

# The Role of Acute Hyperglycemia on the Risk of Malignant Arrhythmia in Acute Myocardial Infarction Patients: A Study of Myocardial Damage, Ion Channel Changes and Inflammatory Factors

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## ABSTRAK

**Latar belakang:** infark miokard akut (IMA) sering kali diikuti oleh hiperglikemia. Sampai saat ini, belum ada penelitian terkait peran kerusakan miokard, perubahan saluran ion dan peningkatan respons inflamasi sebagai patomekanisme aritmia ganas akibat hiperglikemia pada pasien IMA. Tujuan penelitian ini untuk mengetahui pengaruh hiperglikemia akut pada kejadian aritmia ganas, troponin I, VLP, galur ekokardiografi, perubahan saluran ion (CaMKII) dan hsCRP. Penelitian ini juga bertujuan untuk menilai efek troponin I, VLP, GLS, CaMKII dan hsCRP pada terjadinya aritmia ganas pada pasien IMA dengan hiperglikemia akut. **Metode:** studi potong lintang diikuti oleh studi kohort dilakukan pada pasien IMA yang dirawat di ICCU RS Cipto Mangunkusumo Jakarta selama periode November 2018 hingga Mei 2019. Pasien dengan infeksi parah dan mengalami aritmia ganas tidak diikutsertakan dalam penelitian ini. Terjadinya aritmia ganas sebagai hasil utama dari penelitian ini dan tingkat CaMKII dinilai pada hari kelima pengobatan. Pasien yang meninggal sebelum hari kelima pengobatan karena penyebab selain aritmia ganas dikeluarkan dari analisis. Hubungan antara hiperglikemia akut dengan VLP dan kejadian aritmia ganas dianalisis melalui uji chi-square, sedangkan perbedaan antara troponin I, GLS, CaMKII dan hsCRP, berdasarkan status hiperglikemia pasien, dianalisis oleh uji U Mann-Whitney. **Hasil:** total 110 pasien dilibatkan dalam penelitian ini. Dua pasien meninggal pada hari ketiga pengamatan karena aritmia ganas. Tidak ditemukan hubungan bermakna antara hiperglikemia akut pada IMA dan aritmia ganas (RR=1,38, 95% CI 0,503,77). Ada perbedaan tingkat CaMKII pada hari-1 dan hari-5 antara mereka yang mengalami aritmia ganas dan mereka yang tidak (p-value untuk perbedaan masing-masing adalah 0,03 dan 0,01. Pada kelompok hiperglikemia akut, ada perbedaan tingkat CaMKII hari ke-5 antara VLP positif dan negatif (p=0,03). **Kesimpulan:** tahap awal IMA menyebabkan kerusakan miokard yang lebih dominan, dibandingkan dengan faktor metabolik. Pada tahap IMA berikutnya, hiperglikemia akut meningkatkan ROS dan aktivasi perubahan saluran

ion yang dijelaskan oleh CaMKII. Perubahan ini menghasilkan remodeling elektrofisiologis jantung, seperti yang terlihat pada gambar VLP pada SA-ECG.

