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Comp Less Recognized ECG Changes Associated with Significant Ischemia, Concerning the Minnesota Coding System

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Abstract

Background: An electrocardiogram (ECG) is a commonly used, noninvasive, cost-effective tool widely available for diagnosing patients with coronary artery disease. It is associated with significant myocardial ischemia due to Coronary artery disease (CAD), which is associated with specific ECG changes.

Objectives: The goals were to determine less well-known ECG changes associated with significant ischemia and assess their potential value as early markers for diagnosing myocardial ischemia in patients with CAD.

Methods: Data were obtained from participants in the MASHAD cohort study. The characteristics obtained, including fasting blood glucose, lipid profile, history of diabetes mellitus, history of hypertension, and history of previous CVD, were recorded. A 12-lead ECG was also obtained for each subject and coded for specific ECG changes using Minnesota (MN) codes. Patients were divided into two groups based on MN coding for significant ischemia. A p-value less than 0.05 was considered significant.

Results: Out of 9035 coded ECGs,1276 (14.1%) had significant myocardial ischemia. After applying backward binary logistic regression, left- and right-axis deviations were significantly associated with significant ischemia (OR=2.482, p<0.001; OR=2.757, p=0.023, respectively). Left Ventricular (OR=2.171, p=0.020) and right ventricular hypertrophy (OR=5.747, p=0.004) showed significant associations. Other indicators, including minor T-wave abnormalities (OR=3.249, p<0.001), left anterior hemiblock (OR=4.711, p=0.001), and notched and widened P wave (OR=2.415, p<0.001), were also significantly associated with significant ischemia.

Conclusion: These findings suggest that the identified ECG changes may serve as novel indicators or associated markers of central ischemia. However, more longitudinal studies are needed to evaluate each of these abnormalities in patients with CAD.

Keywords: Coronary Artery Disease, Electrocardiogram, Minnesota Codes, Myocardial Ischemia

1. Background

Cardiovascular disease (CVD), including ischemic heart disease, stroke, peripheral arterial disease, heart failure, and various other vascular and cardiac issues, stands as

the primary cause of death worldwide (1). Coronary artery disease (CAD), also referred to as atherosclerotic heart disease (AHD), coronary heart disease (CHD), and ischemic heart disease (IHD), is the most prevalent form of cardiac pathology that accounts for more than half of all CVD deaths (2, 3).

An electrocardiogram (ECG) is a commonly used noninvasive test performed on individuals suspected of cardiac disease and is a fundamental diagnostic tool (4). It is the most readily available and cost-effective diagnostic assessment in cardiology. The ECG provides insights into the heart's electrical function by displaying its component waves: P, QRS, and T. Extracting ECG features is vital for diagnosing various cardiac conditions. Over the last few years, the publication of numerous innovative ECG parameters and patterns has enabled us to perform a more advanced evaluation of cardiac function (5, 6).

The Minnesota (MN) code provides an objective system for classifying ECG patterns, suitable for use in human studies and subsequent statistical analysis. It comprises nine main classes, each objectively describing an aspect of the ECG. Additionally, it encompasses various ECG codification classes (7).

Standard ECG interpretation is considered a sensitive and specific tool for diagnosing CAD (8). In this study, we aimed to shed light on the intricate relationship between ECG changes according to the MN coding system and the presence of significant ischemia. Alterations in the Q wave, ST segment, and T wave defined significant ischemic changes in the ECG. This exploration not only contributes to the theoretical foundations of cardiology but also has practical implications for the clinical management of patients with CAD and related ischemic conditions, ultimately advancing the landscape of cardiovascular care.

2. Objective

In this study, the attempt is to reveal some less prominent ECG alterations that could possibly be linked to severe myocardial ischemia in patients with CAD, using the Minnesota Code. This would help investigate the possibility of employing such least recognized ECG anomalies for the earliest detection of ischemia.

