed to provide a better understanding of the risk factors influencing major cardiovascular events, thereby serving as a foundation for more effective management of NSTE-ACS patients.

RESULTS AND DISCUSSION

Basic Characteristics of SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital

Based on the research conducted, it was found that the number of patients who experienced SKA-NSTE at Prof. Dr. R. D. Kandou Manado Hospital from January to December 2023 and met the inclusion criteria was 85 patients. Of the 85 patients, there were 36 patients (42.35%) who experienced major cardiovascular events and 49 patients (57.65%) who did not experience major cardiovascular events. The following are the characteristics of SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital from January to December 2023.

Table 1. Basic Characteristics of SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital

Basic Characteristics	MOH (n=36)	No KKM (n=49)	Total (n=85)	P value
***Demographic Characteristics**				
Age (*mean+SD*)	67,31+7,32	64,18+9,67	65,51+8,84	0,610**
Gender				0,080***
Man	26 (43,3%)	34 (56,7%)	60 (70,6%)	
Woman	10 (40%)	15 (60%)	25 (29,4%)	
***Age Category**				0,193**
Young Adult (<55 yrs)	1 (11,1%)	8 (88,9%)	9 (10,6%)	
Older Adult (55-64 yrs)	11 (45,8%)	13 (54,2%)	24 (28,2%)	
Old-Young (65-74 yrs)Old-	18 (43,9%)	23 (56,1%)	41 (48,2%)	
Medium (75-84 yrs)	6 (60,0%)	4 (40,0%)	10 (11,8%)	
Oldest (>85 yrs)	0 (0,0%)	1 (100%)	1 (1,2%)	
***Risk Factors for Coronary Heart Disease**				
Male >45 years old & female >55 years old	36 (43,4%)	47 (56,6%)	83 (97,6%)	0,506**
Male gender	26 (43,3%)	34 (56,7%)	60 (70,6%)	0,814***
Family History	0 (0,0%)	0 (0,0%)	0 (0,0%)	-
Early menopause	0 (0,0%)	0 (0,0%)	0 (0,0%)	-
Smoke	6 (37,5%)	10 (62,5%)	16 (18,8%)	0,782***
Hypertension	24 (28,2%)	39 (45,9%)	63 (74,1%)	0,215***
Dyslipidemia	11 (42,3%)	15 (57,7%)	26 (30,6%)	1.000***
Diabates Mellitus	17 (51,5%)	16 (48,5%)	33 (38,8%)	0,186***
***Laboratory Results**				
CK-MB				0,326***
Usual	12 (52,2%)	11 (47,8%)	23 (27,1%)	
Tall	24 (38,7%)	38 (61,3%)	62 (72,9%)	
Troponin T				1,000**

Usual	0 (0,0%)	0 (0,0%)	0 (0,0%)	
Tall	36 (42,4%)	49 (57,6%)	85 (100%)	
***Echocardiography* (*Left Ventricle Ejection Fraction*)**				**0,006****
***Reduced* LVEF**	23 (59%)	16 (41%)	39 (45,9%)	
***Mildly Reduced* LVEF**	8 (40%)	12 (60%)	20 (23,5%)	
***Preserved* LVEF**	5 (19,2%)	21 (80,8%)	26 (30,6%)	
***Revascularization Type**				0,077***
Non-Restructuring	20 (54,1%)	17 (45,9%)	37 (43,5%)	
Culprit Revascularization	16 (33,3%)	32 (66,7%)	48 (56,6%)	
Total Rescuralization	0 (0,0%)	0 (0,0%)	0 (0,0%)	
***Pharmacotherapy**				
Aspilet	27 (38%)	44 (62%)	71 (83,5%)	0,083***
Clopidogrel	34 (43%)	45(57%)	79 (92,9%)	1.000**
Statins	33 (40,7%)	48 (59,3%)	81 (95,3%)	0,307**
Nitrate	33 (44%)	42 (56%)	75 (88,2%)	0,507**
ß-Blocker	23 (39%)	36 (61%)	59 (69,4%)	0,475***
ACE/ARB	35 (43,2%)	46 (56,8%)	81 (95,3%)	0,262**
Aldosterone Antagonists	21 (53,8%)	18 (46,2%)	39 (45,9%)	0,660***