**Kata kunci:** hiperglikemia akut, infark miokard akut (IMA), CaMKII, hsCRP, aritmia ganas, VLP.

## ABSTRACT

**Background:** acute myocardial infarction (AMI) is often followed by hyperglycemia. To date, there is no study that examine the role of myocardial damage, ion channel changes and increased inflammatory response as a pathomechanism of malignant arrhythmias due to hyperglycemia in AMI patients. The aim of this study is to determine the effect of acute hyperglycemia on the occurrence of malignant arrhythmias, troponin I, VLP, echocardiographic strain, ion channel changes (CaMKII) and hsCRP. This study also aims to assess the effect of troponin I, VLP, GLS, CaMKII and hsCRP on the occurrence of malignant arrhythmias in AMI patients with acute hyperglycemia. **Methods:** a cross-sectional study followed by a cohort study was conducted on AMI patients treated at ICCU Cipto Mangunkusumo Hospital Jakarta during November 2018 to May 2019 period. Patients with severe infections and who had experienced malignant arrhythmias at admission were excluded from the study. The occurrence of malignant arrhythmias as the main outcome of this study and CaMKII level were assessed on the fifth day of treatment. Patients who died before the fifth day of treatment due to causes other than malignant arrhythmias were excluded from analysis. The association between acute hyperglycemia with VLP and the occurrence of malignant arrhythmias was analyzed through a chi-square test, whereas the differences between troponin I, GLS, CaMKII and hsCRP, based on the hyperglycemia status of the patient, were analyzed by Mann-Whitney U test. **Results:** a total of 110 patients were included in the study. Two patients died on the third day of observation due to malignant arrhythmias. No significant relationship was found between acute hyperglycemia in AMI and malignant arrhythmias (RR = 1,38, 95%CI 0.50–3.77). There were differences of CaMKII level on day-1 and day-5 between those who were experienced malignant arrhythmia and those who were not (p-value for differences are 0,03 and 0,01, respectively). In the acute hyperglycemia group, there was difference of CaMKII day-5 levels between positive and negative VLP (p = 0.03). **Conclusion:** it was concluded that the initial stage of AMI causes more dominant myocardial damage, as compared to metabolic factors. In the next stage of AMI, acute hyperglycemia increases ROS and the activation of ion channel changes described by CaMKII. This change results in electrophysiological remodeling of the heart, as seen in the VLP image on SA-ECG.

**Keywords:** acute hyperglycemia, AMI, CaMKII, hsCRP, malignant arrhythmias, VLP.

## INTRODUCTION

Acute Myocardial Infarction (AMI) is often followed by various cardiac complications such as atrial and ventricular arrhythmias, haemodynamic disorders, conduction disorders, heart failure, ventricular aneurysms and myocardial rupture. Cardiac complications that can result in sudden cardiac death (SCD) are malignant ventricular arrhythmias like ventricular fibrillation (VF), persistent ventricular tachycardia (ventricular tachycardia, VT) and non persistent ventricular tachycardia (non-sustained ventricular VT). In severe stress such as acute myocardial infarction (AMI), the body often demonstrates an increase in blood glucose levels at the time of hospital admission, also called acute hyperglycemia. Acute hyperglycemia responses are mediated

by the activation of the sympathetic nervous system and the hypothalamic-pituitary axis, which stimulates the release of catecholamines and cortisol. As a result, an increasing process of gluconeogenesis, glycogenolysis and lipolysis occurs. In ICCU Cipto Mangunkusumo Hospital, Jakarta, the prevalence of acute hyperglycemia (plasma glucose >140 mg/dL) in ACS cases has been reported to reach 50.4%.<sup>1</sup>

Patients with AMI and hyperglycemia at admission will have myocardial dysfunction as showed by electrophysiological remodeling, as well as a disruption to left ventricular systolic function. Myocardial damage and dysfunction will trigger higher malignant ventricular arrhythmias. Myocardial dysfunction can be assessed through several examinations, namely

electrocardiographic features such as Signal Averaged Electrocardiography (SA-ECG) and echocardiographic strain. SA-ECG examination is a holter ECG examination that can assess the electrophysiological function of the cardiac muscle in 15–20 minutes described by ventricular late potential (VLP). Several studies have shown that myocardial damage in AMI may vary as functional impairment or electrophysiological remodeling which results in impairment of cardiac electrical conductivity and at risk of arrhythmias especially malignant arrhythmias that will increase the risk of sudden cardiac death.<sup>2,3</sup>

Echocardiographic strain examination can be assessed through a Global Longitudinal Strain (GLS). GLS is more sensitive than an examination of the left ventricular ejection fraction (LVEF), which is usually conducted during routine echocardiographic examinations. In AMI there will be some cellular alteration in ion channels, especially calcium, which can cause complications, especially malignant arrhythmias. When myocardial lesions occur, they increase levels of reactive oxygen species (ROS) and activate Ca<sup>2+</sup>/calmodulin-dependent protein kinase II (CaMKII), a protein enzyme classified as serine/threonine kinase that plays a role in several human physiological processes in the heart and brain.<sup>4</sup> The process of autophosphorylation, glycosylation and oxidation will increase CaMKII levels and increase the risk of malignant arrhythmias through changes in the calcium ion channel.<sup>5</sup>

AMI consists of a series of inflammatory processes that increase inflammatory markers. This study found that several inflammatory markers, which increased at the time of AMI including hsCRP, IL-6, TNF- $\alpha$  were associated with more frequent and severe complications.<sup>6</sup> Levels of hsCRP are also increased in hyperglycemia due to acute stress, which then increases the risk of malignant arrhythmias.<sup>7,8</sup> However, studies have not been conducted as to whether increasing hsCRP as an inflammatory marker plays a role in the mechanism of malignant arrhythmias in AMI patients with acute hyperglycemia. Thus, we conducted this study to determine the role of acute hyperglycemia against the risk of

malignant arrhythmias, and the related processes: myocardial damage and dysfunction, cardiac electrophysiological remodeling, ion channel changes and inflammatory response.

