

Original Article



The Impact of Time Interval From Symptom Onset to Primary Coronary Angioplasty on Heart Rate Variability in Patients With ST-Elevation Myocardial Infarction: A Single-Center Study

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Abstract

Background and aims: Heart rate variability (HRV) is recognized as an independent risk factor for predicting sudden cardiac death in patients with coronary artery disease. The present study aimed to investigate the impact of the time interval between the onset of symptoms in patients experiencing ST-segment elevation myocardial infarction (STEMI) and the subsequent primary coronary angioplasty on HRV.

Methods: A cross-sectional study was conducted involving 65 patients diagnosed with acute MI who were referred to Shahrekord Hajar University Hospital for primary coronary angioplasty. The angiographic findings of the patients, as well as electrophysiological data collected one week and one month post-acute MI, were reviewed and extracted by a cardiologist specializing in electrophysiology. Finally, the data were analyzed using SPSS.

Results: The results demonstrated the right and left coronary arterial dominance in 96.8% and 1.3% of cases, respectively, while a co-dominant pattern was present in 1.3% of patients. The SDNN index and SDNN decreased one month after acute MI ($P=0.396$ and $P=0.378$, respectively). In contrast, the rMSSD and pNN50 indices showed slight increases ($P=0.568$ and $P=0.847$, respectively). The triangle index increased significantly ($P<0.001$), whereas the high-frequency index represented a decrease ($P=0.282$). Eventually, low-frequency and very low-frequency indices did not exhibit significant increases ($P=0.102$ and $P=0.051$, respectively).

Conclusion: Changes in HRV indicators in patients with STEMI significantly differed when comparing data collected one week and one month after primary coronary angioplasty. While high levels of HRV are generally associated with optimal responsiveness of the cardiac autonomic nervous system, the present study's findings do not support the prognostic value of this established electrophysiological principle.

Keywords: Heart rate variability, Cardiac arrhythmia, Angioplasty, Vascular occlusion

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Introduction

Coronary artery disease (CAD), along with its associated acute myocardial infarctions (MIs), is one of the leading causes of premature mortality worldwide (1-3). The dysfunction of the cardiac autonomic nervous system is recognized as a significant risk factor for CAD (4). Heart rate variability (HRV) is an electrophysiological phenomenon characterized by fluctuations in the time intervals between heartbeats. It serves as a non-invasive diagnostic tool for assessing disorders of the cardiac autonomic system (5). HRV is a reliable indicator of autonomic nervous system activity, influenced by both sympathetic and parasympathetic components (6, 7). It has been established that reductions in HRV serve as

an independent prognostic factor for predicting sudden cardiac death in patients with heart failure and indicate a poor prognosis in individuals who have sustained an MI. Conversely, increases in HRV are associated with worse prognostic outcomes in diabetic patients, suggesting a higher risk of cardiovascular complications (8-12). Numerous clinical and laboratory trials have been published regarding HRV measurement methods; however, these findings have yet to be translated into routine clinical practice (4, 13-15). This limitation is attributed to several factors. The clinical applications of HRV assessment are confined to a few standard methods, and underlying diseases can interfere with various parameters, including patient gender and age (14). The

accuracy of risk assessment in patients with cardiovascular disease based on the clinical application of HRV is not widely accepted or generalized in current clinical practice. Regarding the sensitivity, specificity, and predictive accuracy of HRV for assessing risk in patients with CAD, there remains considerable uncertainty regarding the reported findings. The accuracy of HRV in predicting positive cases approaches a moderate level (14–40%), while its ability to predict negative cases is significantly higher (77–98%). Furthermore, there is a consensus that information obtained from HRV measurements alone may not be sufficient for risk assessment in high-risk patients. Combining HRV findings with other risk assessment methods (e.g., evaluating left ventricular systolic function, malignant ventricular tachycardia, and pressure-sensitive receptor sensitivity) may effectively enhance the overall predictive power of both positive and negative values (14, 16–32).

Given the ongoing expectations surrounding the predictive value of HRV in patients with CAD and its wide availability, the objective is to leverage the advantages of HRV in clinical applications to enhance the prediction of patient outcomes and the likelihood of adverse events. This approach aims to better tailor appropriate preventive and therapeutic measures for patients experiencing acute ST-segment elevation myocardial infarction (STEMI) who are undergoing primary coronary intervention (PCI) at Hajar University Hospital in Shahrekord, Chahmahal and Bakhtiari Province, Iran. Specifically, this study will investigate the effect of the timing of PCI on HRV.