3. Methods

Study design and data collection

In this cross-sectional study, data were collected from a population-based cohort (MASHAD) that began in 2010 (9). Using stratified cluster random sampling, 9,704 subjects aged 35-65 were recruited for this study from three urban regions of Mashhad (the second-largest city in Iran). Participants' demographics, physical exercise, nutritional intake, anthropometric, and disease history were recorded. Fasting blood glucose (FBG) and lipid profile, history of diabetes mellitus (DM), hypertension (HTN), and CVD, and resting 12-lead ECG, and their relative coding based on the MN coding system (10), were performed according to the procedure used in our previous study (11). In brief, 9035 available standard 12-lead ECGs were coded. Ten trained medical students generated ECG codes, and three cardiologists confirmed 5% of all ECGs. The study protocol was approved by Mashhad University of Medical Sciences (MUMS) (IR.MUMS.MEDICAL.REC.1399.783) in accordance with the Helsinki ethical principles for medical research. Informed consent was taken from all the subjects.

Significant ischemia changes in the ECG

Significant ischemic changes in ECG were defined using specific MN codes including (1) significant Q-wave abnormalities (MN-1-1 and MN-1-2); (2) minor Q-wave abnormalities (MN-1-3) plus ST segment

and T-wave abnormalities (MN-4-1, MN-4-2, MN-5-1, and MN-5-2); and (3) significant isolated ST segment and T wave abnormalities (MN-4-1, MN-4-2, MN-5-1, and MN-5-2). The definitions of each code are shown in Table 1.

Table 1. Summarized definition of MN codes used to specify significant ischemia in ECG (10)

MN code	Definition
MN-1-1	Q/R amplitude ratio ≥ 1/3 s, plus Q duration ≥ 0.03 s in any leads I,II, V1-V6 or Q duration ≥ 0.04 s in any leads I, II, V1-V6 or Q duration ≥ 0.04 s plus R amplitude ≥ 3 mm in lead aVL
MN-1-2	Q/R amplitude ratio ≥ 1/3, plus Q duration ≥ 0.02 s and < 0.03 s in any leads I, II, V1-V6 or Q duration ≥ 0.03 s and < 0.04 s in any leads I, II, V1-V6 or QS pattern in any leads I, II, V1-V3 (if complete left bundle branch block is not present) or Q duration ≥ 0.04 s and < 0.05 s in lead III, plus a Q-wave ≥ 1.0 mm amplitude in lead aVF or Q duration ≥ 0.04 s and < 0.05 s in lead aVF
MN-1-3	Q/R amplitude ratio ≥ 1/5 and < 1/3, plus Q duration ≥ 0.02 s and < 0.03 s in any leads of I, II, or V2-V5 or QS pattern in each lead of III, aVF, V1, and V2 (if left ventricular hypertrophia or complete left bundle branch block are not present) or Q duration ≥ 0.03 s and < 0.04 s, plus R amplitude ≥ 3 mm in lead aVL
MN-4-1	STJ depression ≥ 1.0 mm, and ST segment horizontal or downward sloping in any leads I, II, aVF, aVL, or V1-V6
MN-4-2	STJ depression ≥ 0.5 mm but < 1.0 mm and ST segment horizontal or downward sloping in any leads I, II, aVF, aVL, or V1-V6
MN-5-1	T amplitude negative 5.0 mm or more in any leads I, II, aVF, aVL, or V1-V5 when R amplitude is ≥ 5.0 mm.
MN-5-2	T amplitude negative or diphasic (positive–negative or negative–positive type) with negative phase at least 1.0 mm but not as deep as 5.0 mm, any leads I, II, aVF, aVL, or V1-V5 when R amplitude is ≥ 5.0 mm
Abbreviation: MN, Minnesota	

Statistical analysis

All data analyses were conducted using SPSS software version 25. Results are shown as absolute numbers (n), mean ± standard deviation, and frequencies (%). To compare ECG changes between participants with and without significant ischemic changes, the chi-squared test was used. Furthermore, to construct a model and feature selection, backward binary logistic regression was applied to the data. Significance was described as $p < 0.05$.

4.Result

A total of 9035 readable ECGs were included, comprising 3615 (40.0%) males and 5420 (60.0%) females. The average age for participants was 48.91 ± 8.40 years in men and 47.60 ± 8.09 years in women. Baseline characteristics, including employment status, smoking habits, body mass index (BMI), diabetes mellitus, hypertension, and CVD, are presented in Table 2.