## METHODS

We conducted a cross sectional followed by a prospective cohort study in AMI (NSTEMI and STEMI) patients who were consecutively sampled from November 2018 to May 2019 at ICCU of Cipto Mangunkusumo Hospital, Jakarta. Those with severe infection and malignant arrhythmias at hospital admission were excluded from the study. One patient in this study died before the fifth day of treatment from causes other than a malignant arrhythmia. This study has been approved by the Ethics Committee of Faculty of Medicine Universitas Indonesia (Reference no. 1093/UN2.F1/ETIK/2018).

### Definition of Study Variables

Acute hyperglycemia is defined by a blood glucose level >140 mg/dL at initial patient admission. Blood glucose, troponin, hsCRP, and CaMKII levels were obtained from blood samples and measured at the Cipto Mangunkusumo Hospital Clinical Pathology Laboratory. Ventricular late potential (VLP) and echocardiographic strain (GLS) were obtained from examination of SAECG and echocardiographic performed at ICCU. SA-ECG is an electrocardiogram that show cardiac electrophysiology remodeling by evaluating VLP. Ventricular late potentials were considered positive when  $\geq 2$  of the following criteria were fulfilled: QRSTT  $\geq 120$  ms, LAS40  $\geq 40$  ms, and RMS40  $\leq 25$   $\mu$ V. Echocardiographic strain is a strain changes in myocardium contraction that showed with echocardiography. Blood glucose, troponin, hsCRP, SAECG and GLS levels were assessed on the first day of treatment. CaMKII was assessed on the first and fifth days of treatment. Malignant arrhythmia which are non sustained ventricular tachycardia, ventricular tachycardia and ventricular fibrillation is observed 24 hours in electrocardiogram monitor during five days treatment at ICCU.

### Data Analysis

A data normality test was conducted using the Kolmogorov-Smirnov test. Data was analyzed