**: Fisher's *Exact Test*
: *Chi-Square Test*

Based on demographic characteristics, it was found that the average age of SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital for the January-December 2023 period was 65.51 years with the average for patients who experienced KKM was 67.31 years and the average for patients who did not experience KKM was 64.18 years. Male patients were obtained as many as 60 patients (70.6%), of which 26 patients (43.3%) experienced KKM and 34 (56.7%) did not experience KKM. Female patients were obtained as many as 25 patients (29.4%), of which 10 patients (40%) experienced KKM and 15 patients (60%) did not experience KKM.

Next, the categorization of patients based on age category, the young adult category there were 9 patients (10.6%), of which 1 patient (11.1%) experienced KKM and 8 patients (88.9%) did not experience KKM. In the elderly adult category, there were 24 patients (28.2%), of which 11 patients (45.8%) experienced KKM and 13 patients (54.2%) did not experience KKM. In the old-young category, there were 41 patients (48.2%), of which 18 patients (43.9%) experienced KKM and 23 patients (56.1%) did not experience KKM. In the elderly-medium category, there were 10 patients (11.8%), of which 6 patients (60%) experienced KKM and 4 patients (40%) did not experience KKM. Lastly, the oldest-oldest category has 1 patient (100%) and patients who do not experience KKM are not present (0.0%).

Based on CHD risk factors, male patients aged >45 years and female patients aged >55 years had 83 patients (97.6%), of which 36 patients (43.4%) experienced KKM and 47 patients (56.6%) did not experience KKM. There were 60 patients (70.6%) male, of which 26 patients (43.3%) experienced KKM and 34 (56.7%) did not experience KKM. There were no patients (0.0%) who had a family history and experienced early menopause. For modifiable risk factors, 16 patients (18.8%) had a history of smoking with 6 patients (37.5%) experiencing KKM and

10 patients (62.5%) not experiencing KKM. There were 63 patients (74.1%) who had a history of hypertension with 24 patients (28.2%) experiencing KKM and 39 patients (45.9%) not experiencing KKM. Patients with a history of dyslipidemia were found to be 26 patients (30.6%) with 11 patients (42.3%) experiencing KKM and 15 patients (57.7%) not experiencing KKM. Meanwhile, for patients with diabetes mellitus, there were 33 patients (38.8%) with 17 patients (51.5%) experiencing KKM and 16 patients (48.5%) not experiencing KKM.

From the research that has been conducted, SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital for the January-December 2023 period are divided into 23 patients with normal CK-MB levels (27.1%) and patients with high CK-MB levels as many as 62 patients (72.9%). From the group of patients with normal CK-MB levels, 12 patients (52.2%) experienced KKM and 11 patients (47.8%) did not experience KKM. Meanwhile, in the group of patients with high CK-MB levels, there were 24 patients (38.7%) who experienced KKM and 38 patients (61.3%) who did not experience KKM. In this study, no SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital for the January-December 2023 period had normal Troponin T values, but 36 patients (42.4%) with high Troponin T values experienced KKM and 49 patients (57.6%) did not experience KKM.

Based on the results of the *echocardiography* examination carried out, SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital during the period of January to December 2023 were classified into three categories, namely: patients with *reduced left ventricle ejection fraction, mildly reduced left ventricle ejection fraction*, and *preserved left ventricle ejection fraction*. The results showed that there were 39 patients (45.9%) with *reduced left ventricle ejection fraction*, of which 23 patients (59%) experienced KKM, while 16 patients (41%) did not experience KKM. In the *mildly reduced left ventricle ejection fraction group*, 20 patients were found, with 8 patients (40%) experiencing KKM and 12 patients (60%) not experiencing KKM. Meanwhile, there were 26 patients (30.6%) with *preserved left ventricle ejection fraction*, of which 5 patients (19.2%) experienced KKM and 21 patients (80.8%) did not experience KKM.