Materials and Methods

A cross-sectional study was performed to determine the effect of the timing of primary PCI on HRV. The study included 69 patients who sustained STEMI and underwent PCI at Hajar University Hospital from July 2019 to December 2019. Using an approved checklist, the required data were prospectively extracted from patients' medical records simultaneously by an internist and an electrophysiologist cardiologist. Demographic variables included age, gender, and body surface area, as well as family history of cardiovascular disease (including sudden cardiac death and cardiac arrhythmias). Additionally, patients' medical history was recorded, encompassing substance abuse, diabetes mellitus, chronic kidney disease, and systemic hypertension. Information regarding medication intake (e.g., statins and beta-blockers) and laboratory findings at the time of admission (including plasma troponin-I levels, hemoglobin levels, hematocrit percentages, and white blood cell and platelet counts) was gathered as well. Interventional cardiology parameters were recorded, including the procedural status, which comprised primary percutaneous coronary intervention (PPCI), rescue PCI, and early urgent PCI. Additionally, the time intervals from the onset of symptoms to the various PCI statuses were noted, along with the left ventricular ejection fraction.

The investigated electrophysiological parameters included the rate of ventricular fibrillation, as well as HRV assessed using both frequency-based and time-based methods. The time-based parameters of HRV were as follows:

SDNN: The standard deviation (SD) of the intervals between two normal beats (measured in ms)

SDANN: The average SD of the R-wave intervals compared to the subsequent R-wave intervals (measured in ms)

RMSSD: The square root of the mean squared differences of the R-wave intervals compared to the subsequent R-wave intervals (measured in ms)

pNN50: The proportion of pairs of consecutive normal-to-normal (NN) intervals that differ by more than 50 ms, expressed as the average number of occurrences per hour

The frequency parameters of HRV included:

LF: Low-frequency waves, measured in the range of 0.04–0.15 Hz (ms^2)

HF: High-frequency waves, measured in the range of 0.15–0.40 Hz (ms^2)

LF/HF Ratio: The ratio of the amplitude of low-frequency waves to the amplitude of high-frequency waves

TP: Total power, which represents the variance of all normal heartbeat intervals (measured in ms^2).

The data were entered and analyzed using the SPSS statistical program (version 26). Descriptive statistics were employed to summarize the data, including frequency counts for qualitative variables and means \pm SDs for quantitative variables. Finally, paired t-tests and analysis of variance were utilized to compare differences between quantitative variables. A significance level of $P < 0.05$ was considered statistically significant.

Results

Table 1 presents the frequency distribution of demographic data, including values related to age, height, weight, and body surface area. It also includes the period from symptom onset to hospital admission, the number of previously performed PCIs, plasma levels of creatinine, and the rate of creatinine clearance at the time of patient admission prior to coronary angiography. Additionally, the table outlines the time frame from symptom onset to hospital admission (door-to-needle time), the number of PCIs performed during hospitalization, the length of stay in the coronary care unit, and the total length of hospital stay.

Table 2 provides the results of time-based parameters, including SDNN, SDNN index, rMSSD, and pNN50, measured one week and one month after STEMI. The highest frequency for the SDNN parameter was observed in the range of 50–70 ms one week after the MI, while the most common range was 70–100 ms one month later. The SDNN values ranged from a minimum of 36 ms to a maximum of 442 ms one week post-MI and from 14 to 238 ms one month post-MI. Additionally, the results related to the SDNN index (the SD of the N-N interval

Table 1. Demographic and Clinical Data

Variable	Min.	Max.	Mean \pm SD
Age	26	87	60.8 \pm 11.3
Height	155	185	169.6 \pm 6.9
Weight	60	103	73.8 \pm 8.3
BSA	1.61	2.18	1.84 \pm 0.13
SDT	0.3	72	11.5 \pm 14.8
Number of previous PCI	0	1	0.2 \pm 0.4
Pre-angiography creatinine	0.5	1.5	0.92 \pm 0.19
Pre-angiography creatinine clearance	36.01	146.23	87.96 \pm 23
DNT	0.1	45	1.5 \pm 5.5
SNT	0.05	4.3	0.82 \pm 0.87
In-patient number of affected PCIs	0	3	1.1 \pm 0.5
CCU length of stay	2	15	3.7 \pm 2.1
Hospital length of stay	2	20	3.8 \pm 2.6