**Table 1.** Characteristics of the study population at baseline.

Characteristics	Total Subject (n = 110)	Acute Hyperglycemia (n = 65)	Normoglycemia (n = 45)
Gender, male - n (%)	88 (80)	51 (78.5)	37 (82.2)
Age (years), mean (SD)	57.38 (10)	57.83 (9.83)	56.73 (10.9)
Risk Factor, n (%)			
- Diabetes mellitus	44 (40)	35 (53.8)	9 (20)
- Dyslipidemia	57 (51.8)	37 (56.9)	20 (44.4)
- Hypertension	62 (56.4)	38 (58.5)	24 (53.3)
- Obesity	13 (11.8)	11 (16.9)	2 (4.4)
- Smoker	73 (66.4)	40 (61.5)	33 (73.3)
- History of Coronary Heart Disease	21 (19.1)	16 (24.6)	5 (11.1)
- History of Revascularization	14 (12.7)	12 (18.5)	2 (4.4)
- Stroke	9 (8.2)	6 (9.2)	3 (6.7)
Number of Risk Factor, n (%)			
- 1 Risk Factor	21 (19.1)	8 (12.3)	13 (28.9)
- 2 Risk Factor	34 (30.9)	16 (24.6)	18 (40)
- ≥ 3 Risk Factor	55 (50.0)	41 (63.1)	14 (31.1)
AMI, STEMI - n (%)	70 (63.6)	40 (61.5)	30 (66.7)
GRACE Score, median (interquartile range)	113.5 (48)	116.5 (48)	110.5 (47)
Killip Classification, n (%)			
- Class 1	50 (46.7)	28 (44.4)	22 (50)
- Class 2	23 (21.5)	14 (22.2)	9 (20.5)
- Class 3	20 (18.7)	11 (17.5)	9 (20.5)
- Class 4	14 (13.1)	10 (15.9)	4 (9.1)
Cardiac Marker			
- Troponin I, pg/mL, median (interquartile range)	6954 (57562.8)	3617.7 (70947.9)	8380 (42279.3)
Cardiac Troponin I			
- Normal, ≤ 30 pg/mL, n (%)	2 (1.8)	2 (3.1)	0 (0)
- Elevated, > 30 pg/mL, n (%)	108 (98.2)	63 (96.9)	45 (100)
Echocardiography			
- Ejection Fraction, %, mean (SD)	45.7 (13.7)	46 (14.3)	47 (13.1)
- Systolic Function, n (%)			
- Preserved, ≥ 50%	47 (42.7)	29 (44.6)	18 (40)
- Low, < 50%	63 (57.3)	36 (55.4)	27 (60)
Diastolic Function			
- Normal, n (%)	11 (11.5)	7 (12.3)	4 (10.3)
- Impaired Relaxation, n (%)	40 (41.7)	24 (42.1)	16 (41.0)
- Pseudonormal, n (%)	38 (39.6)	20 (35.1)	18 (46.2)
- Restrictive, n (%)	7 (7.3)	6 (10.5)	1 (2.6)
RBG, mg/dL, median (interquartile range)	149.5(81.3)	191.1 (115.5)	119 (20.8)
- Normoglycemia, ≤ 140 mg/dL, n (%)	45 (40.9)		
- Acute Hyperglycemia, > 140 mg/dL, n (%)	65 (59.1)		
FPG, mg/dL, median (interquartile range), n = 100	118 (52.7)	133 (90.2)	99 (34.25)
PPG, mg/dL, median (interquartile range), n = 90	136.5 (99.75)	167 (106)	108 (45.5)
HbA1c, %, median (interquartile range), n = 104	5.8 (1.38)	6.4 (2.8)	5.4 (0.5)
Normal, < 6.5%, n (%)	71 (68.3)	32 (51.6)	39 (92.9)
Diabetes Mellitus ≥ 6.5%, n (%)	33 (31.7)	30 (48.4)	3 (7.1)

AMI = Acute Myocardial Infarction; STEMI = ST segment elevation myocardial infarction; NSTEMI = Non-ST segment elevation myocardial infarction; GRACE = The Global Registry of Acute Coronary Events; RBG = Random Blood Glucose; FPG = Fasting Plasma Glucose; PPG = Post Prandial Glucose; SD = Standard Deviation.

using a chi-square, Mann Whitney U-test and Independent T-tests. The correlation between acute hyperglycemia with VLP and the occurrence of malignant arrhythmias was analyzed by chi-square test, whereas troponin I, GLS, CaMKII and hsCRP based on the hyperglycemia status were tested by t-test of Mann-Whitney test.

## RESULTS

There were 110 patients consisting of 88 males (80%) and 22 females (20%). The average age was 38 years old with the youngest being 29 years old and the oldest being 83 years old. (Table 1)

From this study, the common risk factor was smoking, with 73 patients (66.4%) reported as smokers. The median GRACE score was 113.5 and the common Killip score was Class 1 Killip (46.7%). The subject of this study was also divided into two groups – the acute hyperglycemia group (> 140 mg/dL), with 65 subjects, and the normoglycemia group (< 140 mg/dL), with 45 subjects. The median troponin value was 3617.7 in the acute hyperglycemia group and 8380 in the normoglycemia group. The average ejection fraction in this study was 45.7%. There were ten patients (15.4%) who had malignant arrhythmias in the acute hyperglycemia

group and five patients (11.1%) who had malignant arrhythmias in the normoglycemia group. There is no significant difference between acute hyperglycemia and malignant arrhythmia (RR 1.38, 95% CI 0.50–3.77,  $p = 0.52$ ). AMI patients with acute hyperglycemia have a higher risk of malignant arrhythmias compared to those with normoglycemia based on electrophysiology remodeling described by VLP based on a SA-ECG assessment (RR = 2.3, 95% CI 0.59–7.25,  $p = 0.25$ ). There is no significant difference between acute hyperglycemia in AMI patients on troponin I, GLS, CaMKII day one and five and hsCRP and patients in the normoglycemia group. (Table 2)