For grouping based on the type of revascularization undergone by SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital during the period of January to December 2023, it is classified into three categories, namely: patients who do not undergo revascularization, undergo culprit revascularization, and undergo total revascularization. In the non-revasculation group, 37 patients (43.5%) were found, of which 20 patients (54.1%) experienced KKM and 17 patients (45.9%) did not experience KKM. Then the culprit revascularization group had 48 patients (56.6%), of which 16 patients (33.3%) experienced KKM and 32 patients (66.7%) did not experience KKM. Meanwhile, the total revascularization group did not find patients (0.0%).

Then for pharmacotherapy given to patients, it was found that 71 (83.5%) patients were given aspileps with 27 patients (38%) experiencing KKM and 44 patients (62%) not experiencing KKM. 79 patients (92.9%) were given *clopidogrel* of which 34 patients (43%) had KKM and 45 patients (57%) did not have KKM. 81 patients (95.3%) were given statins, of which 33 patients (40.7%) had KKM and 48 patients (59.3%) did not have KKM. 75 patients

(88.2%) were given nitrates, of which 33 patients (44%) had KKM and 42 patients (56%) did not have KKM. 59 patients (69.4%) were given ß-blockers, Among them, 23 patients (39%) experienced KKM and 36 patients (61%) did not experience KKM. 81 patients (95.3%) were given ACE/ARB, of which 35 patients (43.2%) experienced KKM and 46 patients (56.8%) did not experience KKM. 39 patients (45.9%) were given the antagonist aldosterone, of which 21 patients (53.8%) experienced KKM and 18 patients (46.2%) did not experience KKM.

Major Cardiovascular Incidence in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital

Distribution of Major Cardiovascular Events in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital

Table 2. Distribution of Major Cardiovascular Events in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Hospital

Types of KKM	Number (n=36)	Percentage(%)
Death	8	22,2
Recurrent Myocardial Inphylaxis	4	11,1
Stroke	4	11,1
Recurring Rehospitalization	17	47,2
Recurring Rescumenization	3	8,3

From the research that has been conducted, it was found that 36 patients (42.4%) experienced KKM, including 8 patients (22.2%) died, 4 patients (11.1%) experienced recurrent myocardial infarction, 4 patients (11.1%) experienced stroke, 17 patients (47.2%) experienced repeated rehospitalization due to heart failure, and 3 patients (8.3%) experienced repeated revascularization.

Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on the Value of the Left Ventricular Ejection Fraction

Table 3. Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on the Value of the Left Ventricular Ejection Fraction

	MOH (n=36)	NON KKM (n=49)	TOTAL (n=85)
***Reduced* LVEF**	23 (59%)	16 (41%)	39 (45,9%)
***Mildly Reduced* LVEF**	8 (40%)	12 (60%)	20 (23,5%)

***Preserved* LVEF**	5 (19,2%)	21 (80,8%)	26 (30,6%)

Based on the medical record analysis of Prof. Dr. R. D. Kandou Manado Hospital, it was found that 36 SKA-NSTE patients (42.4%) experienced KKM and 49 patients (57.6%) did not experience KKM. SKA-NSTE patients with *reduced* LVEF were 39 patients with 23 patients (59%) experiencing KKM and 16 patients (41%) not experiencing KKM. 20 patients (23.5%) of SKA-NSTE with *mildly reduced* LVEF were obtained, of which 8 patients (40%) experienced KKM and 12 patients (60%) did not experience KKM. Furthermore, there were 26 SKA-NSTE patients (30.6%) with *preserved*, of which 5 patients (19.2%) experienced KKM and 21 patients (80.8%) did not experience KKM.