Note. Min.: Minimum; Max.: Maximum; SD: Standard deviation; SDT: Symptom-to-door time; PPCI: Primary percutaneous coronary intervention; PCI: Primary coronary intervention; BSA: Body surface area; CCU: Coronary care unit; DNT: Door-to-needle time (the time interval from emergency department admission to PPCI angiography); TSD: Time symptom to door (the time interval from symptom onset to emergency department admission); SNT: Symptom onset to needle time (the time interval from symptom onset to primary angiography).

index) indicated that the highest recorded frequency was less than 50 ms both one week and one month after the MI. One week after MI, the range of the SDNN index was from a minimum of 17 ms to a maximum of 278 ms, while one month after MI, its range was from 14 ms to 155 ms. Consequently, the highest frequency of rMSSD was recorded as less than 50 ms both one week and one month after the MI. One week after MI, the range of rMSSD was from a minimum of 10 ms to a maximum of 167 ms, and one month after MI, it ranged from 10 ms to 91 ms. Regarding the pNN50 parameter, the highest recorded frequency was less than 10 occurrences one week and one month after the MI. One week after MI, the range of pNN50 was from 0 to a maximum of 62 occurrences. However, one month after MI, it ranged from 0 to 66 occurrences.

Table 3 summarizes the results of frequency-based parameters, including high frequency (HF), low frequency (LF), and very low frequency (VLF), measured one week and one month after MI in patients with STEMI. For the HF parameter, the highest frequency was associated with fluctuations in the range of 100–200 Hz, both one week and one month after the MI. One week after MI, the HF range was from a minimum of 11.3 Hz to a maximum of 2051.8 Hz, while one month after MI, it ranged from 8.7 Hz to 1313.9 Hz. Regarding the LF parameter, the highest frequency related to oscillations was observed to be more than 300 Hz both one week and one month after the MI. The LF amplitude ranged from a minimum of 13.7 Hz to a maximum of 2288.7 Hz one week after MI, while it ranged from 1.8 Hz to 1948.4 Hz one month after MI. In terms of VLF, the results from patients with STEMI at Shahrekord Hajar Hospital confirmed that the highest frequency of

Table 2. Frequency Distribution of Time-Based Parameters One Week and One Month After MI in Patients With STEMI

Time Axes Parameters	Variables	After One Week	After One Month
		n (%)	n (%)
SDNN	< 50	9 (13)	4 (5.8)
	50-70	23 (33.3)	15 (21.7)
	70-100	17 (24.6)	25 (36.2)
	100-150	11 (15.9)	16 (23.2)
	> 150	9 (13)	9 (13)
SDNN index	< 50	40 (58)	36 (52.2)
	50-70	12 (17.4)	21 (30.4)
	70-100	6 (8.7)	6 (8.7)
	100-150	8 (11.6)	5 (7.2)
	> 150	3 (4.3)	1 (1.4)
rMSSD	< 50	58 (84.1)	58 (84.1)
	50-70	5 (7.2)	6 (8.7)
	70-100	4 (5.8)	5 (7.2)
	100-150	1 (1.4)	0 (0)
	> 150	1 (1.4)	0 (0)
pNN50	< 10	47 (68.1)	45 (65.2)
	10-20	10 (14.5)	12 (17.4)
	20-30	7 (10.1)	6 (8.7)
	> 30	5 (7.2)	6 (8.7)

Note. MI: Myocardial infarction; STEMI: ST-segment elevation myocardial infarction; SDNN: Standard deviation of normal-to-normal intervals. rMSSD: The root mean square of successive differences; pNN50: The percentage of successive RR intervals that differ by more than 50 ms.

VLF was less than 500 Hz one week after MI, and it was in the range of 500–1000 Hz one month after MI. One week after MI, the VLF amplitude ranged from a minimum of 43.4 Hz to a maximum of 2923 Hz, while one month after MI, it ranged from 1.94 Hz to 14697.4 Hz.

Table 4 lists the comparison results related to average heart rate indices one week and one month after MI in patients with STEMI. Although the values of the SDNN and the SDNN index were lower one month after MI than those recorded one week after MI, there was no statistically significant difference between the values at these two time points ($P=0.396$ and $P=0.378$, respectively). The mean values of rMSSD and pNN50 showed a slight increase one month after MI; however, this change was not statistically significant ($P=0.568$ and $P=0.847$, respectively). Conversely, one month after MI, the average triangle index was significantly higher than the value recorded one week after MI ($P<0.001$). The mean indices of HF, LF, and VLF did not differ significantly ($P>0.05$).

