ORIGINAL ARTICLE

Journal of the ASEAN Federation of Endocrine Societies

The Relationship Between Admission Insulin Resistance Index (AIRI) and In-Hospital Outcome in Non-Diabetic Acute Coronary Syndrome

Jorianto Muntari,[1] Husaini Umar,[1] Pendrik Tandean,[1] Syakib Bakri,[1] Himawan Sanusi,[1] Nur Ahmad Tabri,[1] Arifin Seweng[2]

[1]*Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia*
[2]*Public Health and Community, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia*

Abstract

Background. Acute coronary syndrome (ACS) is a major cardiovascular problem due to its high hospitalization and mortality rates. One of the risk factors for atherosclerosis that leads to ACS is insulin resistance (IR) which plays a role in the pathogenesis and development of cardiovascular events. This study aims to determine the relationship between IR and in-hospital outcomes in non-diabetic patients with ACS.

Methodology. This was a cohort study conducted from January-June 2021. Insulin resistance was assessed using the Admission insulin resistance index (AIRI). This measurement was performed once during the patient's admission, and then the outcome was observed during hospitalization. The observed in-hospital outcomes were composite outcomes; namely, heart failure, arrhythmia, cardiogenic shock, and death. The statistical tests used were ANOVA, independent T and Chi-Square tests. Statistical test results were considered significant if $p<0.05$.

Results. This study included 60 subjects (51 males and 9 females). Analysis revealed that AIRI was higher in patients with composite outcomes (mean 9.97 ± 4.08) than in patients without composite outcomes (mean 7.71 ± 4.06) ($p<0.05$); AIRI was higher in patients with heart failure (mean 10.72 ± 3.83) than in patients without heart failure (mean 7.25 ± 3.84) ($p<0.001$). Patients with IR had a higher rate of heart failure complications [OR 5.5 95% CI (1.56-19.38) ($p=0.005$)].

Conclusion. There is an association between AIRI and composite outcomes. Patients with IR have 5.5 times the risk of developing heart failure.

Key words: insulin resistance, acute coronary syndrome, in-hospital outcome, AIRI

INTRODUCTION

Insulin resistance (IR) pertains to impaired insulin sensitivity in maintaining plasma glucose concentrations which causes compensatory hyperinsulinemia.[1] It plays a vital role in the pathogenesis and development of cardiovascular events. Thus, fasting glycemia, post-prandial glycemia, and insulin levels can be positively correlated with new cardiac complications in ACS patients.[2]

Atherosclerosis is the main driver of clinical manifestations such as transient ischemic attack, ischemic stroke, peripheral arterial disease, angina pectoris, acute myocardial infarction, heart failure, arrhythmias, and sudden cardiac death.[2] Various studies have proven the relationship between IR and vascular disease and include IR as a new risk factor for atherosclerosis.[3,4] Insulin resistance causes atherosclerosis either directly or indirectly. Directly, IR disrupts the intracellular phosphorylase pathways PI-3-kinase and Akt, resulting in a decrease in nitric oxide (NO) production,and increasing the activation of the MAP kinase pathway, which causes smooth muscle cell proliferation and prothrombic conditions.[5] Indirectly, IR facilitates the occurrence of hyperlipidemia, hypertension, and diabetes, components of the metabolic syndrome that increase the risk of atherosclerosis which is the trigger of ACS.[3]

Admission insulin resistance index (AIRI) is an insulin resistance test measuring insulin levels at admission [insulin at admission (μIU/ml) x plasma glucose at admission (mmol/L)/22.5].[6] This has a correlation with the insulin resistance syndrome and can be used as a poor prognostic predictor in patients with ACS.[7]

eISSN 2308-118x (Online)
Printed in the Philippines

Received: August 11, 2022. Accepted: November 17, 2022.
Published online first: February 8, 2023.
https://doi.org/10.15605/jafes.038.01.03

Corresponding author: Jorianto Muntari, MD
Department of Internal Medicine, Faculty of Medicine,
Hasanuddin University, Rumah Sakit Universitas Hasanuddin
Lt. 5 Gedung A RS. Unhas, Jalan Perintis Kemerdekaan Km 11
Tamalanrea, Makassar 90245, Indonesia
Tel. No.: 0411-586533
E-mail: drjorianto89@gmail.com
ORCiD: https://orcid.org/0000-0002-6472-9787