Table 4. Distribution of Major Cardiovascular Incidence Types in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on the Value of Left Ventricular Ejection Fraction

Types of KKM / LVEF	Death	Recurrent Myocardial Inphylaxis	Stroke	Rehospitalization Recurring	Recurring Rescumenization	Total
Reduced	5 (21,7%)	2 (8,7%)	1 (4,3%)	14 (60,9%)	1 (4,3%)	23 (63,9%)
Mildly Reduced	2 (25%)	2 (25%)	1 (12,5%)	2 (25%)	1 (12,5%)	8 (22,2%)
Preserved	1 (20%)	0 (0,0%)	2 (40%)	1 (20%)	1 (20%)	5 (13,9%)

Based on the value of the left ventricle ejection fraction, 23 patients (63.9%) were found with *reduced left ventricle ejection fraction*, of which 5 patients (21.7%) died, 2 patients (8.7%) experienced recurrent myocardial infarction, 1 patient (4.3%) had a stroke, 14 patients (60.9%) were rehospitalized due to heart failure, and 1 patient (4.3%) had repeated revascularization. Furthermore, patients with *mildly reduced left ventricle ejection fraction* were found to be 8 patients (22.2%), of which 2 patients (25%) died, 2 patients (25%) experienced recurrent myocardial infarction, 1 patient (12.5%) had a stroke, 2 patients (25%) experienced repeated rehospitalization due to heart failure, and 1 patient (12.5%) experienced repeated revascularization. The last category, preserved *left ventricle ejection fraction*, was found in 5 patients (13.9%), of which 1 patient (20%) died, no patient (0%) was found with myocardial infarction, 2 patients (40%) had stroke, 1 patient (20%) had repeated rehospitalization due to heart failure, and 1 patient (20%) had repeated revascularization.

Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on Age

Table 5. Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on Age

	MOH (n=36)	Non-KKM (n=49)	TOTAL (n=85)
***Age Category**			
<55 years	1 (11,1%)	8 (88,9%)	9 (10,6%)
55-64 years old	11 (45,8%)	13 (54,2%)	24 (28,2%)
65-74 years old	18 (43,9%)	23 (56,1%)	41 (48,2%)
75-84 years old	6 (60%)	4 (40%)	10 (11,8%)
>85 years	0 (0,0%)	1 (100%)	1 (1,2%)

Based on the results of the medical record review of Prof. Dr. R. D. Kandou Manado Hospital, 85 patients were found which could be divided based on age categories into 5 categories, namely: young adults (<55 years old), old adults (55-64 years old), young adults (65-74 years old), medium old (75-84 years old), and oldest old people (>85 years old). There were 9 young adult patients (10.6%), of which 1 patient (11.1%) experienced KKM and 8 patients (88.9%) did not experience KKM. In the elderly adult category, there were 24 patients, of which 11 patients (45.8%) experienced KKM and 13 patients (54.2%) did not experience KKM. Patients with old age and young age were collected as many as 41 patients (48.2%) with 18 patients (43.9%) experiencing KKM and 23 patients (56.1%) not experiencing KKM. Furthermore, in the old and medium category, there are 10 patients (11.8%), of which 6 patients (60%) experience KKM and 4 patients (40%) do not experience KKM. The last category, namely the oldest age, was found to be 1 patient (100%) and did not experience KKM.