Table 2. Baseline characteristics of the studied population

Baseline characteristics		Men	Women
Age (mean±SD)(year)		48.91±8.40	47.60±8.09
Employment status N (%)	Student	10 (0.3)	8 (0.1)
	Employment	2627 (73.5)	693 (13.0)
	Unemployment	284 (7.9)	4393 (82.3)
	Retired	653 (18.3)	243 (4.6)
Smoking N (%)	Non-smoker	2075 (58.0)	4064 (76.1)
	Ex-smoker	538 (15.0)	331 (6.2)
	Current smoker	962 (26.9)	945 (17.7)
BMI (mean±SD)(kg/m^2)		26.34±4.15	28.91±4.83
Diabetes mellitus N (%)		479 (13.6)	769 (14.6)
Hypertension N (%)		1031(28.9)	1712 (32.1)
Cardiovascular diseases N (%)		91 (2.5)	59 (1.1)

The relation between significant ischemia in the ECG and the Minnesota codes

Out of 9035 participants, 1276 (14.1%) had significant myocardial ischemia according to the MN coding system. The detailed prevalence of Minnesota codes for significant ischemia is shown in Table 3.

Table 3. Relation between significant ischemia in ECG and Minnesota codes

Code		Significant ischemia in ECG*		P value#
		No (N= 7759)	Yes (N=1276)	
QRS axis deviation				
2-1	Left axis deviation	242 (3.1)	104 (8.2)	<0.001
2-2	Right axis deviation	18 (0.2)	7 (0.5)	0.053
2-3	Right axis deviation	19 (0.2)	23 (1.8)	<0.001
2-4	Extreme axis deviation	2 (0.0)	4 (0.3)	0.005
2-5	Intermediate axis	6 (0.1)	9 (0.7)	<0.001
Ventricular hypertrophy				
3-1	Left	34 (0.4)	13 (1.0)	0.011
3-2	Right	6 (0.1)	5 (0.4)	0.012
Minor ST-segment abnormalities				
4-3		6 (0.1)	1 (0.1)	0.656
4-4		43 (0.6)	5 (0.4)	0.311
Minor T-wave abnormalities				
5-3		146 (1.9)	75 (5.9)	<0.001
5-4		39 (0.5)	16 (1.3)	0.003
A-V conduction defect				
6-2-1	Mobitz type II	2 (0.0)	0 (0.0)	0.737
6-2-3	Wenckebach's Phenomenon	1 (0.0)	0 (0.0)	0.859
6-3	PR interval >0.22 s	22 (0.3)	3 (0.2)	0.521
6-5	Short PR interval	11 (0.1)	1 (0.1)	0.478
Ventricular conduction defect				
7-1-1	LBBB	33 (0.4)	12 (0.9)	0.019
7-1-2	Intermittent LBBB	2 (0.0)	0 (0.0)	0.737
7-2-1	RBBB	20 (0.3)	6 (0.5)	0.151
7-3	Intermittent RBBB	6 (0.1)	2 (0.2)	0.315
7-4	Intraventricular block	3 (0.0)	0 (0.0)	0.633
7-5	R-R′ pattern	41 (0.5)	12 (0.9)	0.062
7-6	Incomplete LBBB	8 (0.1)	2 (0.2)	0.423
7-7	LAH	8 (0.1)	12 (0.9)	<0.001
7-9-1	Type 1 Brugada pattern	0 (0.0)	1 (0.1)	0.141
7-9-2	Type 2 Brugada pattern	15 (0.2)	1 (0.1)	0.318
7-9-3	Type 3 Brugada pattern	10 (0.1)	0 (0.0)	0.218
7-10	Fragmented QRS	125 (1.6)	24 (1.9)	0.274
Arrhythmias				
8-1-1	PAC	23 (0.3)	4 (0.3)	0.542
8-1-2	PVC	90 (1.2)	18 (1.4)	0.445
8-1-4	Wandering pacemaker	1 (0.0)	0 (0.0)	0.859
8-1-5	Premature beats	1 (0.0)	0 (0.0)	0.859
8-2-2	Persistent ventricular (idio-ventricular) rhythm	0 (0.0)	1 (0.1)	0.141
8-2-3	Intermittent VT	1 (0.0)	0 (0.0)	0.859
8-2-4	Ventricular parasystole	1 (0.0)	0 (0.0)	0.859
8-4-1	SV rhythm persistent	4 (0.1)	0 (0.0)	0.544
8-3-1	AF	1 (0.0)	3 (0.2)	0.010
8-3-3	Intermittent AF	0 (0.0)	1 (0.1)	0.141
8-5-1	Sinoatrial arrest	3 (0.0)	2 (0.2)	0.149
8-5-2	Sinoatrial block	8 (0.1)	0 (0.0)	0.296
8-7	Sinus tachycardia	121 (1.6)	19 (1.5)	0.850
8-8	Sinus bradycardia	207 (2.7)	46 (3.6)	0.040
8-9	Arrhythmias	3 (0.0)	1 (0.1)	0.456