Discussion

The present study investigated the effect of the timing of PPCI on fluctuations in the electrical activity of the heart following the onset of symptoms in patients with STEMI. The results demonstrated that none of the patients had a history of coronary artery bypass grafting (CABG); however, 16.4% of the patients reported a history of PCI.

Table 3. Frequency Distribution of Frequency-Based Parameters One Week and One Month After MI in Patients With STEMI

Time Axes Parameters	Variables	After One Week	After One Month
		n (%)	n (%)
HF	<50	13 (18.8)	10 (1.5)
	50-100	16 (23.2)	17 (24.6)
	100-200	17 (24.6)	18 (26.1)
	200-300	7 (10.1)	8 (11.6)
	>300	16 (23.2)	16 (23.2)
LF	<50	6 (8.7)	4 (5.8)
	50-100	12 (17.4)	6 (8.7)
	100-200	15 (21.7)	12 (17.4)
	200-300	10 (1.5)	12 (17.4)
	>300	26 (37.7)	35 (50.7)
VLF	<500	38 (55.1)	18 (26.1)
	500-1000	20 (29)	31 (44.9)
	1000-2000	6 (8.7)	15 (21.7)
	>2000	5 (7.2)	5 (7.2)

Note. MI: Myocardial infarction; STEMI: ST-Segment elevation myocardial infarction; HF: High frequency; LF: Low frequency; VLF: Very low frequency.

In terms of coronary artery involvement, 58.9%, 20.5%, and 4.1% of patients had one vessel, two vessels, and three coronary vessels affected, respectively. Additionally, complete vessel occlusion was observed in 46.6% of patients, while proximal arterial occlusion was noted in 50.7% of cases. Following hospital admission, PCI and CABG were performed in 95.1% and 1.4% of patients, respectively. In addition to controlling risk factors, the management of CAD encompasses pharmacotherapy and the restoration of coronary flow in affected arteries through CABG and/or PCI. Although pharmacotherapy remains the cornerstone of treatment for patients with CAD, many individuals can be effectively treated with PCI (33). The therapeutic efficacy of primary PCI in patients with STEMI has been well established; however, ongoing studies are expected to provide further insights into the optimal clinical pathways for managing STEMI (34).

Our findings revealed that the average creatinine level before angiography was 0.92 mg/dL, with a creatinine clearance of 87.96 mL/minute. Moreover, 52.3% of patients exhibited a creatinine clearance greater than 85 mL/minute, while 47.7% had values between 35 mL/minute and 85 mL/minute. Renal injury caused by contrast agents is the third most common cause of acute renal failure, following hypotension and surgical procedures in a hospital setting. Individuals with a history of renal failure, particularly those with diabetic nephropathy, congestive heart failure, hypotension, high volumes of contrast agent exposure, and concurrent use of nephrotoxic medications, are at increased risk (35). The precise mechanism underlying renal impairment due to contrast agents remains unclear; however, it is believed to be associated with the toxic effects of these agents on renal tubular cells and increased oxidative stress. Various substances have been investigated

Table 4. Comparison Results of Average Indicators of Heart Electrical Activity Fluctuations One Week and One Month After MI

Variables	After One Week	After One Month	P value
	Mean \pm SD	Mean \pm SD	
SDNN	115.7 \pm 160.3	99.1 \pm 41.5	0.396
SDNN index	57.3 \pm 4.1	52.8 \pm 27.2	0.378
rMSSD	34.3 \pm 25.4	32.8 \pm 17.3	0.568
pNN50	10.5 \pm 13	10.7 \pm 13.2	0.847
Triangle	14.9 \pm 6.8	19.7 \pm 7.8	0.001
HF	257.8 \pm 389.3	238.3 \pm 288.4	0.282
LF	342.6 \pm 387.5	433.8 \pm 380.5	0.102
VLF	650.2 \pm 637.4	1085.3 \pm 1756.7	0.051

Note. MI: Myocardial infarction; SD: Standard deviation; SDNN: Standard deviation of normal-to-normal intervals; rMSSD: The root mean square of successive differences; pNN50: The percentage of successive RR intervals that differ by more than 50 ms; HF: High frequency; LF: Low frequency; VLF: Very low frequency.

for their potential to mitigate the adverse effects of contrast agents on renal function. Among them, N-acetylcysteine, theophylline, sodium bicarbonate, HMG-CoA reductase inhibitors, ascorbic acid, diuretics, and phenol-dopamine have undergone evaluation (36, 37).