Table 6. Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on Age

Types of KKM / Age	Death	Recurrent Myocardial Inphylaxis	Stroke	Rehospitalization Recurring	Recurring Rescumenization	Total
< 55 years	0 (0,0%)	0 (0,0%)	0 (0,0%)	1 (100%)	0 (0,0%)	1 (2,8%)
55-64 years old	1 (9,1%)	2 (18,2%)	3 (27,3%)	4 (36,4%)	1 (9,1%)	11 (30,6%)
65-74 years old	6 (33,3%)	1 (5,6%)	1 (5,6%)	8 (44,4%)	2 (11,1%)	18 (50,0%)
75-84 years old	1 (16,7%)	1 (16,7%)	0 (0,0%)	4 (66,7%)	0 (0,0%)	6 (16,7%)
>85 years old	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)

Based on the age category, 1 patient (100%) with the age of <55 years or young adults who experienced repeated rehospitalization due to heart failure was found. This study obtained 11 patients aged 55-64 years or older adults, including 1 patient (9.1%) who died, 2 patients

(18.2%) who had recurrent myocardial infarction, 3 patients (27.3%) who had stroke, 4 patients (36.4%) who had recurrent rehospitalization due to heart failure, and 1 patient (9.1%) who had recurrent revascularization. In the age category of 65-74 years old, 18 patients (50%) were obtained, of which 6 patients (33.3%) died, 1 patient (5.6%) experienced recurrent myocardial infarction, 1 patient (5.6%) had a stroke, 8 patients (44.4%) experienced recurrent rehospitalization due to heart failure, and 2 patients (11.1%) experienced repeated revascularization. The next category, namely the elderly, medium or 75-84 years old, was obtained by 6 patients with 1 patient (16.7%) experiencing death, 1 patient (16.7%) experiencing recurrent myocardial infarction, and 4 patients (66.7%) experiencing repeated rehospitalization due to heart failure. As for the oldest age category or ≥85 years old , no patients were found who experienced KKM.

Distribution of Major Cardiovascular Events in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on Left Ventricular Ejection Fraction Value and Age

Table 7. Distribution of KKM in SKA-NSTE Patients at Prof. Dr. R. D. Kandou Manado Hospital Based on Left Ventricular Ejection Fraction Value and Age

LVEF * Age Category	**Major Cardiovascular Events**					**Total**
	Death	Recurrent Myocardial Inphylaxis	Stroke	Recurring Rehospitalization	Recurring Rescumenization	
***Reduced* LVEF**						
Young Adults	0 (0,0%)	0 (0,0%) 2 (40,0%)	0 (0,0%)	1 (100%) 3 (60,0%)	0 (0,0%) 0 (0,0%)	1 (4,3%)
Older Adult	0 (0,0%)	0 (0,0%) 0 (0,0%)	0 (0,0%)	7 (53,8%) 3 (75,0%)	1 (7,7%) 0 (0,0%)	5 (21,7%)
Young and Old Medium Old	4 (30,8%) 1 (25,0%)	0 (0,0%)	1 (7,7%) 0 (0,0%)	0 (0,0%)	0 (0,0%)	13 (56,5%) 4 (17,4%)
The Oldest Elder	0 (0,0%)		0 (0,0%)			0 (0,0%)
***Mildly Reduced* LVEF**						

Young	0	0 (0,0%)	0	0 (0,0%)	0 (0,0%)	0
Adults	(0,0%)	0 (0,0%)	(0,0%)	1 (33,3%)	0 (0,0%)	(0,0%)
Older	1	1 (25,0%)	1	1 (25,0%)	1 (25,0%)	3
Adult	(33,3%)	1 (100%)	(33,3%)	0 (0,0%)	0 (0,0%)	(37,5%)
Young	1	0 (0,0%)	0	0 (0,0%)	0 (0,0%)	4
and Old	(25,0%)		(0,0%)			(50,0%)
Medium	0		0			1
Old	(0,0%)		(0,0%)			(12,5%)
The	0		0			0
Oldest	(0,0%)		(0,0%)			(0,0%)
Elder						
***Preserved* LVEF**						
Young	0	0 (0,0%)	0	0 (0,0%)	0 (0,0%)	0
Adults	(0,0%)	0 (0,0%)	(0,0%)	0 (0,0%)	1 (33,3%)	(0,0%)
Older	0	0 (0,0%)	2	0 (0,0%)	0 (0,0%)	3
Adult	(0,0%)	0 (0,0%)	(66,7%)	1 (100%)	0 (0,0%)	(60,0%)
Young	1	0 (0,0%)	0	0 (0,0%)	0 (0,0%)	1
and Old	(100%)		(0,0%)			(20,0%)
Medium	0		0			1
Old	(0,0%)		(0,0%)			(20,0%)
The	0		0			0
Oldest	(0,0%)		(0,0%)			(0,0%)
Elder						