Several studies show that AIRI can be used as a prognostic tool for patients with myocardial infarction. Stubbs et al., concluded that AIRI in patients with myocardial infarction predicts poor outcomes and is superior to glucose measurement at admission.[7]

Içli et al., found higher AIRI values in patients with acute myocardial infarction than in unstable angina pectoris (7.2 ± 5.3 versus 5.2 ± 4.4, $p<0.01$). Admission insulin resistance index was significantly correlated with heart failure (r=0.42, $p<0.0001$), atrial fibrillation (r=0.35, $p=0.002$) and reinfarction (r=0.23, $p=0.04$) in patients with acute myocardial infarction (AMI).[8] Sanjuan et al., in a study of 518 patients with AMI with or without diabetes mellitus found that the mortality rate increased with increasing IR values, from 3% at IR values <2 to 18% at IR values >3. Admission insulin resistance index is a simple measure to identify IR states. The presence of IR in ACS has a role in identifying the extent of coronary vessel affectation in non-diabetic patients. [9]

This study aimed to observe the relationship between AIRI and in-hospital outcomes in non-diabetic patients with ACS. The academic benefit of the study is that the results can be serve as reference for further research on the topic.

METHODOLOGY

Study design

The design was a prospective cohort study. Insulin resistance was assessed using the admission insulin resistance index (AIRI). This measurement was performed upon the patient's admission, and the outcome was observed during hospitalization. The observed in-hospital outcomes were composite outcomes; namely, heart failure, arrhythmia, cardiogenic shock, and death.

Research subject and sample size

Subjects in this study were patients who met the inclusion criteria: aged >18 years old who had a diagnosis of acute coronary syndrome [unstable angina pectoris (UAP), non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI)] at the time of admission, with no history of diabetes mellitus or heart disease, and who were willing to participate in the study.

The estimated number of samples required in this study was calculated based on the formula:

$$n = \frac{\left(Z_{1-\alpha/2}\sqrt{(1+k)\bar{\lambda}^2} + Z_{1-\beta}\sqrt{k\lambda_1^2+\lambda_2^2}\right)^2}{k\left(\lambda_1-\lambda_2\right)^2}$$

Based on this formula, the minimum sample size is 20 participants.

Data collection

Data was collected from the Emergency Department of the Dr. Wahidin Sudirohusodo Hospital from January-June 2021. History taking, physical examination, ECG, and troponin I examinations were used to diagnose ACS.

The subjects' venous blood were taken and blood glucoses were checked by the hexokinase-glucose-6-phosphate dehydrogenase method, which was expressed in mg/dL units, and converted to mmol/L units using the formula: blood glucose (mmol/L) = admission blood glucose (mg/dL)/18. The insulin level was checked using the ELISA kit 96T brand Demeditec and expressed in IU/L; then, the results were incorporated into the formula AIRI = random blood glucose (mmol/L) x random insulin (μIU/L) / 22.5.

Admission insulin resistance index is an insulin resistance test that does not require fasting insulin. It is obtained by checking insulin and plasma glucose at the time of admission or at any time. Although its sensitivity and specificity are still unknown, the AIRI value has a significant correlation with HOMA-IR and the insulin resistance syndrome.[7]

The gold standard examination for assessing IR is the hyperinsulinemic euglycemic clamp (HEC). Unfortunately, this examination is invasive, entails high costs, and takes a long time, so is impractical in the clinical setting. Another test that is relatively inexpensive and is easier to perform is the homeostasis model assessment-insulin resistance (HOMA-IR), which involves checking fasting insulin and plasma glucose, then entering these values into the formula: fasting insulin (μIU/ml) x glucose plasma (mmol/L)/22.5.[10–12] However, there is currently no standardized HOMA-IR cut-off for determining insulin resistance, and its utility is limited because it requires both glucose and fasting insulin.