Based on our results, electrocardiogram (ECG) changes were observed in 82.2% of patients. Conduction disturbances were noted in 5.5% of patients, while atrial and ventricular fibrillation rhythm disturbances occurred in 1.4% and 2.7%, respectively. ST-segment elevation affected the inferior and anterior leads in 32.3% and 58.5% of patients, respectively. The incidence of supraventricular arrhythmias before and after STEMI was 4.1%. Premature ventricular contractions were observed in 6.8% of patients before STEMI and in 8.2% after STEMI. Additionally, premature atrial contractions were present in 4.1% and 7.2% of patients before and after STEMI, respectively.

The primary focus is to manage acute coronary syndrome (ACS) in patients admitted to cardiology emergency units. Therefore, accurately estimating the prognosis of each patient with ACS is of significant importance in daily clinical practice (38). ACS encompasses three electrophysiological entities, namely, unstable angina, non-STEMI, and STEMI (39, 40). The results reported by Savonitto et al demonstrated the feasibility of estimating a patient's prognosis with a high degree of accuracy based on the admission ECG (41). Factors such as the patient's vital signs, ECG changes, cardiac enzyme levels, and results from echocardiography and exercise tests contribute to the patient's prognosis (41). The results of the study by Miri et al indicated that the presence of ST-segment elevation and depression, whether alone or in combination, was associated with increased overall mortality. In contrast, an inverted T wave was not linked to a worse prognosis. Among the ECG disturbances related to ACS, ST-segment depression was associated with the worst prognosis, while the presence of an inverted T wave was associated with the best prognosis (42). Cohen et al (1991) found a negative correlation between the number of leads exhibiting ST-

segment changes at patient admission and the incidence of major adverse cardiac events (38). Several factors contribute to the better prognosis of patients with inverted T-waves compared to the higher mortality rates observed in patients with ST-segment elevation or depression, either alone or in combination. One key reason is that inverted T-waves typically indicate only myocardial ischemia or limited necrosis, which allows for the timely initiation of appropriate anti-ischemic therapy. In contrast, ST-segment changes reflect more severe ischemia and a larger area of jeopardized myocardium (42).

The findings of the current study identified the left anterior descending (LAD) and the right coronary artery as the most frequently involved culprit arteries in cases of STEMI, with stenosis ranging from 70% to 100%. Regarding coronary dominance, right dominance was observed in 93.8% of the coronary angiographies performed, followed by left dominance. In terms of anatomical lesion topography, 50.7% of the vascular stenosis occurred in the middle segment, while 26% was found in the distal segment of the culprit arteries. Abdollahi et al reported that the incidence of culprit lesions with less than 50% stenosis involving the LAD, right coronary artery, left circumflex artery, and obtuse marginal branches was 28.1%, 16%, 25.8%, and 39%, respectively (43). Nozari et al concluded that the highest percentages of culprit lesions affecting the left circumflex artery and the LAD branches were 62.5% and 20.2%, respectively (44). Given the wide spectrum of possible combinations of culprit lesions observed at the time of ACS presentation, a thorough analysis of lesion anatomy is valuable for scoring systems (45). The ACS scoring systems primarily consider the number of involved vessels, the severity of stenosis, the anatomical topography of culprit lesions, and the length of the lesions. Additionally, the location of the stenosis—whether distal or proximal—and the feasibility of performing PPCI play a critical role in patient prognosis. Therefore, an accurate pre-procedural assessment of the anatomical characteristics of the culprit lesions significantly enhances PCI outcomes while reducing associated complications (46).

Conclusion

The results revealed that there was no significant difference in HRV indices in patients suffering from STEMI one week and one month after the MI. Although changes in SDNN and the SDNN index did not reach statistical significance, the averages for the rMSSD and pNN50 increased non-significantly one month after the occurrence of STEMI. Additionally, HFV decreased one month after the MI, while LF and VLF components increased non-significantly. The triangle index showed a significant increase one month after the MI. Despite the association of low HRV with sustained underlying ischemia and high HRV reflecting optimal responsiveness of the cardiac autonomic nervous system, the results demonstrated no significant predictive value for HRV following STEMI.

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Competing Interests

The second author of this article serves as the deputy editor of the journal; however, the evaluation and review process for this article was conducted in the same manner as for all other submissions. There is no conflict of interests to report regarding this matter.

Ethical Approval

This study was approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1399.166).