Miscellaneous				
9-1	Low QRS amplitude	140 (1.8)	19 (1.5)	0.427
9-2	STE	359 (4.6)	77 (6.0)	0.020
9-3	Tall P wave	31 (0.4)	6 (0.5)	۰/۴۲۶
9-5	Tall T-wave	60 (0.8)	8 (0.6)	0.363
9-6	Notched and widened P wave	148 (1.9)	59 (4.6)	<0.001
9-7-1	Definite ER	44 (0.6)	3 (0.2)	0.085
9-7-2	Probable ER	49 (0.6)	1 (0.1)	<0.004

*** Expressed as a number (percent)**
 # p-value according to the chi-square test
Abbreviations: LBBB, left bundle branch block; RBBB, right bundle branch block; LAH, Left anterior hemi-block; PAC, premature atrial complex; PVC, premature ventricular complex; VT, Ventricular tachycardia; SV, Supraventricular AF, Atrial fibrillation; AFL, Atrial flutter; STE, ST segment elevation; Tall P wave, P-wave amplitude ≥ 2.5 mm; Tall T-wave, T wave amplitude > 12 mm; ER, early repolarization.

QRS Axis Deviation

Among QRS axis deviations, left and right (from +90° through +119°) QRS axis deviations were more prevalent. Left QRS axis deviation, right QRS axis deviation, and indeterminate QRS axis had a significant relationship with ischemia (p<0.001). Extreme axis deviation was also a significant indicator of ischemia (p=0.005). Right QRS axis deviation (from +120° to –150°) was more prevalent among patients with significant ischemia. In univariate analysis, Right Axis Deviation did not reach statistical significance (p=0.053); however, it showed a significant association in the multivariate regression model (p=0.023).

High Amplitude R Waves

Left ventricular hypertrophy (LVH) and right ventricular hypertrophy showed a significant relationship with ischemia (p=0.011 and p=0.012, respectively).

Minor ST Junction (J) and Segment Depression

Minor ST junction and segment depression is represented by STJ depression as much as 0.5 mm, but ST segment downward sloping and segment or T-wave nadir ≥ 0.5 mm below P-R baseline (4-3) and STJ depression ≥ 1.0 mm and ST segment upward sloping, or U-shaped (4-4). Code 4-3 occurred with the same frequency in patients with significant ischemia and in those with non-significant ischemia (p=0.656). The other code, 4-4, had a higher prevalence in the non-significant ischemia group, but the association was not statistically significant (p=0.311).

Minor T-Wave changes

Minnesota code 5-3: T-wave amplitude of 0 (flat), or negative, or biphasic (negative-positive pattern only) with less than 1.0 mm of negative phase in lead I or V6, or in lead aVL if R-wave amplitude is 5.0 or more: T-wave amplitude positive, and ratio of T-wave to R-wave amplitude less than 1/20 in any of leads I, aVL, or V6 if R-wave amplitude is 10.0 or more, is given by 5-4. Both 5-3 and 5-4 were strongly predictive of significant ischemia (P < 0.001, 5-3; P = 0.003, 5-4).