As with HOMA-IR, there is no AIRI cut-off value to diagnose insulin resistance. To assess whether the AIRI taken as a criterion for insulin resistance can reflect variations in the AIRI value of the population studied, we classified the AIRI values of the entire study population into tertiles, with these values: tertile-1 (<6.73), tertile-2 (6.73-10.84), and tertile-3 (>10.84) values. Tertile-3 is considered as AIRI above the normal limit; therefore, the value of 10.84 was set as the threshold for insulin resistance.

The HbA1C level was obtained using chromatography with the Konelab Prime 60 tool and expressed as a percentage (%). Subjects with HbA1c levels greater than or equal to 6.5% were excluded from the study.

After the examination, the patient was observed for in-hospital outcomes, specifically arrhythmia, heart failure, cardiogenic shock and death.

In this study, we used a composite outcome which refers to an outcome consisting of two or more component outcomes. Patients who have experienced one of the events defined

by the component categorized as a composite outcome. The main benefits of utilizing component outcomes include increased statistical efficiency, the potential to increase overall event rates when individual event rates are low, and the improved resource efficiency of trials.[13]

The following were considered arrhythmias in this study: atrial flutter, atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, ventricular fibrillation, and AV block grade 2-3.

The forms of heart failure considered in the outcomes are: heart failure with preserved ejection fraction (HFpEF), heart failure with mid-range ejection fraction (HFmrEF), and heart failure with reduced ejection fraction (HFrEF).[14]

The criteria for diagnosing cardiogenic shock according to the KAMIR-NIH (2018) guidelines are systolic blood pressure (SBP) <90 mmHg for >30 minutes or the use of supportive interventions to maintain SBP >90 mmHg, evidence of end-organ damage (impaired mental status, urine output <30 mL/hour, or the presence of cold extremities).[15]

Table 1. Data variable description

Characteristics	N (60)	%
Sex		
Male	51	85.0
Female	9	15.0
Diagnosis		
UAP	9	15.0
NSTEMI	27	45.0
STEMI	24	40.0
Thrombolytics		
Yes	7	11.7
No	53	88.3
Primary Cutaneous Intervention		
Yes	22	36.7
No	38	63.3
Complication		
Yes	40	66.7
No	20	33.3
Arrhythmias		
Yes	9	15.0
No	51	85.0
Heart Failure		
Yes	34	56.7
No	26	43.3
Cardiogenic Shock		
Yes	7	11.7
No	53	88.3
Death		
Yes	9	8.8
No	51	91.2

Data analysis

Data analysis was performed using SPSS version 25. The descriptive method aims to obtain general information about the research sample. Mean values, standard deviation (SD) and the frequency distribution of the sample were obtained as descriptive statistics. The statistical tests that we used were ANOVA, independent T-test, and Chi-Square tests. Statistical test results were considered as significant results if $p<0.05$.

In this study, a normality test was carried out on the AIRI value with Kolmogorov-Smirnov obtained $p>0.05$, which means that the AIRI value is normally distributed; therefore, the statistical test used is a parametric test. Subsequently, the mean AIRI was tested using ANOVA for variables consisting of more than 2 groups, while the independent T-test was used for variables made up of 2 groups.

Research permission and ethical approval

Before conducting the research, an ethical clearance approval from the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar was obtained. The research ethics approval recommendation number is 799/UN4.6.4.5.31/PP36/2020.

RESULTS

Subject characteristics

Data analysis was conducted on 60 subjects (51 males and 9 females), ages 30-79 years old (55.98 ± 12.39 years old). In this study, the average serum insulin level was 27.68 ± 13.83 mIU/L, the average blood glucose was 8.07 ± 3.32 mmol/L, and the AIRI index was 9.22 ± 4.18 (Table 1). To date, there is no set cutoff of the AIRI value to confirm the presence of IR; therefore, in this study, we classified the AIRI values based on tertiles: tertile-1 (<6.73), tertile-2 (6.73-10.84), and tertile-3 (>10.84) values. Tertile-3 is considered as AIRI above the normal limit; thus, the value of 10.84 was set as the threshold for insulin resistance in this study.