There is a Troponin I level difference between malignant and no malignant arrhythmia in AMI patients within the normoglycemia group. This difference is not seen within acute hyperglycemia patients. (Table 3)

There are also differences of CaMKII, as marker of Calcium ion channel changes, between AMI patients with and without malignant arrhythmia on day-1 and day 5. Subgroup analysis showed that the differences also seen on normoglycemia patients on day 5. (Table 4)

There is an increase risk of malignant arrhythmia in IMA patients with cardiac electrophysiology remodeling (VLP positive)

**Table 2.** Relationship of acute hyperglycemia on troponin I, GLS, CaMKII day 1, CaMKII day 5, and hsCRP levels.

Variables	RBG Status		p
	Acute Hyperglycemia, n = 65	Normoglycemia, n = 45	
Troponin I, pg/mL, median (IQR)	3617.7 (70947.9)	8380 (42279.3)	0.56*
GLS, mean (SD)	11.65 (4.14)	11.44 (4.69)	0.81**
CaMKII 1, ng/mL, median (IQR)	0.24 (0.52)	0.19 (0.25)	0.09*
CaMKII 5, ng/mL, median (IQR)	0.19 (0.3)	0.15 (0.32)	0.25*
hsCRP, ng/mL, median (IQR)	18.88 (103)	13.66 (48)	0.59*

GLS = Global Longitudinal Strain; CaMKII 1 = Calcium/Calmodulin-dependent Protein Kinase Type II Day 1; CaMKII 5 = Calcium/Calmodulin-dependent Protein Kinase Type II Day 5; hsCRP = High Sensitivity C-reactive Protein; RBG = Random Blood Glucose; SD = Standard Deviation. \*Mann-Whitney test. \*\*Independent T Test.

**Table 3.** Differences in troponin I levels between malignant arrhythmia and non-malignant arrhythmia in acute hyperglycemia group and normoglycemia

Blood Glucose Status	Troponin I, pg/ml, median (interquartile range)		p
	Malignant arrhythmia	No Malignant arrhythmias	
Acute Hyperglycemia, n = 65	4534.55 (100537.5)	3617.7 (66330.8)	0.44*
Normoglycemia, n = 45	83473.5 (334657.5)	7921.95 (31036.0)	0.04*
Total, n = 100	7579.7 (159586.7)	5471 (46840.2)	0.10*

\*Mann-Whitney test

**Table 4.** Differences in CaMKII levels between malignant arrhythmia and non-malignant arrhythmia with CaMKII in acute hyperglycemia group and normoglycemia

Blood Glucose Status	Collection Day	CaMKII, ng/ml, median (interquartile range)		p
		Malignant arrhythmia	No Malignant arrhythmia	
Acute Hyperglycemia n = 65	Day-1	0.33 (0.53)	0.23 (0.48)	0.13*
	Day-5	0.28 (0.32)	0.18 (0.29)	0.20*
Normoglycemia n = 45	Day-1	0.40 (0.82)	0.18 (0.23)	0.20*
	Day-5	0.53 (0.63)	0.15 (0.33)	0.02*
Total n = 110	Day-1	0.40 (0.52)	0.22 (0.32)	0.03*
	Day-5	0.33 (0.50)	0.17 (0.27)	0.01*

CaMKII = Calcium/Calmodulin-dependent Protein Kinase Type II. \* Mann-Whitney Test

**Table 5.** The Associations between Electrophysiological Remodeling with the Occurrence of Malignant Arrhythmia in Acute Hyperglycemia Group and Normoglycemia.

Blood Glucose Status	Cardiac Electrophysiology Remodeling	Malignant arrhythmia	No Malignant arrhythmia	RR (CI 95%)	P value
Acute Hyperglycemia (n = 65)	VLP positive. n (%)	3 (33.3)	6 (66.7)	2.64 (0.84-8.46)	0.09*
	VLP negative. n (%)	7 (12.5)	49 (87.5)		
Normoglycemia (n = 45)	VLP positive. n (%)	0 (0.0)	4 (100.0)	-	1*
	VLP negative. n (%)	5 (12.2)	36 (87.8)		
Total (n = 110)	VLP positive. n (%)	3 (25.0)	9 (75.0)	2.04 (0.67-6.21)	0.21*
	VLP negative. n (%)	12 (12.2)	86 (87.8)		

