ORIGINAL ARTICLE

FREQUENCY AND FACTORS ASSOCIATED WITH EARLY REPOLARIZATION CHANGES IN ECG IN PATIENTS PRESENTING WITH CHEST PAIN

Anoshi Anoshi[1], Shakir Zada[1], Kamran Ahmed Khan[1], Sumera Rajpoot[1], Poonam Bai[1], Paras Nazir[1], Sorath Sorath[2], Pashmina Kumari[3]

[1]National Institute of Cardiovascular Diseases, Karachi, Pakistan, [2]Jinnah Sindh Medical University, Karachi, Pakistan, [3]Jinnah Postgraduate Medical Centre, Karachi, Pakistan

Objectives: The "early repolarization (ER)" pattern, previously regarded as benign, has recently shown associations with adverse outcomes, including all-cause, arrhythmic and cardiac mortality. This study aimed to assess the prevalence and factors linked to ER changes in the ECG among chest pain patients at a tertiary cardiac center.

Methodology: We enrolled 271 patients aged 18-80 with chest pain complaints. Baseline 12-lead ECGs were used to assess the ER pattern. Multivariable binary logistic regression was conducted, and "odds ratios (OR)" with 95% "confidence intervals (CI)" were reported.

Results: Of the 271 patients, 162 (59.8%) were male, with a mean age of 55.3 ± 10 years, and 40 (14.8%) were ≤45 years old. The ER pattern was present in 92 (33.9%) patients. The ER pattern was associated with low "body mass index (BMI)" (OR=0.85 [95% CI: 0.77 - 0.94; p=0.002]), shorter T-wave duration (OR=0.99 [95% CI: 0.98 - 1.00; p=0.008]), and lower heart rate (OR=0.94 [95% CI: 0.90 - 0.98; p=0.007]). Additionally, the odds of ER pattern were lower in patients with "ST-elevation myocardial infarction (STEMI)" (OR=0.23 [95% CI: 0.07 - 0.72; p=0.012]) and non-STEMI (OR=0.21 [95% CI: 0.07 - 0.63; p=0.006]) compared to non-cardiac chest pain.

Conclusion: Early repolarization is a common ECG pattern in one-third of chest pain patients. Associated factors include low BMI, shorter T-wave duration, and lower heart rate, and it is less frequent in patients with STEMI and non-STEMI.

Keywords: chest pain, early repolarization, ECG, non-cardiac chest pain

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INTRODUCTION

Chest pain is a common chief complaint in emergency departments worldwide, accounting for millions of patient visits annually. It is a symptom that can arise from a myriad of underlying causes, ranging from benign conditions to life-threatening cardiac events.[1] Early recognition of cardiac etiologies is of paramount importance to ensure timely and appropriate intervention, given that "acute myocardial infarction (AMI)", commonly known as a heart attack, is a leading cause of global mortality and morbidity.[1-3] Electrocardiography (ECG) is an invaluable tool for evaluating patients presenting with chest pain, aiding in the differentiation of benign chest pain from potentially life-threatening cardiac events.[1-3]

An intriguing facet of interpreting electrocardiograms (ECGs) in individuals presenting with chest pain involves the recognition of early repolarization (ER) changes. Initially, the ER pattern was described as an ST-segment elevation in one or more leads on the 12-lead ECG, particularly in the absence of conduction abnormalities or when chest pain occurred, often in young individuals with bradycardia. Traditionally, ER patterns were considered harmless.[4] However, recent investigations have unveiled a spectrum of associations, both positive and negative, as well as some neutral, between ER patterns and various clinical outcomes, including overall mortality, cardiac events, and arrhythmic incidents.[4]

Multiple definitions have been proposed to characterize ER patterns.[5-8] Recent studies have introduced more intricate and diverse definitions of ER, which may encompass features like “J-wave or J-point elevation, QRS complex notching or slurring, and concomitant ST-segment elevation”.[9] Moreover, some research has established a heightened prevalence of ER patterns in individuals who have survived cardiac arrest or spontaneous ventricular fibrillation (VF).[4]

The clinical relevance of early repolarization lies in its potential to mimic the ECG manifestations of myocardial infarction.[8] This resemblance can confound the diagnosis and management of patients with chest pain, as well as lead to unwarranted interventions and hospital admissions. Recent studies have attempted to elucidate the frequency of early repolarization changes in patients presenting with chest pain and identify factors associated with this ECG pattern.[10,11] Understanding the factors associated with early repolarization changes in ECG in patients presenting with chest pain is not only a matter of academic interest but has profound implications for clinical practice. Accurate identification and risk stratification of patients with early repolarization patterns are essential to avoid unnecessary diagnostic tests, hospital admissions, and interventional procedures.[11]