In this study, 7 patients received thrombolytics and 22 received primary cutaneous intervention. All patients received dual antiplatelet and anticoagulant therapy. Patients with UAP and NSTEMI were subjected to individual risk stratification. For those deemed to be at

Table 2. Subject characteristics at the Emergency Department, Dr. Wahidin Sudirohusodo Hospital, from January-June 2021

	N	Minimum	Maximum	Mean	Std. deviation
Age (year)	60	30.00	79.00	55.9833	12.39258
Insulin Serum (µIU/ml)	60	10.04	77.61	27.6805	13.83629
GDS (mmol/L)	60	3.89	21.39	8.0796	3.32095
AIRI	60	2.03	24.32	9.2244	4.18206

high and very high-risk, coronary angiography and optimal revascularization were performed. Patients with STEMI received immediate reperfusion therapy, either through PCI or fibrinolysis (Table 2).

Analysis of the relationship between AIRI and the presentation of non-diabetic patients with ACS

The ANOVA test was used to analyze the relationship between AIRI and the presentation of ACS by comparing the mean AIRI values in UAP, NSTEMI, and STEMI. The results of the analysis showed no relationship between AIRI and the different types of ACS (p>0.05) (Table 3).

Analysis of the relationship between AIRI with composite outcomes and in-hospital outcomes in non-diabetic patients with ACS

The relationship between AIRI and composite outcomes during the hospitalization was analyzed. In the group with composite outcomes, the mean AIRI value was 9.97 ± 4.08 higher than in the group without composite outcomes 7.71 ± 4.06, which showed a significant relationship between AIRI and composite outcomes (p=0.047) (Table 3).

The relationship between AIRI and in-hospital outcomes was analyzed by stratifying the mean AIRI values associated with the percentage of in-hospital outcomes, such as heart failure, arrhythmias, cardiogenic shock, and death. Our results did not find any significant difference in AIRI value with arrhythmia, cardiogenic shock, and death (p>0.05), but we found a significant relationship between AIRI value and heart failure (p 0.001). In Table 3, the mean AIRI value in patients with ACS and heart failure is 10.72 ± 3.83, which is higher than in patients with ACS but without heart failure, which is 7.25 ± 3.84.

Table 3. Relationship between mean AIRI and variables

Variable	N	Mean AIRI (SD)	p*
Diagnosis			
UAP	9	9.33 (4.27)	0.942**
NSTEMI	27	9.01 (4.72)	
STEMI	24	9.41 (3.63)	
Composite outcome			0.047*
Yes	40	9.97 (4.08)	
No	20	7.71 (4.06)	
Heart Failure			0.001*
Yes	34	10.72 (3.83)	
No	26	7.25 (3.84)	
Arrhythmias			0.925*
Yes	9	9.24 (4.17)	
No	51	9.10 (4.45)	
Cardiogenic Shock			0.765*
Yes	7	9.67 (4.11)	
No	53	9.16 (4.22)	
Death			0.056*
Yes	9	11.67 (5.47)	
No	51	8.79 (3.81)	

*Independent T-test, **Annova Test

The correlation between IR and heart failure was assessed using the Chi-Square and Cochran's & Mantel-Haenszel tests, which revealed a higher rate of heart failure outcomes in those with insulin resistance (Table 4). Patients who had insulin resistance also had an increased rate of heart failure complications. [OR 5.5 CI 95% (1.56-19.38) (p=0.005)].

DISCUSSION

Our study demonstrated that the group with composite outcomes had a higher AIRI value than the group without composite outcomes. The mean AIRI value of 9.97 ± 4.08 was higher than the average AIRI in the group without the composite outcomes at 7.71 ± 4.06. This points to a significant relationship between AIRI and the presence of composite outcomes (p<0.05) (Table 3). This result is similar to that of several studies which found an association between IR and cardiovascular complications.[6,16]

A cross-sectional study by Refaie et al., on 120 non-diabetic patients showed a linear relationship between AIRI value and the number of coronary artery involvement, suggesting a role of AIRI in identifying the extent of coronary artery involvement in ACS.[6] Likewise, a cohort study by Yun et al., of 98 non-diabetic patients who underwent elective coronary angiography found that a HOMA-IR of ≥2.6, was significantly associated with adverse cardiac events (MACE) in 30 days, with a rate 27.8% higher than in those with HOMA -IR <2.6, i.e., 2.4% (p=0.008).[16]