Based on the distribution of the left ventricular ejection fraction value and age to major cardiovascular events, 23 patients (63.9%) with *reduced* LVEF experienced KKM. Among them, 1 patient (100%) young adults (<55 years old) experienced repeated rehospitalization due to heart failure, 2 patients (40%) elderly adults (55-64 years old) experienced recurrent myocardial infarction, 3 patients (60%) elderly adults experienced repeated rehospitalization due to heart failure, 4 patients (30%) young adults (65-74 years old) experienced death, 1 patient (7.7%) young elderly experienced stroke, 7 patients (53.8%) of the elderly experienced recurrent rehospitalization due to heart failure, 1 patient (7.7%) of the young elderly experienced repeated revascularization, 1 patient (25%) of the moderate elderly (75-84 years) died, and 3 patients (75%) of the elderly experienced repeated rehospitalization due to heart failure.

In the next category, 8 patients (22.2%) with *mildly reduced* LVEF experienced major cardiovascular events. Among them, 1 patient (14.3%) of old age died, 1 patient (33.3%) of

old age died, 1 patient (33.3%) of old age experienced stroke, 1 patient (33.3%) of old age experienced recurrent rehospitalization due to heart failure, 1 patient (25%) of young age experienced death, 1 patient (25%) of young age experienced recurrent myocardial infarction, 1 patient (25%) of young age experienced repeated rehospitalization due to heart failure, 1 patient (25%) of young age experienced recurrent revascularization, and 1 patient (100%) of moderate elderly age experienced recurrent myocardial infarction.

For the last category, 5 patients (13.9%) with *preserved* LVEF experienced major cardiovascular events. Among them, 2 patients (66.7%) of elderly adults experienced stroke, patients (33.3%) of elderly adults experienced repeated revascularization, 1 patient (100%) of young adults experienced death, and 1 patient (100%) of elderly age experienced repeated rehospitalization due to heart failure.

Results of Bivariate Analysis

Bivariate analysis was carried out to see the relationship between the value of the left ventricular ejection fraction and age to major cardiovascular events in SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital for the period January to December 2023. This analysis uses *the Chi Square* Test and *Fisher's Exact Test* to determine the relationship between the three variables. The following are the results of the analysis of the data.

Table 8. Bivariate Analysis of the Relationship between Left Ventral Ejection Fraction Value and Age on Major Cardiovascular Incidence

	Major Cardiovascular Events						
	Death	Recurrent Myocardial Inphylaxis	Stroke	Recurring Rehospitalization	Recurring Rescumenization	**Total**	**p Value**
***Left Ventricular Ejection Faction Value**							**0.012** **
***Reduced* LVEF**	5 (12,8%)	2 (5,1%)	1 (2,6%)	14 (35,9%)	1 (2,6%)	23 (59%)	
***Mildly Reduced* LVEF**	2 (10,0%)	2 (10,0%)	1 (5,0%)	2 (10,0%)	1 (5,0%)	8 (40%)	
***Preserved* LVEF**	1 (3,8%)	0 (0,0%)	2 (7,7%)	1 (3,8%)	1 (3,8%)	5 (19,1%)	
***Age Category**							0,706 **