Factors that may influence early repolarization changes in the ECG include age, gender, underlying cardiac comorbidities, and other clinical risk factors.[12-13] Additionally, the role of genetic and hereditary factors in developing early repolarization patterns is a topic of ongoing research interest.[14-15] This study aims to contribute to the growing body of knowledge on early repolarization patterns in patients with chest pain, helping to refine diagnostic algorithms and improve the management of these patients in the emergency department and beyond. Furthermore, local data and clinical evidence for this important ECG pattern are very limited. Understanding and evaluating in our local context can be helpful in risk stratification of the patients in a cardiac emergency room. Therefore, this study aimed to determine the frequency and factors associated with early repolarization changes in ECG in patients presenting with chest pain at a tertiary care cardiac center.

METHODOLOGY

This descriptive cross-sectional study was conducted at the "National Institute of Cardiovascular Diseases" in Karachi, Pakistan, over a six-month period, spanning from 24th January 2023 to 23rd July 2023. In order to ensure a representative sample, non-probability consecutive sampling was employed, including patients of both genders aged between 18 and 80 years who presented to the emergency department with complaints of chest pain. Excluded from the study were individuals with a history of prior cardiac-related surgery or intervention and those who declined to provide consent for participation.

Before data collection, the institutional review board approval was obtained (ERC/07/2023), and verbal informed consent was secured from all patients. A 12-lead ECG was performed, recording the early repolarization pattern along with other ECG findings such as QTc intervals (ms), QRS duration (ms), R-R interval (ms), P-R interval (ms), T-wave duration (ms), heart rate (bpm), and the presence of left ventricular hypertrophy (yes/no). Demographic details, including gender and age (in years), were gathered upon hospital arrival, and body mass index (BMI) in kg/m² was calculated following an established definition. Additional patient history was collected, encompassing information about hypertension, diabetes mellitus, family history, smoking habits, and obesity. All patients received care in accordance with clinical practice guidelines and hospital protocols.

The ER pattern was defined as "an elevation of the QRS-ST junction (J point) by ≥0.1 mV above the baseline, and/or either notching or slurring morphology of the terminal portion of QRS at ≥2 inferior (II, III, and aVF) and/or lateral (I, aVL, and V4-V6) leads".[16] The final diagnosis, categorizing patients as having “ST-segment elevation myocardial infarction (STEMI)”, “non-ST elevation myocardial infarction (NSTEMI)”, unstable angina, or non-cardiac chest pain, was determined based on baseline 12-lead ECG findings, chest pain duration, and changes in cardiac biomarker levels, specifically high-sensitivity troponin.

The sample size for this study was determined based on a study by Chen Q et al.[16], which reported an early repolarization pattern in 12.5% of consecutive patients with acute anterior STEMI. The required sample size of N=263 was calculated at a 95% confidence level (CI) and a margin of error of 4%. However, data from 271 patients were included in the analysis.

Data were analyzed using SPSS version-21 ("IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp"). The “Shapiro-Wilk test” was applied to assess the normality hypothesis for various variables. Descriptive statistics, including mean ± SD or median (IQR), were computed based on the distribution of the variables. Categorical variables, such as gender, age group, final diagnosis, hypertension, diabetes mellitus, family history, obesity, smoking, left ventricular hypertrophy, and early repolarization, were summarized with frequency and percentages.

Patients were stratified into two groups, depending on the presence or absence of the early repolarization pattern. Characteristics such as gender, age group, hypertension, diabetes mellitus, family history, smoking, obesity, ECG parameters, and final diagnosis were compared between the two groups using appropriate statistical tests, including Chi-square tests or t-tests/Mann-Whitney tests. To assess the clinical factors associated with the early repolarization pattern, a multivariable binary logistic regression analysis was performed using backward conditional variable selection methods, and "odds ratios (OR)" with 95% CI were calculated. Statistical significance was set at a two-sided p-value of ≤ 0.05.

RESULTS

A total of 271 patients were enrolled in this study, comprising 162 males (59.8%). Their mean age was 55.3 years, with a standard deviation of 10 years. Among the participants, 40 (14.8%) were aged 45 years or younger. The final diagnoses revealed that 25 patients (9.2%) had non-cardiac conditions, 172 patients (63.5%) were diagnosed with NSTEMI, 57 patients (21%) had STEMI, and the remaining 17 patients (6.3%) were diagnosed with unstable angina.