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References

1. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: epidemiological update. *Eur Heart J*. 2014;35(42):2950-9. doi: [10.1093/eurheartj/ehu299](https://doi.org/10.1093/eurheartj/ehu299).
2. Bonnemeier H, Hartmann F, Wiegand UK, Irmer C, Kurz T, Tölg R, et al. Heart rate variability in patients with acute myocardial infarction undergoing primary coronary angioplasty. *Am J Cardiol*. 2000;85(7):815-20. doi: [10.1016/s0002-9149\(99\)00873-5](https://doi.org/10.1016/s0002-9149(99)00873-5).
3. Pipilis A, Flather M, Ormerod O, Sleight P. Heart rate variability in acute myocardial infarction and its association with infarct site and clinical course. *Am J Cardiol*. 1991;67(13):1137-9. doi: [10.1016/0002-9149\(91\)90880-t](https://doi.org/10.1016/0002-9149(91)90880-t).
4. Feng J, Wang A, Gao C, Zhang J, Chen Z, Hou L, et al. Altered heart rate variability depend on the characteristics of coronary lesions in stable angina pectoris. *Anatol J Cardiol*. 2015;15(6):496-501. doi: [10.5152/akd.2014.5642](https://doi.org/10.5152/akd.2014.5642).
5. Oktaramdani T, Mudjaddid E, Muhadi, Shatri H. Increased heart rate variability following elective percutaneous coronary intervention in patients with stable coronary artery disease and preprocedural anxiety. *Cardiol Res Pract*. 2019;2019:3696825. doi: [10.1155/2019/3696825](https://doi.org/10.1155/2019/3696825).