Young Adults	0 (0,0%)	0 (0,0%)	0 (0,0%)	1 (11,1%)	0 (0,0%)	1 (11,1%)
Older Adult	1 (4,2%)	2 (8,3%)	3 (12,5%)	4 (16,7%)	1 (4,2%)	11 (45,9%)
Young and Old	6 (14,6%)	1 (2,4%)	1 (2,4%)	8 (19,5%)	2 (4,9%)	18 (43,8%)
Medium Old	1 (10,0%)	1 (10,0%)	0 (0,0%)	4 (40,0%)	0 (0,0%)	6 (60,0%)
The Oldest Elder	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)	0 (0,0%)

**: Fisher*'s Exact Test*

Based on the bivariate analysis that has been carried out, it was found that the relationship between the value of the left ventricular ejection fraction and the major cardiovascular incidence in SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital has a value of P = 0.012 which proves that the value of the left ventricular ejection fraction has a meaningful relationship with major cardiovascular events. In addition, the results of the study found that the relationship between age and major cardiovascular events in SKA-NSTE patients at Prof. Dr. R. D. Kandou Manado Hospital had a value of P = 0.706 which proved that age did not have a meaningful relationship with major cardiovascular events.

Discussion

Basic Characteristics of NSTE-ACS Patients at Prof. Dr. R. D. Kandou General Hospital

The majority of NSTE-ACS patients at Prof. Dr. R. D. Kandou General Hospital were male (70.6%), with an average age of 65.51 years. Patients who experienced major adverse cardiovascular events (MACE) had a higher average age (67.31 years) compared to those without MACE (64.18 years). These findings align with the literature indicating that men and older individuals are more vulnerable to cardiovascular events due to physiological changes and higher risk factors.

Major Cardiovascular Incidence in NSTE-ACS Patients at Prof. Dr. R. D. Kandou General Hospital

The incidence of MACE among NSTE-ACS patients was 42.35%, with rehospitalization due to heart failure being the most common event (47.2%), followed by death (22.2%), stroke (11.1%), recurrent myocardial infarction (11.1%), and repeat revascularization (8.3%). Patients

with low LVEF showed a higher risk for all MACE categories, particularly rehospitalization and death. These findings underscore the importance of intensive monitoring for patients with low LVEF to prevent further complications.

The Relationship Between Left Ventricular Ejection Fraction and Major Cardiovascular Incidence in NSTE-ACS Patients

Patients with lower LVEF (<40%) had a significantly higher incidence of MACE (59%) compared to those with normal or mildly reduced LVEF. This relationship was statistically significant (p=0.006), indicating that low LVEF is a strong risk indicator for MACE. Low LVEF reflects impaired left ventricular systolic function, which increases the risk of heart failure, arrhythmias, and other cardiovascular complications.

Age Relationship with Major Cardiovascular Incidence in NSTE-ACS Patients

Older age was also associated with an increased risk of MACE, although this relationship was not statistically significant across all age categories (p>0.05). Patients in the "old-medium" age group (75–84 years) had the highest MACE incidence (60%), reflecting the impact of aging on cardiovascular function, including reduced vascular elasticity and left ventricular performance.

CONCLUSION

This study demonstrates that reduced left ventricular ejection fraction (LVEF) and advanced age are significantly associated with an increased risk of major adverse cardiovascular events (MACE) in patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS). Among the studied population, 42.35% of patients experienced MACE, with rehospitalization due to heart failure being the most common event, followed by death, stroke, recurrent myocardial infarction, and repeat revascularization. Patients with reduced LVEF (<40%) showed the highest incidence of MACE, particularly rehospitalization and death, emphasizing the critical role of LVEF as a predictor of cardiovascular outcomes. Additionally, older patients, especially those in the "old-medium" age group (75–84 years), exhibited a higher tendency for MACE, highlighting the impact of aging on cardiovascular health. These findings underscore the importance of early evaluation and management of LVEF and age-related risk factors in the clinical care of NSTE-ACS patients to reduce the likelihood of adverse cardiovascular outcomes.

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