Early repolarization patterns were identified in 92 patients, accounting for 33.9% of the study population. These patterns were significantly associated with specific factors, including low body mass index (p<0.001), reduced T-wave duration (p=0.001), lower heart rate (p=0.001), and the final diagnosis of conditions other than STEMI (p=0.046). For more details, please refer to Table 1.

In the multivariable binary logistic regression model, the presence of an early repolarization pattern was found to be significantly associated with several factors. Notably, low body mass index (BMI) exhibited an odds ratio (OR) of 0.85 (95% CI: 0.77 - 0.94; p=0.002), indicating a robust association.

Table 1: Comparison of clinical data, ECG findings, and final diagnosis between patients with and without early repolarization pattern

	Total	Early repolarization pattern		P-value
		Absent	Present	
Total (N)	**271**	**179 (66.1%)**	**92 (33.9%)**	-
Gender				
Male	162 (59.8%)	104 (58.1%)	58 (63%)	0.432
Female	109 (40.2%)	75 (41.9%)	34 (37%)	
Age (years)	55.3 ± 10	56 ± 9.7	54 ± 10.6	0.109
≤45 years	40 (14.8%)	21 (11.7%)	19 (20.7%)	0.215
46-55 years	100 (36.9%)	66 (36.9%)	34 (37%)	
56-65 years	94 (34.7%)	65 (36.3%)	29 (31.5%)	
> 65 years	37 (13.7%)	27 (15.1%)	10 (10.9%)	
Body mass index (kg/m^2)	25.9 ± 3.4	26.4 ± 3.6	24.8 ± 2.8	<0.001
ECG parameters				
QTc intervals (ms)	320 [290-380]	320 [290-389]	320 [285-360]	0.161
QRS duration (ms)	80 [70-100]	80 [70-100]	80 [60-100]	0.509
R–R interval (sec)	0.76 [0.68-0.8]	0.75 [0.66-0.8]	0.77 [0.69-0.8]	0.079
P–R interval (ms)	150 [120-160]	150 [120-160]	140 [120-160]	0.076
T-wave duration (ms)	110 [80-160]	110 [80-160]	90 [80-120]	0.001
Heart rate (bpm)	78.3 ± 9.1	79.6 ± 9.8	75.9 ± 6.9	0.001
Left ventricular hypertrophy	15 (5.5%)	10 (5.6%)	5 (5.4%)	0.959
Co-morbid conditions				
Hypertension	164 (60.5%)	114 (63.7%)	50 (54.3%)	0.136
Diabetes mellitus	103 (38%)	67 (37.4%)	36 (39.1%)	0.785
Smoking	70 (25.8%)	44 (24.6%)	26 (28.3%)	0.512
Obesity	33 (12.2%)	29 (16.2%)	4 (4.3%)	0.005
Family history of CAD	13 (4.8%)	7 (3.9%)	6 (6.5%)	0.341
Final Diagnosis				
Unstable Angina	17 (6.3%)	11 (6.1%)	6 (6.5%)	0.904
STEMI	57 (21%)	44 (24.6%)	13 (14.1%)	0.046
NSTEMI	172 (63.5%)	111 (62%)	61 (66.3%)	0.487
Non-cardiac	25 (9.2%)	13 (7.3%)	12 (13%)	0.119

CAD= "coronary artery diseases", STEMI="ST elevation myocardial infarction", NSTEMI= "non-ST elevation myocardial infarction"

Table 2: Multivariable binary logistic regression analysis model for the assessment of factors associated with early repolarization pattern

Characteristics	Initial Model		Final Model	
	Odds ratio [95% CI]	P-value	Odds ratio [95% CI]	P-value
Female	0.49 [0.24 - 0.99]	0.048	0.54 [0.29 - 1.02]	0.056
Age (years)	0.99 [0.96 - 1.02]	0.476	-	-
Body mass index (kg/m^2)	0.86 [0.75 - 0.98]	0.025	0.85 [0.77 - 0.94]	0.002
ECG parameters				
QTc intervals (ms)	1.00 [0.99 - 1.01]	0.707	-	-
QRS duration (ms)	1.00 [0.99 - 1.02]	0.745	-	-
R–R interval (sec)	10.13 [0.45 - 227.08]	0.144	-	-
P–R interval (ms)	1.00 [0.99 - 1.01]	0.771	-	-
T-wave duration (ms)	0.99 [0.98 - 1.00]	0.007	0.99 [0.98 - 1.00]	0.008
Heart rate (bpm)	0.96 [0.91 - 1.01]	0.086	0.94 [0.90 - 0.98]	0.007
Left ventricular hypertrophy	1.33 [0.37 - 4.75]	0.658	-	-
Co-morbid conditions				
Hypertension	0.74 [0.40 - 1.37]	0.333	-	-
Diabetes mellitus	1.62 [0.83 - 3.18]	0.157	1.76 [0.95 - 3.25]	0.072
Smoking	0.77 [0.37 - 1.63]	0.501	-	-
Obesity	0.56 [0.14 - 2.16]	0.397	-	-
Family history of CAD	0.65 [0.16 - 2.63]	0.547	-	-
Final diagnosis				
Non-cardiac	Reference category		Reference category	
Unstable Angina	0.43 [0.09 - 2.10]	0.300	0.40 [0.10 - 1.71]	0.217
STEMI	0.25 [0.07 - 0.89]	0.032	0.23 [0.07 - 0.72]	0.012
NSTEMI	0.20 [0.06 - 0.67]	0.010	0.21 [0.07 - 0.63]	0.006