On the other hand, the results of our study differ from that of the study of Salehiomran and Jafari (2009), which found no significant difference between the mean AIRI in patients with complications (7.9 ± 9.1) and without complications (8.7 ± 8.8).[17]

In this study, there was a correlation between insulin resistance reflected by an elevated AIRI and heart failure, but there was no correlation between insulin resistance and arrhythmias, cardiogenic shock, and death. The results of this study are similar to a study by Içli et al., in 160 non-diabetic patients, where 72 of the 160 patients

Table 4. Relationship between insulin resistance and heart failure outcome

			Heart Failure		Total	p*
			Yes	No		OR** (CI 95%)
Insulin Resistance	Yes	N	17	4	21	
		%	81%	19%	100%	0.005
	No	N	17	22	39	5.5 (1.56-19.38)
		%	43.6%	56.4%	100%	
Total		N	34	26	60	
		%	56.7%	43.3%	100%	

*Chi-Square Test, **Cochran's and Mantel-Haenszel Test

were diagnosed with acute myocardial infarction in the Coronary Intensive Care Unit. Patients were then followed up for the development of heart failure, atrial fibrillation, life-threatening ventricular arrhythmias, atrioventricular block, reinfarction, and death. Admission insulin resistance index was found to be significantly correlated with heart failure (r=0.42, p<0.0001), atrial fibrillation (r=0.35, p=0.002) and reinfarction (r=0.23, p=0.04).[8]

Insulin resistance is closely related to heart failure and is the main factor that drives heart failure both directly and indirectly.[18] Directly, IR brings about changes in intracellular metabolism, such as a decrease in intracellular glycogen and impaired glucose delivery to ischemic myocytes, thereby exacerbating the injury from infarction. Acute myocardial infarction results in cardiac dysfunction.[7,19] Indirectly, IR causes atherosclerosis which is the forerunner of acute myocardial infarction. Reduced coronary blood flow causes myocardial ischemia, where in the oxygen supply of the heart stops for approximately 20 minutes, leading to myocardium necrosis and pump failure that ultimately cause heart failure.[5,18-20]

In this study, AIRI was not correlated with arrhythmias, in contrast to the study by Sanjuan et al., which found that 20% (254/1258) of patients with acute myocardial infarction experienced high-risk ventricular tachyarrhythmias during treatment and the mortality rate (115/1,258) was higher in patients with high-risk ventricular tachyarrhythmias.[21] The pathogenic mechanism of arrhythmias due to ACS is multifactorial, including ischemia, hemodynamic and electrolyte disturbances, reentry rhythms, and automatization disorders.[22] In our study, no correlation was observed. The presence of confounding factors such as hemodynamic and electrolyte disturbances may have contributed to the lack of correlation seen in this cohort study.

The correlation between AIRI and mortality was also assessed in this study using the independent T-test and no correlation between AIRI and mortality (p > 0.05) was seen. It is consistent with the findings by Caccamo et al., which found that mortality did not appear to be significantly associated with IR (p=0.07).[2] Pathophysiological mechanisms driving the association between IR, hyperglycemia, and death in patients with acute myocardial infarction are not fully understood.[23,24]

Many studies have used the AIRI value as a predictor of outcome in ACS patients. A meta-analysis by Gast et al., with 516,325 participants from 65 studies, demonstrated that IR is a predictor of cardiovascular events.[25] Likewise, a prospective study, Insulin Resistance Atherosclerosis Study (IRAS) with 2938 patients found that IR is a significant risk factor for cardiovascular disease.[19]

Atherosclerosis is the main driver of clinical manifestations and a major cause of ischemic cardiac events such as angina pectoris, acute myocardial infarction, heart failure, arrhythmias, and sudden cardiac death. Recent data indicate that IR plays a significant role both in the pathogenesis of the metabolic syndrome and in the prediction of cardiovascular events, so that fasting glycemia, post-prandial glycemia, and insulin levels have a positive correlation with the incidence of new heart disease in ACS patients.[2,8]

Admission insulin resistance index can be used at the early stage as a predictor in high-risk patients with ACS. The AIRI value is a practical parameter that is easy to calculate and is an independent risk factor that can predict the prognosis of patients with ACS.[12] In addition, the AIRI value also has a better predictive value than blood glucose for patients with ACS.[7]

CONCLUSION

There is a relationship between the AIRI and the composite outcome of ACS which is heart failure. However, there is no correlation between AIRI and arrhythmias, cardiogenic shock, and death. Patients with IR have 5.5 times the risk of heart failure. There is no difference in AIRI value among the different types of ACS (UAP, NSTEMI, and STEMI).