A-V Conduction Defect

There was no significant association between Mobitz II, Wenckebach's Phenomenon, 1st-degree atrial block, and Wolff-Parkinson-White pattern with significant ischemia (p=0.737, p=0.859, p=0.521, and p=0.478, respectively).

Ventricular Conduction Defect

Among ventricular ECG abnormalities, left anterior hemiblock (LAH) was the most significant indicator of ischemia (p<0.001). The second most significant abnormality was the complete left bundle branch block (LBBB) (p=0.019). Other aberrations in this category, including intermittent LBBB, complete right bundle branch block (RBBB), incomplete RBBB, intraventricular block, R-R' pattern, incomplete LBBB, Brugada pattern, and Fragmented QRS, were not significantly associated with ischemia.

Arrhythmias

In this category of Minnesota codes, persistent atrial fibrillation (AF) (p=0.010) and sinus bradycardia with heart rate ≤50/min (p=0.040) were significantly more frequent in patients with significant ischemia. Others like premature ventricular complex, premature atrial complex, wandering pacemaker, persistent ventricular idio-ventricular rhythm, intermittent ventricular tachycardia VT, premature beats, ventricular parasystole, persistent supraventricular rhythm, intermittent AF, sinoatrial arrest, sinus tachycardia, sinoatrial block and other arrhythmias did not show significant correlation with significant ischemia.

ST-Segment Elevation

ST-segment elevation (9-2) was frequently observed in patients with significant ischemia, with a statistically significant relationship (p=0.020).

Miscellaneous Items

Low QRS amplitude (9-1), tall T wave (9-5), and definite early repolarization (ER) (9-7-1) were more frequent in the non-significant ischemia group and did not show any significant correlation with significant ischemia. The tall P wave (9-3) was not significantly correlated with ischemia. However, notched and widened P waves (9-6) were statistically significant indicators of ischemia (p<0.001). At the same time, probable early repolarization ER (9-7-2) was more frequent in subjects with non-significant ischemia (p<0.004).

Detailed results of the Minnesota codes for significant ischemia after backward binary logistic regression are shown in Table 4. Left QRS axis deviation (2-1) exhibited a substantial association with significant ischemia, demonstrating an odds ratio of 2.482 (95% CI: 1.933-3.186, p<0.001). Similarly, the right QRS axis deviation (2-2, QRS axis from +120˚ through -150˚ in leads I, II, III) was significantly associated with ischemia, reflected in an odds ratio of 2.757 (95% CI: 1.149-6.618, p=0.023). For left ventricular hypertrophy (LVH) (3-1), an odds ratio of 2.171 (95% CI: 1.127-4.180, p=0.020) showed a significant association with significant ischemia. Also, RVH (3-2) showed a significant association with ischemia, with an odds ratio of 5.747 (95% CI: 1.749-18.889, p=0.004). Code 5-3 showed a significant association with significant ischemia with an odds ratio of 3.249 (95% CI: 2.433-4.337, p<0.001). Similarly, LAH (7-7) demonstrated a significant association with significant ischemia with an odds ratio of 4.711 (95% CI: 1.848-12.006, p=0.001). While sinus bradycardia with a heart rate <50/min (8-8) had an odds ratio of 1.354 (95% CI: 0.973-1.884), it did not show a statistically significant association with ischemia (p=0.072). Lastly, notched and widened P wave (9-6) exhibited a significant association with significant ischemia, indicated by an odds ratio of 2.415 (95% CI: 1.764-3.304, p<0.001). A summary of the study is illustrated in Figure 1.