CAD= "coronary artery diseases", STEMI="ST elevation myocardial infarction", NSTEMI= "non-ST elevation myocardial infarction"

Additionally, reduced T-wave duration was associated with an OR of 0.99 (95% CI: 0.98 - 1.00; p=0.008), emphasizing its significance. Likewise, a lower heart rate demonstrated an OR of 0.94 (95% CI: 0.90 - 0.98; p=0.007), underscoring its role in this association (Table 2

Furthermore, the likelihood of an early repolarization pattern was notably less common in patients diagnosed with STEMI (OR=0.23 [95% CI: 0.07 - 0.72; p=0.012]) and NSTEMI (OR=0.21 [95% CI: 0.07 - 0.63; p=0.006]) in comparison to those with non-cardiac findings. Please refer to Table 2 for a comprehensive presentation of these results.

A notably higher likelihood of encountering an early repolarization pattern was evident in the 1st quartile (< 23.4) and 2nd quartile (23.4-25.6) of BMI in comparison to the 4th quartile (> 27.8), showcasing OR of 3.68 [95% CI: 1.68 - 8.09; p=0.001] and 3.56 [95% CI: 1.62 - 7.84; p=0.002], respectively.

Additionally, a significantly greater probability of observing an early repolarization pattern was observed in the 1st quartile (< 75) of heart rate when contrasted with the 4th quartile (> 80), with an OR of 2.35 [95% CI: 1.22 - 4.55; p=0.011].

Similarly, the odds of encountering an early repolarization pattern were elevated in the 1st quartile (< 80) and the 2nd quartile (80-109) of T-wave duration (ms) when compared to the 4th quartile (> 160), with OR of 3.35 [95% CI: 1.21 - 9.29; p=0.020] and 2.93 [95% CI: 1.50 - 5.69; p=0.002], respectively. For a comprehensive summary, please consult Table 3.

Table 3: Binary logistic regression analysis model for the assessment of association between early repolarization pattern and BMI, T-wave duration, and heart rate

Parameters	Odds ratio [95% CI]	P-value
Body mass index (kg/m^2)		
1st quartile (< 23.4)	3.68 [1.68 - 8.09]	0.001
2nd quartile (23.4-25.6)	3.56 [1.62 - 7.84]	0.002
3rd quartile (25.7-27.8)	2.09 [0.93 - 4.68]	0.075
4th quartile (> 27.8)	Reference category	
T-wave duration (ms)		
1st quartile (< 80)	3.35 [1.21 - 9.29]	0.020
2nd quartile (80-109)	2.93 [1.50 - 5.69]	0.002
3rd quartile (110-160)	1.28 [0.58 - 2.83]	0.538
4th quartile (> 160)	Reference category	
Heart rate (bpm)		
1st quartile (< 75)	2.35 [1.22 - 4.55]	0.011
2nd quartile (75-77)	1.51 [0.75 - 3.05]	0.252
3rd quartile (78-80)	1.67 [0.80 - 3.50]	0.170
4th quartile (> 80)	Reference category	

DISCUSSION

We conducted this study to investigate the frequency of ER changes among patients presenting with chest pain and to explore the factors associated with these ECG patterns. The study revealed that the early repolarization pattern was observed in approximately one-third (33.9%) of the patients. This frequency is notable and warrants attention, as recent research has highlighted the potential clinical implications of ER changes.[4]

The prevalence of ER patterns in our study is much higher than the reported prevalence in past studies. Chen Q et al.[16] conducted a study in 1,460 consecutive patients with acute anterior STEMI, and an ER pattern was identified in 183 patients, making up 12.5%. In the comparison of the propensity-matched cohort, an increased risk of sustained VT/VF was associated with the presence of ER with a hazard ratio of 2.915 (95% CI: 1.520–5.588, P=0.001).