VLP = Ventricular Late Potential; RR = Risk Ratio; CI = Confidence Interval. \* Chi-Square Test

**Table 6.** The Differences of Ion Channel Changes between Positive and Negative VLP in Patients with Acute Hyperglycemia Group and normoglycemia

Blood Glucose Status	Collection Day	CaMKII, ng/ml, median (Interquartile Range)		P value
		Positive VLP	Negative VLP	
Acute Hyperglycemia (n = 65)	Day-1	0.27 (0.41)	0.23 (0.55)	0.56*
	Day-5	0.40 (0.55)	0.18 (0.26)	0.03*
Normoglycemia (n = 45)	Day-1	0.23 (0.00)	0.18 (0.24)	0.98*
	Day-5	0.31 (0.00)	0.15 (0.31)	0.98*
Total (n = 110)	Day-1	0.27 (0.38)	0.22 (0.34)	0.44*
	Day-5	0.32 (0.41)	0.18 (0.29)	0.05*

CaMKII = Calcium/Calmodulin-dependent Protein Kinase Type II; VLP = Ventricular Late Potential. \* Mann-Whitney Test.

compared to VLP negative, but this increase not statistically significant. The increase is seen only in patients with acute hyperglycemia. (Table 5)

There is no differences of Global Longitudinal Strain (GLS) and inflammatory marker (hsCRP) between AMI patients with and without malignant arrhythmia. Analysis of ion channel changes on the first day (CaMKII day one) through electrophysiological remodeling showed no significant difference in all subjects, including the acute hyperglycemia and normoglycemia

groups. However, there was a significant difference between CaMKII day five with electrophysiological remodeling in the acute hyperglycemia group (p = 0.03). (Table 6)

## DISCUSSION

To our knowledge, this is the first study exploring the risk of malignant arrhythmia in hyperglycemia through multiple mechanisms in setting of AMI. Out of 110 AMI patients included in this study, the common risk factors found

were smoking (66.4%), hypertension (56.4%), dyslipidemia (51.8%) and diabetes mellitus (40%). This result was consistent with previous studies in terms of the common risk factors for AMI which are smoking, hypertension, low physical activity and dyslipidemia.<sup>3</sup> This study showed that the median troponin I level in all subjects was 6945 pg/mL, 3617.7 pg/mL in acute hyperglycemia group and 8380 pg/mL in normoglycemia group.

This study found there is no association between hyperglycemia status on admission and the occurrence of malignant arrhythmia, which is not conform with results from previous studies.<sup>1,9</sup> Further analysis showed that in AMI patients with acute hyperglycemia there is risk increase electrophysiological remodeling compared to those who normoglycemi on admission, although not statistically significant. Electrophysiologic remodeling (represent by VLP examination) is a marker for increasing risk of malignant arrhythmia. Myocardial infarction results in electrophysiological remodelling caused by excessive myocardial structural changes generates inhomogeneous electrical impulses conduction within myocardial structure leads to arrhythmia.<sup>10</sup> There is no previous study explored the risk of malignant arrhythmia in hyperglycemia patients using VLP assessment, which is a sensitive parameter to detect the risk for malignant arrhythmia. Eventhough our results did not attain statistically significant, but the estimation risk (relative risk 2.3) is clinically important. We suggest this association is not significant because inadequate sample sizes.

We found that in normoglycemic patients, there is a significant difference of Troponin I level between those who are develop malignant arrhythmia and not. This difference was not seen in acute hyperglycemic grup as well as in total group. This may occur because median levels of troponin I in the normoglycemia group were almost three times higher than in the. acute hyperglycemia group There was no previous study which have been explored this phenomenon, we suggest further research about the correlation between the extent of infarct lesion and malignant arrhythmia. These results explain that the influence of myocardial

damage is very dominant in the early phase of AMI compared to metabolic factors which is blood glucose status (acute hyperglycemia or normoglycemia).

Another mechanism studied is the role of ion channel changes, represent by CaMKII level, on the development of malignant arrhythmia in AMI patients with hyperglycemia. We found there are significant differences of CaMKII level between malignant arrhythmia and no malignant arrhythmia patients, both in first day of and fifth day after admission. Further analysis showed that the differences specially found in normoglycemic patients on fifth day after admission. Based on this result, we suggest that metabolic factors are not the main cause of malignant arrhythmias in the early phase of AMI. Cellular influences, including ion channel changes, seems consistently statistically significant as a dominant factor in the mechanism of malignant arrhythmias.