Table 4. Association of significant ischemia in ECG and Minnesota codes applying backward binary logistic regression

Abnormality (MN Code)	Odds ratio (95% confidence interval)	P value
Left QRS axis deviation (2-1)	2.482(1.933-3.186)	<0.001
Right QRS axis deviation (2-2)	2.757(1.149-6.618)	0.023
LVH (3-1)	2.171(1.127-4.180)	0.020
RVH (3-2)	5.747(1.749-18.889)	0.004
Minor T-wave abnormalities (5-3)	3.249(2.433-4.337)	<0.001
LAH (7-7)	4.711(1.848-12.006)	0.001
Sinus bradycardia (8-8)	1.354(0.973-1.884)	0.072
Notched and widened P wave (9-6)	2.415(1.764-3.304)	<0.001

Abbreviations: LVH, left ventricular hypertrophy; RVH, Right ventricular hypertrophy; LAH, Left anterior hemi-block

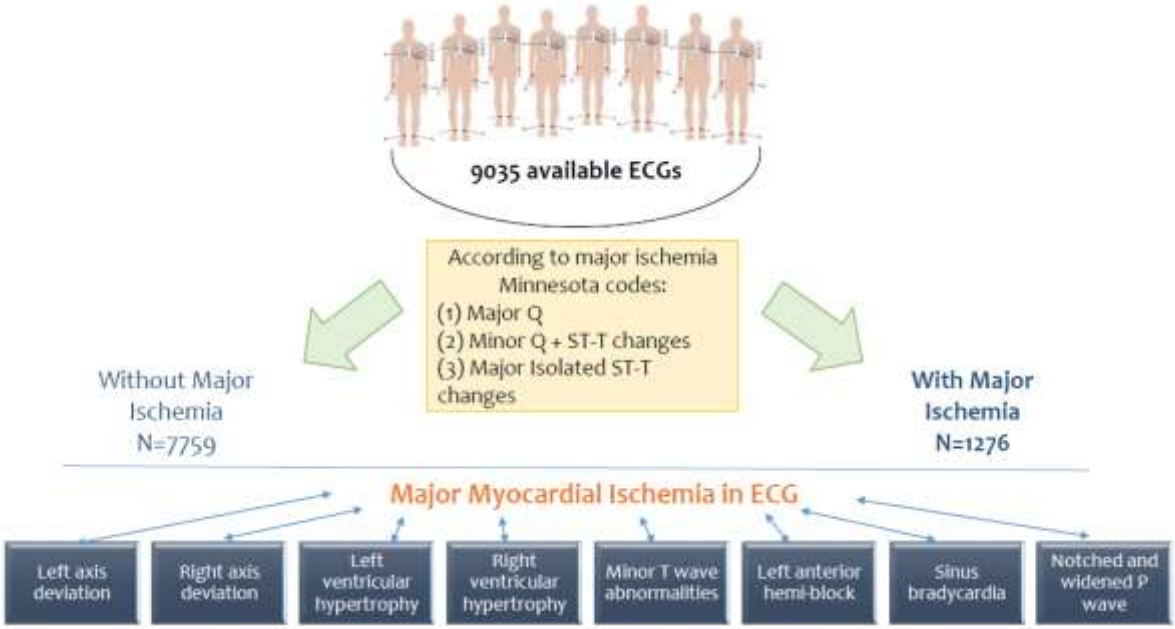

Figure1- Summary of the study.

5. Discussion

Significant heart ischemia is a descriptor of an event in which coronary blood flow is reduced due to plaque formation in coronary arteries, and Q and ST-T changes in the Twelve-lead ECG are one of the routine, low-cost methods for diagnosis (12). It has been shown that specific ECG changes are highly indicative of unique heart disease, and ECG is widely used in clinical practice. For instance, myocardial infarction is significantly associated with specific ECG changes, such as ST-segment elevation, as observed in our investigation (13). However, in the present investigation, our objective is to elucidate the accuracy of ECG coding systems in identifying CAD. Specifically, we aimed to investigate the relationship between the Minnesota coding system and significant ischemia, a significant manifestation of CAD. This inquiry not only enriches the theoretical underpinnings of cardiology but also has direct relevance to the clinical care of individuals with CAD and its associated ischemic pathologies, thereby fostering advancements in cardiovascular medicine. Therefore, we included the general population aged 35-65 years and investigated the association between significant ischemia-related ECG changes, defined by MN codes, and other possible ECG abnormalities. Our initial results indicated that participants were most likely female, with an average age of 48.91 ± 8.39 in males and 47.60 ± 8.09 in females.