In their study, Oka E and colleagues [17] explored the occurrence and importance of the ER-ECG pattern, delving into its mechanistic underpinnings by examining cardiac magnetic resonance findings in individuals with acute myocarditis. Their findings indicated the presence of the ER-ECG pattern in 30.0% of cases, and they inferred that this pattern might be attributed to inflammation and swelling localized to the “left ventricular (LV)” epicardium, caused by acute myocarditis, which in turn could create a voltage gradient traversing the ventricular wall. Importantly, they also observed that the ER-ECG pattern in patients with acute myocarditis was not linked to the occurrence of life-threatening “ventricular tachyarrhythmias (VT)”.[17]

Sucu M et al.[18] in a study reported an association between the J-wave and slurring early repolarization pattern with coronary slow flow phenomenon among patients with positive responses to treadmill testing or chest pain indicative of “stable angina” pectoris. In a different investigation conducted by Kitamura T and colleagues,[19] it was observed that the existence of early repolarization patterns, particularly when they exhibit day-to-day fluctuations, can serve as a valuable predictor for the recurrence of ventricular fibrillation (VF) in individuals with vasospastic angina (VSA). Consequently, for the secondary prevention of VF in high-risk VSA patients, the implantation of an “implantable cardioverter defibrillator (ICD)” is considered a reasonable strategy.

Further in our study, the presence of an ER pattern has a significant association with low BMI. Patients in the lower quartiles of BMI (1st and 2nd quartiles) had significantly higher odds of displaying ER patterns. This finding suggests that lower body mass may be a predisposing factor for ER changes.

The mechanistic underpinning of this association warrants further investigation. Patients with shorter T-wave durations had a higher likelihood of exhibiting ER patterns. This observation underscores the importance of T-wave characteristics in the context of ER changes and may offer insights into the electrophysiological basis of these patterns. Another important finding of our study was that a lower heart rate was associated with an increased likelihood of ER patterns. This relationship between heart rate and ER patterns may have clinical implications for risk stratification and warrants further exploration. A study conducted by Movahed MR et al.[20] on African-American race reported an association between a higher prevalence of ER and lower heart rate. Conversely, they found a positive association between high BMI and an increased prevalence of ER in their population.

Further, the association between ER patterns and the final diagnosis is noteworthy. The odds of having an ER pattern were significantly lower in patients diagnosed with STEMI and NSTEMI compared to non-cardiac findings. Historically, ER patterns were often regarded as benign ECG variants,[4] but the study's results suggest that understanding and recognizing ER patterns is essential, especially in the context of chest pain, to differentiate them from true MI findings. This differentiation is critical as these two conditions' management and clinical implications are distinct. ER is typically an incidental discovery on ECGs and can be present intermittently.[21] It's worth noting that in a study involving 542 subjects with ER, about 20% did not consistently display ER patterns in subsequent ECG measurements.[22]

Even in cases of cardiac arrest where ER syndrome is implicated as the cause, as many as 58% of patients had at least one ECG that did not show the ER pattern during their hospital stay.[21] Currently, no established tests can reliably identify concealed ER. Moreover, we lack practical tools for effectively assessing the risk associated with malignant ER, even though some ECG characteristics have been associated with a higher risk.

Therefore, ECG variations for patients with asymptomatic ER in the absence of a family history of any event of malignant ER should be categorized as normal variation until a more precise and accurate stratification marker or tool becomes available.[23] Regardless of whether ER is symptomatic or not, addressing modifiable cardiac risk factors remains essential.

Several limitations should be considered when interpreting these findings. This was a single-center study, which may limit the generalizability of the results. Additionally, the inherent limitations of cross-sectional study design of the study, such as potential selection bias. Additionally, the study does not address the clinical outcomes of patients with ER patterns.

CONCLUSION

In conclusion, early repolarization is a common ECG pattern observed in one-third of chest pain patients. The ER pattern was more common among patients with non-cardiac chest pain. Low BMI, short T-wave duration, and low heart rate were identified as significant factors associated with ER patterns.

These factors can be further evaluated to differentiate the true MI findings from ER changes. Further research, especially prospective studies with long-term follow-up, is needed to elucidate the clinical implications and mechanisms underlying ER patterns in the context of chest pain.

AUTHORS' CONTRIBUTION

AA and SZ: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. AA, SZ, KAK, SR, PB, PN, SS, and PK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

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Address for Correspondence:
Dr. Anoshi Anoshi, Clinical Fellow at National Institute of Cardiovascular Diseases, Karachi, Pakistan.
Email: anoshikataria0@gmail.com