6. Sztajzel J. Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system. *Swiss Med Wkly.* 2004;134(35-36):514-22. doi: [10.4414/smw.2004.10321](https://doi.org/10.4414/smw.2004.10321).
7. Björkander I, Forslund L, Ericson M, Rehnqvist N, Hjemdahl P, Kahan T. Long-term stability of heart rate variability in chronic stable angina pectoris, and the impact of an acute myocardial infarction. *Clin Physiol Funct Imaging.* 2009;29(3):201-8. doi: [10.1111/j.1475-097X.2009.00857.x](https://doi.org/10.1111/j.1475-097X.2009.00857.x).
8. Musialik-Lydk A, Sredniawa B, Pasyk S. Heart rate variability in heart failure. *Kardiologia Pol.* 2003;58(1):10-6.
9. Buccelletti E, Gilardi E, Scaini E, Galiuto L, Persiani R, Biondi A, et al. Heart rate variability and myocardial infarction: systematic literature review and meta-analysis. *Eur Rev Med Pharmacol Sci.* 2009;13(4):299-307.
10. Futterman LG, Lemberg L. Heart rate variability: prognostic implications. *Am J Crit Care.* 1994;3(6):476-80.
11. Markuszewski L, Bissinger A. [Application of heart rate variability in prognosis of patients with diabetes mellitus]. *Pol Merkuriusz Lekarski.* 2005;19(112):548-52. [Polish].
12. Lombardi F, Sandrone G, Spinnler MT, Torzillo D, Lavezzaro GC, Brusca A, et al. Heart rate variability in the early hours of an acute myocardial infarction. *Am J Cardiol.* 1996;77(12):1037-44. doi: [10.1016/s0002-9149\(96\)00127-0](https://doi.org/10.1016/s0002-9149(96)00127-0).
13. Abrootan S, Yazdankhah S, Payami B, Alasti M. Changes in heart rate variability parameters after elective percutaneous coronary intervention. *J Tehran Heart Cent.* 2015;10(2):80-4.
14. Pivatelli FC, Dos Santos MA, Fernandes GB, Gatti M, de Abreu LC, Valenti VE, et al. Sensitivity, specificity and predictive values of linear and nonlinear indices of heart rate variability in stable angina patients. *Int Arch Med.* 2012;5(1):31. doi: [10.1186/1755-7682-5-31](https://doi.org/10.1186/1755-7682-5-31).
15. Abdelnaby MH. Effect of percutaneous coronary intervention on heart rate variability in coronary artery disease patients. *Eur Cardiol.* 2018;13(1):60-1. doi: [10.15420/eur.2018.13.2](https://doi.org/10.15420/eur.2018.13.2).
16. Odemuyiwa O, Farrell TG, Malik M, Bashir Y, Millane T, Cripps T, et al. Influence of age on the relation between heart rate variability, left ventricular ejection fraction, frequency of ventricular extrasystoles, and sudden death after myocardial infarction. *Br Heart J.* 1992;67(5):387-91. doi: [10.1136/hrt.67.5.387](https://doi.org/10.1136/hrt.67.5.387).
17. Farrell TG, Bashir Y, Cripps T, Malik M, Poloniecki J, Bennett ED, et al. Risk stratification for arrhythmic events in postinfarction patients based on heart rate variability, ambulatory electrocardiographic variables and the signal-averaged electrocardiogram. *J Am Coll Cardiol.* 1991;18(3):687-97. doi: [10.1016/0735-1097\(91\)90791-7](https://doi.org/10.1016/0735-1097(91)90791-7).
18. Ebrahimzadeh E, Pooyan M. Prediction of sudden cardiac death (SCD) using time-frequency analysis of ECG signals. *Comput Intell Electr Eng.* 2013;3(4):15-26. [Persian].
19. Sedziwy E, Olszowska M, Tracz W, Pieniazek P. [Heart rate variability in patients treated with percutaneous transluminal coronary angioplasty]. *Przegl Lek.* 2002;59(9):695-8. [Polish].
20. Sosnowski M, MacFarlane PW, Czyz Z, Skrzypek-Wańha J, Boczkowska-Gaik E, Tendera M. Age-adjustment of HRV measures and its prognostic value for risk assessment in patients late after myocardial infarction. *Int J Cardiol.* 2002;86(2-3):249-58. doi: [10.1016/s0167-5273\(02\)00301-7](https://doi.org/10.1016/s0167-5273(02)00301-7).
21. Janatifard N, Salmani F. The effect of early mobilization program on incidence of arrhythmias in patients after acute myocardial infarction. *Iran J Cardiovasc Nurs.* 2019;8(1):64-71. [Persian].
22. Adnan R, Hashemi Fard A, Saffari SE. The effective factors on the number of hospitalization days for MI patients in Vasei hospital of Sabzevar in 2012 using regression models. *J Sabzevar Univ Med Sci.* 2014;20(4):447-56. [Persian].
23. Mohammadian-Hafshejani A, Baradaran Attar Moghaddam H, Sarrafzadegan N, Asadi Lari M, Roohani M, Allah-Bakhshi F, et al. Secular trend changes in mean age of morbidity and mortality from an acute myocardial infarction during a 10-year period of time in Isfahan and Najaf Abad. *J Shahrekord Univ Med Sci.* 2013;14(6):101-14. [Persian].
24. Mahmoodi MR, Kimiagar SM, Abadi AR. Gender difference in myocardial infarction events between patients with and without conventional risk factors: the Modares Heart Study. *Iranian J Nutr Sci Food Technol.* 2007;2(3):65-72. [Persian].
25. Pinkel D. The use of body surface area as a criterion of drug dosage in cancer chemotherapy. *Cancer Res.* 1958;18(7):853-6.
26. Zafir B, Salman N, Crespo-Leiro MG, Anker SD, Coats AJ, Ferrari R, et al. Body surface area as a prognostic marker in chronic heart failure patients: results from the Heart Failure Registry of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail.* 2016;18(7):859-68. doi: [10.1002/ehf.551](https://doi.org/10.1002/ehf.551).
27. Roy SK, Zeb I, Kadakia J, Li D, Budoff MJ. Body surface area is a predictor of coronary artery calcium, whereas body mass index is not. *Coron Artery Dis.* 2012;23(2):113-7. doi: [10.1097/MCA.0b013e32834f1b72](https://doi.org/10.1097/MCA.0b013e32834f1b72).
28. Poursheykhian M, Moghadamnia MT, Nasirzadeh F. Duration of chest pain to hospitalization in cardiac center, in acute myocardial infarction cases admitted, in Rasht, in 2005. *Sci J Forensic Med.* 2008;13(4):228-34. [Persian].
29. Afrasiabi A, Hasanazadeh Salmasi S. The effect of delay in time from onset of acute chest pain to admission to coronary care unit in patients with acute myocardial infarction. *Med J Tabriz Univ Med Sci.* 2002;36(56):22-6. [Persian].
30. Rafi A, Sayeed Z, Sultana P, Aik S, Hossain G. Pre-hospital delay in patients with myocardial infarction: an observational study in a tertiary care hospital of northern Bangladesh. *BMC Health Serv Res.* 2020;20(1):633. doi: [10.1186/s12913-020-05505-x](https://doi.org/10.1186/s12913-020-05505-x).
31. Ebrahimi K, Khadem Vatan K, Salarilak S, Gharaaghaji R. Epidemiological features of risk factors occurrence and outcomes of myocardial infarction in patients admitted to hospitals in West Azerbaijan province during the years 2011 and 2012. *Stud Med Sci.* 2015;26(8):724-34. [Persian].
32. Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J. *Harrison's Principles of Internal Medicine.* New York: McGraw-Hill Education; 2018.
33. Yousefnejad K, Masoumi S. Long-term clinical outcome after implantation of second-generation bare-metal stents. *J Mazandaran Univ Med Sci.* 2008;17(62):21-30. [Persian].
34. Safi M, Mohammadpour M, Mojtahedzadeh M, Otoukesh S, Vakili H. Comparison between primary PCI and thrombolytic therapy results in patients with acute ST-elevation MI. *Pajooohandeh.* 2010;14(6):332-6. [Persian].
35. Goldenberg I, Shechter M, Matetzky S, Jonas M, Adam M, Pres H, et al. Oral acetylcysteine as an adjunct to saline hydration for the prevention of contrast-induced nephropathy following coronary angiography. A randomized controlled trial and review of the current literature. *Eur Heart J.* 2004;25(3):212-8. doi: [10.1016/j.ehj.2003.11.011](https://doi.org/10.1016/j.ehj.2003.11.011).
36. Ala SH, Mohseni A, Tabiban S, Ghezlbash Z, Hendouie N. The study of the efficacy of N-acetylcysteine for the prevention of contrast induced nephropathy in normal renal functioning patients undergoing coronary angiography. *J Mazandaran Univ Med Sci.* 2007;17(60):102-7. [Persian].
37. Allaqaband S, Tumuluri R, Malik AM, Gupta A, Volkert P, Shalev Y, et al. Prospective randomized study of N-acetylcysteine, fenoldopam, and saline for prevention of radiocontrast-induced nephropathy. *Catheter Cardiovasc Interv.* 2002;57(3):279-83. doi: [10.1002/ccd.10323](https://doi.org/10.1002/ccd.10323).
38. Cohen M, Hawkins L, Greenberg S, Fuster V. Usefulness of ST-segment changes in ≥ 2 leads on the emergency room electrocardiogram in either unstable angina pectoris or