Statement of Authorship
The authors certified fulfillment of ICMJE authorship criteria.

CRediT Author Statement
JM: Conceptualization, Methodology, Software, Formal analysis, Investigation, Resources, Writing - original draft preparation, Supervision, Funding acquisition; **HU:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - review and editing, Supervision, Funding acquisition; **PT:** Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing - review and editing, Supervision, Funding acquisition; **SB:** Conceptualization, Methodology, Resources, Writing - original draft preparation, Supervision, Project administration, Funding acquisition**; HS:** Conceptualization, Validation, Resources, Writing - original draft preparation, Visualization, Supervision, Project administration, Funding acquisition; **NAT:** Conceptualization, Validation, Resources, Writing - review and editing, Visualization, Supervision, Project administration, Funding acquisition; **AS**: Conceptualization, Methodology, Validation, Formal analysis, Data curation, Supervision, Funding acquisition.

Author Disclosure
The authors declared no conflict of interest.

Funding Source
None.

References
1. Wilcox G. Insulin and insulin resistance. Clin Biochem Rev. 2005;26(2):19-39. PMID: 16278749. PMCID: PMC1204764.
2. Caccamo G, Bonura F, Bonura F, et al. Insulin resistance and acute coronary syndrome. Atherosclerosis. 2010;211(2):672-5. PMID: 20466373. https://doi.org/10.1016/j.atherosclerosis.2010.03.033.
3. Semenkovich CF. Insulin Resistance and atherosclerosis. J Clin Invest. 2006;116(7):1813-22. PMID: 16823479. PMCID: PMC1483180. https://doi.org/10.1172/JCI29024.
4. Hacman DG, Anand SS. Emerging risk factors for atherosclerotic vascular disease: A critical review of the evidence. Clin Cardiol. 2003;290(7):932-40. PMID: 12928471. https://doi.org/10.1001/jama.290.7.932.