We found that indeterminate, right (90°-119°), and left QRS axis deviations were more prevalent in subjects with significant ECG ischemia. Extreme axis deviation showed a significant association in univariate analysis (p=0.005) but was not retained in the final regression model. It is worth mentioning that among the three significant comparisons, the prevalence of left axis deviation is higher than that of right or indeterminate axis deviation. In patients with ischemia and MI, as the heart experiences reduced blood supply, remodeling may be initiated (14, 15). During cardiac remodeling, the ventricles become more spherical, which may be due to hypertrophy of remaining myocytes to compensate for the loss of function of necrosed cells **(**16) Thus, due to altered electrical activity, it is expected to observe axis deviations in patients with old

ischemia. However, axis deviation can vary depending on the involved artery (17). During remodeling after MI, depending on the implicated artery and necrosed cardiac site, right- or left-ventricular hypertrophy develops, which gradually leads to left- or right-axis deviation. Hence, the higher incidence of left axis deviation in our study could be explained by a greater number of patients with left ventricular infarction, as supported by the higher incidence of LVH.

As noted in our results, right and left ventricular hypertrophy were substantially more common in cases with significant ischemia, as indicated by MN codes. However, it may also be interpreted as a bidirectional relationship in which patients with ventricular hypertrophy are more likely to have had previous significant ischemic symptoms due to increased blood supply demands and pressure effects on microcoronary arteries (16). In accordance with this hypothesis, recent evidence from Zakeri et al. demonstrated that Left Ventricular Mass (a proxy for LVH) is linearly associated with greater Microvascular Obstruction (MVO) during STEMI (15). This finding supports the concept that increased extravascular compressive forces associated with LVH can contribute to microvascular damage. In another study, the diagnostic significance of electrocardiographic left ventricular hypertrophy (ECG-LVH) for patients suspected of acute myocardial infarction was investigated. However, their findings revealed that the group who experienced ECG-LVH had significantly fewer myocardial infarctions (18). Accordingly, more investigations are needed to determine the diagnostic significance of LVH.

In a normal ECG, a T wave is considered to be a ventricular repolarization. Whenever ischemia occurs in the ventricles, the action potential duration decreases, and consequently, the repolarization time frame decreases, which can be explained by the greater sensitivity of subendocardial cells to ischemia and their earlier repolarization (19, 20). Clinically, significant T-wave changes, such as amplitude of -5.0 mm or more, could be highly representative of MI (18). However, minor T waves have not yet been considered an important sign of MI diagnosis. In this study, our results showed that minor T changes (described earlier as codes 5-3 and 5-4) are significantly associated with severe ischemia. Consistent with our results, another study showed that increased T-wave complexity could predict non-symptomatic MI in men (21). Furthermore, in another study, the authors found that balloon-induced MI was associated with T-wave alterations (21).

Insufficient blood supply may cause conduction defects due to necrosis in the heart conduction system, which finally leads to a group of heart disorders called ventricular conduction defects. In this study, we found that LAH and Left Bundle Branch Block (LBBB) were significantly more common in patients with Electrocardiographic evidence of significant ischemia; however, other conduction disturbances were not significantly higher in the significant ischemia group. In another study, the authors evaluated 20 patients with LAH patterns on ECG. In our study, their findings showed that all 20 patients had a significant lesion in the proximal left anterior descending artery (22-24). In addition, the study of Jain et al. demonstrated that the patients with LBBB were most likely to have higher Thrombolysis In Myocardial Infarction (TIMI) risk scores and higher risk profiles in comparison to patients without LBBB; however, there were no significant differences between these two groups of patients in terms of acute coronary syndrome diagnosis (25). Similarly, in another study, the authors concluded that new LBBB was not associated with a higher risk of MI (26). Consequently, we believe that the greater prevalence of LBBB and LAH in the significant ischemia group in our study could reflect the post-ischemia onset of LBBB and LAH,

reflecting a remodeled heart after prior ischemia.