- non-Q-wave myocardial infarction in predicting outcome. *Am J Cardiol.* 1991;67(16):1368-73. doi: [10.1016/0002-9149\(91\)90467-y](https://doi.org/10.1016/0002-9149(91)90467-y).
39. Bhatheja R, Mukherjee D. Acute coronary syndromes: unstable angina/non-ST elevation myocardial infarction. *Crit Care Clin.* 2007;23(4):709-35. doi: [10.1016/j.ccc.2007.07.003](https://doi.org/10.1016/j.ccc.2007.07.003).
 40. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. *Harrison's Principles of Internal Medicine.* 19th ed. New York: McGraw-Hill; 2015.
 41. Savonitto S, Ardissino D, Granger CB, Morando G, Prando MD, Mafriqi A, et al. Prognostic value of the admission electrocardiogram in acute coronary syndromes. *JAMA.* 1999;281(8):707-13. doi: [10.1001/jama.281.8.707](https://doi.org/10.1001/jama.281.8.707).
 42. Miri R, Asadzadeh R, Mirzaie V. Surveying primary ECG findings in emergency unit and prognosis of acute coronary syndrome. *Pajoohandeh.* 2009;14(4):215-8. [Persian].
 43. Abdollahi AA, Hoseini SA, Salehi A, Behnampour N, Abasi A. Coronary artery lesions and some of its related factors in more than 5000 patients in Kosar angiography center (Golestan province) from 2007 to 2009. *Sci J Kurdistan Univ Med Sci.* 2012;17(1):18-24. [Persian].
 44. Nozari Y, Gaemian A, Safir Mardanloo A. Predictors of Side Branch Compromise and related early complications after percutaneous coronary intervention. *Tehran Univ Med J.* 2007;65(3):30-5. [Persian].
 45. Wilson SH, Celermajer DS, Nakagomi A, Wyndham RN, Janu MR, Ben Freedman S. Vascular risk factors correlate to the extent as well as the severity of coronary atherosclerosis. *Coron Artery Dis.* 1999;10(7):449-53. doi: [10.1097/00019501-199910000-00003](https://doi.org/10.1097/00019501-199910000-00003).
 46. Younessi Heravi MA, Mojdekanlu M, Seyed Sharifi SH, Yaghubi M. Role of cardiovascular risk factors in involvement of coronary arteries a predictive model in angiographic study. *J North Khorasan Univ Med Sci.* 2014;6(1):199-205. doi: [10.29252/jnkums.6.1.199](https://doi.org/10.29252/jnkums.6.1.199). [Persian].