The results show that on the first day, a prominent factor was myocardial damage, in which there was a very high increase in troponin I levels even in the AMI with normoglycemia population. Metabolic factors described by random blood glucose will affect in the following days, and the results were statistically significant on the fifth day of examination.

There are three processes that occur simultaneously during the pathomechanism of malignant arrhythmia during AMI. First, myocardial damage occurs and appears dominant in the early phase of AMI. This theoretically may result in malignant arrhythmias through several processes. Second, changes occur in intracellular calcium ions, which activate CaMKII and subsequently cause electrophysiological remodeling of the myocardial surface, affecting the action potential and influencing proarithmetic. Third, AMI increases the stress hormones glucocorticoid and catecholamine, which trigger acute hyperglycemia and increase the production of Reactive Oxygen Species (ROS) that activate CaMKII via ROS CaMKII. These changes result in electrophysiological remodeling of the heart on the surface as seen in the VLP during the SA-ECG examination which will eventually trigger the occurrence of malignant arrhythmias. **(Figure 1)**

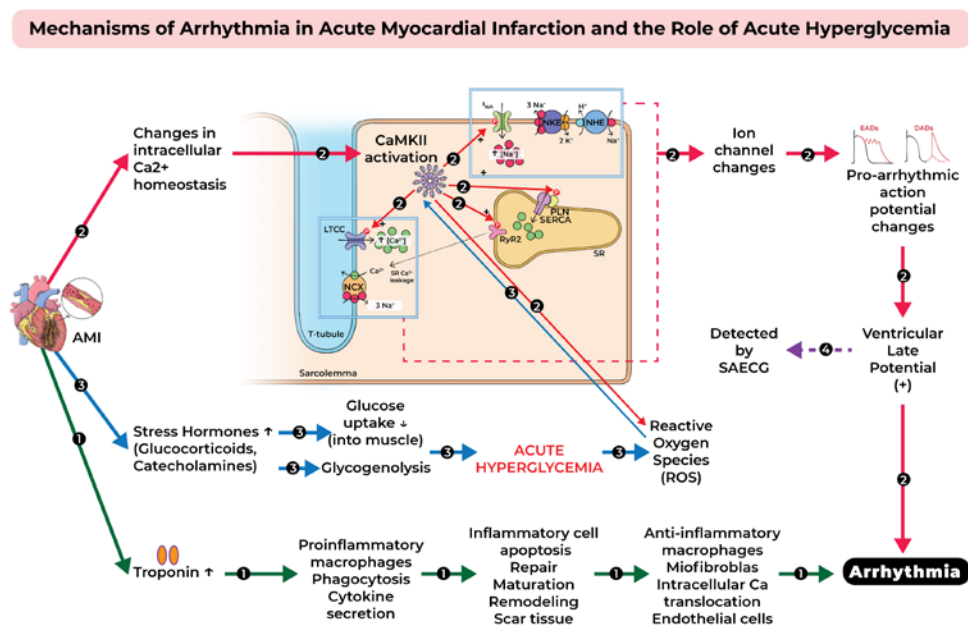


Figure 1. Mechanisms of arrhythmia in acute myocardial infarction and the role of acute hyperglycemia.

### CONCLUSION

This study showed that there was no relationship between acute hyperglycemia in AMI patients and malignant arrhythmias, myocardial damage, electrophysiological remodeling, left ventricular dysfunction, ion channel changes and inflammatory processes compared to AMI patients without acute hyperglycemia. There was no relationship between myocardial damage, cardiac electrophysiological remodeling, left ventricular dysfunction and inflammatory process in IMA, and acute hyperglycemia in the occurrence of malignant arrhythmias.

There were differences between ion channel changes described by CaMKII day one and five, and the occurrence of malignant arrhythmias. However, CaMKII day one is not enough to predict the occurrence of malignant arrhythmias in AMI patients with acute hyperglycemia. There were also differences between ion channel changes described by CaMKII day five and electrophysiological remodeling, which is a risk for malignant arrhythmias. These differences were statistically significant in the acute hyperglycemia group.

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