AF is characterized by high-frequency, dysynchronous atrial excitation, leading to tachycardia and non-functional atrial contraction (27). Regarding our results, AF arrhythmia was associated with significant ischemia. A mutual relationship between significant ischemia and AF justifies this finding, in which both could lead to each other or develop simultaneously due to the same risk factors. Non-functional contraction of the atrium provides an opportunity for thromboembolism formation, which might involve the coronary arteries. In addition, ventricular and atrial contraction incompatibility may lead to inadequate ventricular blood supply. On the other hand, a prolonged remodeling process after ventricular muscle necrosis leads to atrial expansion and the development of AF (28, 29). A bidirectional association between AF and MI has been shown in several studies (30-32).

As we noted in our results, the prevalence of bradycardia was significantly higher in participants with significant ischemia. Consistent with our findings, previous studies have revealed that patients with inferior myocardial infarction could present with bradycardia. Similarly, another study showed that sinus bradycardia is more prevalent in patients with the right coronary artery involved (33), which could be explained by the similar blood supply of the sinus node and the inferior wall (33-35).

ER is regarded as an elevation after the termination of the QRS complex and the onset of the ST segment in two adjacent ECG leads (36). Our study showed that ER is substantially prevalent in patients without significant ischemia. Previous studies strongly suggest that Early Repolarization (ER) is more common in younger people, especially those under 50, suggesting that ER may be a normal variant of ST elevation (36). However, according to our results, the significantly increased prevalence of ER in subjects without significant ischemia is discussable. One reason this manifestation may be justified is the higher prevalence of middle-aged people, with an average age of about 48 years. According to our characteristic data, participants of older age are most likely to have cardiovascular diseases. Thus, it can be concluded that ER is most likely to be present in participants with non-significant ischemia. Furthermore, another study showed that the epicardial injury incidence as a result of acute myocardial infarction increases after the age of 50, while ER declines after the fifth decade (37).

As reported in our results, subjects diagnosed with MI showed a significantly higher number of notched and widened P-waves than other participants, a finding consistent with left atrial enlargement (38). Also, previous studies have indicated that left atrial enlargement demonstrates chronic diastolic dysfunction and imbalanced systolic function, which is caused by myocardial infarction (38-40). Hence, an old myocardial infarction may be the etiological factor underlying this observation. Furthermore, this observation, along with our other findings, supports our argument. Given that, left ventricle hypertrophy due to the remodeling process after MI and elevated left ventricular filling pressure, predisposes the left atrium to enlargement, it rationally explains the higher occurrence of LVH, left bundle branch block (LBBB), and LAH (left anterior block), and left QRS axis deviation in comparison to RVH, RBBB, and right QRS axis deviation in patients with significant ischemia.

After applying logistic regression and backward variable selection, the final model demonstrated that MI-diagnosed participants had significantly higher odds of showing ECG signs of left, right, and extreme axis deviation, LVH, RVH, minor T-wave changes, LAH, and left atrial enlargement. Different studies have evaluated the significance of ECG abnormalities in predicting cardiovascular

events or death. Denes and colleagues found that significant and minor ECG abnormalities in postmenopausal women are independent and could be predictors of increased cardiovascular event risk (16). Similarly, a cohort study showed that ST-segment depression, T-wave inversion, and left axis deviation are indicative of rising mortality among participants (41), with left axis deviation also indicated by another study (42). Additionally, Caird et al demonstrated an association between LAH and mortality in their study (43). In summary, these studies converge to the point that ECG abnormalities may serve as diagnostic, predictive, and prognostic indicators. Nevertheless, further extensive and longitudinal investigations are warranted.

Despite the substantial population under scrutiny in our inquiry, this study was constrained by the dearth of longitudinal and follow-up data. Moreover, our investigation was confined to a single urban area, albeit one of considerable size and population density within Iran. Additionally, the absence of comprehensive participant characteristics, including lipid profile and ethnicity, may have impacted the study's outcomes. Furthermore, the potential influence of various medications on ECG changes warrants careful consideration in future research.

6. Conclusion

In conclusion, to the best of our knowledge, this is the first investigation conducted in Mashhad encompassing a substantial population. Our findings identify novel electrocardiographic irregularities that may indicate myocardial ischemia. Nevertheless, further longitudinal inquiry is imperative to clarify the diagnostic and prognostic implications of these irregularities.

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