5. Razani B, Chakravarthy MV, Semenkovich CF. Insulin resistance and atherosclerosis. Endocrinol Metab Clin North Am. 2008;37(3): 603-21. PMID: 18775354. PMCID: PMC2639785. https://doi.org/10.1016/j.ecl.2008.05.001.
6. Refaie W, Elewa A. Admission insulin resistance index in non diabetic patients with acute coronary syndrome: Clinical and angiographic features. Egypt J Intern Med. 2013;25:42-6. https://doi.org/10.7123/01.EJIM.0000425959.76987.c5.
7. Stubbs PJ, Alaghband-Zadeh J, Laycock JF, Collinson PO, Carter GD, Noble MI. Significance of an index of insulin resistance on admission in non-diabetic patients with acute coronary syndromes. 1999;82(4):443-7. PMID: 10490558. PMCID: PMC1760262. https://doi.org/10.1136/hrt.82.4.443.
8. Içli A, Gök H, Altunkeser BB, et al. Evaluation of "admission index of insulin resistance (AIRI)" as an early stage risk predictor in nondiabetic acute coronary syndromes. Anadolu Kardiyol Derg. 2002;2(3):194-201. PMID: 12223324.
9. Sanjuan R, Blasco ML, Huerta R, et al. Insulin resistance and short-term mortality in patients with acute myocardial infarction. Int J Cardiol. 2014;172(2):e269-70. PMID: 24485226. https://doi.org/10.1016/j.ijcard.2013.12.207.
10. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. Indian J Endocrinol Metab. 2015;19(1): 160-4. PMID: 25593845. PMCID: PMC4287763. https://doi.org/10.4103/2230-8210.146874.
11. Souza AL, Batista GA, Alegre SM. Assessment of insulin sensitivity by the hyperinsulinemic euglycemic clamp: Comparison with the spectral analysis of photoplethysmography. J Diab Complications. 2017;31(1):128-33. PMID: 27839921. https://doi.org/10.1016/j.jdiacomp.2016.10.018.
12. Horáková D, Štěpánek L, Jonout V, et al. Optimal homeostasis model assessment of insulin resistance (HOMA-IR) cut-offs: A cross-sectional study in the Czech Population. Medicine (Kaunas). 2019;55(5):158. PMID: 31108989. PMCID: PMC6571793. https://doi.org/10.3390/medicina55050158.
13. Dash K, Goodacre S, Sutton L. Composite outcomes in clinical prediction modeling: Are we trying to predict apples and oranges? Ann Emerg Med. 2022;80(1):12-9. PMID: 35339284. https://doi.org/10.1016/j.annemergmed.2022.01.046.
14. Ponikowski P, Voors AA, Anker SA, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J. 2016;37(27):2129-200. PMID: 27206819. https://doi.org/10.1093/eurheartj/ehw128.
15. Vahdatpour C, Collins D, Goldberg S. Cardiogenic shock. J Am Heart Assoc. 2019;8(8):e011991. PMID: 30947630. PMCID: PMC6507212. https://doi.org/10.1161/JAHA.119.011991.
16. Yun KH, Jeong MH, Kim KH, et al. The effect of insulin resistance on prognosis of non-diabetic patients who underwent percutaneous coronary intervention. J Korean Med Sci. 2006;21(2):212-6. PMID: 16614503. PMCID: PMC2733993. https://doi.org/10.3346/jkms.2006.21.2.212.
17. Salehiomran MT, Jafari S. Association of admission insulin resistance index with early cardiac complications in non diabetic patients with acute coronary syndrome. J Babol Univ Med Sci. 2009;10(6):62-6.
18. Aroor AR, Mandavia CH, Sowers JR. Insulin resistance and heart failure: Molecular mechanisms. Heart Fail Clin. 2012;8(4):609-17. PMID: 22999243. PMCID: PMC3457065. https://doi.org/10.1016/j.hfc.2012.06.005.
19. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17(1):122. PMID: 30170598. PMCID: PMC6119242. https://doi.org/10.1186/s12933-018-0762-4.
20. Juzar DA, Danny SS, Irmalita, Firdaus I, Widyantoro B. Pedoman Tatalaksana Sindrom Koroner Akut. 4th ed. Jakarta:PERKI; 2018.
21. Sanjuan R, Blasco ML, Martinez-maicas H, et al. Acute myocardial infarction : High risk ventricular tachyarrhythmias and admission glucose level in patients with and without diabetes mellitus. Curr Diabetes Rev. 2011;7(2):126-34. PMID: 21348814. https://doi.org/10.2174/157339911794940675.
22. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation, 2013;127(4):e362.425. PMID: 23247304. https://doi.org/10.1161/CIR.0b013e3182742cf6.
23. Lazzeri C, Sori A, Chiostri M, Gensini GF, Valente S. Prognostic role of insulin resistance as assessed by homeostatic model assessment index in the acute phase of myocardial infarction in nondiabetic patients submitted to percutaneous coronary intervention. Eur J Anaesthesiol. 2009;26(10):856-62. PMID: 19367169. https://doi.org/10.1097/EJA.0b013e32832a235c.
24. García RG, Rincón MY, Arenas WD, et al. Hyperinsulinemia is a predictor of new cardiovascular events in Colombian patients with a first myocardial infarction. Int J Cardiol. 2011;148(1):85-90. PMID: 19923024. https://doi.org/10.1016/j.ijcard.2009.10.030.
25. Gast KB, Tjeerdema N, Stijnen T, Smit JWA, Dekkers OM. Insulin resistance and risk of incident cardiovascular events in adults without diabetes: Meta-analysis. PLoS One. 2012;7(12):e52036. PMID: 23300589. PMCID: PMC3532497. https://doi.org/10.1371/journal.pone.0052036.