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Impact of Early Complete Coronary Revascularization on Non-Invasive Risk Factors for Sudden Cardiac Death in Post-Myocardial Infarction Patients with Preserved and Mildly Reduced Left Ventricular Ejection Fraction

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Abstract

Background: *Recent studies show that coronary revascularization in myocardial infarction (MI) patients improves survival, but its effect on sudden cardiac death (SCD) remains unclear. This study assessed the impact of complete anatomical revascularization at varying post-MI intervals on the dynamics of non-invasive risk factors (NIRFs) for SCD.*

Methods and Results: *A total of 110 post-MI patients with preserved or moderately reduced left ventricular ejection fraction (LVEF) underwent percutaneous coronary intervention (PCI) 40 days after MI. Based on the time from MI to PCI, patients were divided into two groups: Early revascularization (n=55, median 67.5 days) and Late revascularization (n=55, median 580 days). Six NIRFs were assessed by 24-hour Holter ECG monitoring before and one year after PCI: ventricular ectopy (VE) >10/hour, non-sustained ventricular tachycardia (NSVT), potentially life-threatening VE (PLTVE), reduced heart rate variability (HRV), abnormal heart rate turbulence (HRT), and prolonged QTc. Reduced HRV was most common (90%). One year later, early revascularization significantly reduced total NIRFs, notably PLTVE (p=0.043) and VE (p=0.038), compared to late PCI.*

Conclusion: *Early complete anatomical revascularization post-MI in patients with preserved or mildly reduced LVEF is linked to greater improvement in NIRFs for SCD, suggesting early ischemia relief may better modify the arrhythmogenic substrate.*

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Abbreviations: ACE - angiotensin converting enzyme, ARA - angiotensin receptor antagonist, ARNI - angiotensin receptor and neprilysin inhibitor, CVDs - cardiovascular disease, BMI - body mass index, DCA – damaged coronary arteries, iLVMM - left ventricular myocardial mass index, LVEF – left ventricular ejection fraction, MI - myocardial infarction, NIRFs - noninvasive risk factors, NSVT - non-sustained ventricular tachycardia, PCI - percutaneous intervention, PLTVE - potentially life-threatening ventricular extrasystoles, SCD - sudden cardiac death, SDNN – standard deviation NN interval, SS- syntax score, HMECG - holter monitoring electrocardiography, HRT – heart rate turbulence, HRV – heart rate variability, VE- ventricular extrasystole

Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide. According to international epidemiological data, in 2019 alone, CVDs were responsible for approximately 18.6 million deaths globally, with 85% of these attributed to myocardial infarction (MI) and stroke [1]. Among cardiovascular conditions, MI and its potentially fatal complication—sudden arrhythmic death (SAD)—represent some of the most prevalent and clinically significant pathologies. Alarmingly, between 25% and 50% of patients with MI succumb to sudden cardiac arrest caused by ventricular arrhythmias [2].

Each year, nearly 4-5 million individuals worldwide experience sudden cardiac arrest, yet survival rates remain below 10% [3]. Consequently, the prevention of sudden cardiac death (SCD) is recognized as a critical public health priority, with profound medical and socio-economic implications.

In recent years, international research has increasingly focused on identifying high-risk populations—particularly those with preserved left ventricular ejection fraction (LVEF)—through non-invasive diagnostic methods, with the aim of implementing timely interventions to prevent SCD. Holter monitoring electrocardiography (HMECG) has emerged as a valuable tool for detecting non-invasive risk factors (NIRFs), including reduced heart rate variability (HRV), abnormal heart rate turbulence (HRT), potentially life-threatening ventricular extrasystoles (PLTVE), and prolonged corrected QT interval, among others [4].

Despite these advancements, a universally accepted risk stratification model for predicting SAD in patients with preserved LVEF has yet to be established. Moreover, current invasive preventive strategies for SCD often fall short in terms of efficacy and cost-effectiveness. Emerging evidence, however, suggests that the integration of multiple NIRFs may significantly enhance the predictive power for SCD [5].

In this context, the present study proposes a novel investigative approach by stratifying patients according to the timing of post-MI revascularization (i.e., early vs. late stenting) and assessing the influence of coronary stenting on the dynamics of NIRFs. This approach offers meaningful scientific and clinical potential to optimize the timing of coronary revascularization and improve the effectiveness of SCD prevention strategies in patients with MI and preserved or mildly reduced LVEF.

Materials and Methods

This prospective clinical study included 110 patients (both male and female), aged 45 to 72 years (median age: 61 years), admitted to the inpatient departments of the Republican Specialized Scientific and Practical Medical Center of Cardiology. All participants underwent evaluation in the Department of Cardiac Arrhythmias. Eligible patients had preserved or mildly reduced LVEF, assessed 40 days after an acute MI. The mean duration from MI to revascularization was 145 days.

Study Groups: to assess the impact of revascularization timing on NIRFs for SCD, patients were stratified into two groups based on the interval between MI and percutaneous coronary intervention (PCI):

- **Group 1 – Early Revascularization (n = 55):** Patients underwent coronary stenting at a median of 67.5 days post-MI (range: 40–267 days).
- **Group 2 – Late Revascularization (n = 55):** Patients received stenting at a median of 580 days post-MI (range: 266–1410 days).

Baseline Evaluation: on admission, all patients underwent a comprehensive clinical evaluation according to international guidelines for chronic coronary syndrome [6]. This included medical history, physical examination, laboratory testing, instrumental diagnostics, and specialist consultations as necessary.

Assessment of Non-Invasive Risk Factors (NIRFs): six NIRFs for SCD were assessed individually and in combination using HMECG, both at baseline and one year after intervention. The following parameters were evaluated:

- Frequent VE: >10 episodes per hour (Bigger's criteria)
- NSVT
- PLTVE: Lown-Wolf classes III, IVA, or IVB
- HRV: SDNNi <70 ms
- Abnormal HRT: Turbulence onset (To) > 0% and turbulence slope (Ts) < 2.5 ms/RR
- Prolonged corrected QT interval (QTc): >440 ms for both men and women

Coronary Angiography and Intervention: all patients underwent coronary angiography (CAG) to assess coronary anatomy. Hemodynamically significant stenosis was defined as luminal narrowing >50%. The mean number of significantly affected coronary arteries was 1.63 ± 0.70. All patients received complete anatomical revascularization using drug-eluting stents, achieving a 100% procedural success rate in both groups.

Medical Therapy and Follow-Up: following PCI, all patients received standard guideline-directed medical therapy. Individualized discharge treatment plans were prescribed in accordance with current clinical recommendations [7]. Patients were followed up for one year on an outpatient basis. Follow-up evaluation included lipid profiling, transthoracic echocardiography, and repeat 24 - hour HMECG for reassessment of NIRFs.

Data analysis was performed using IBM SPSS Statistics v29.0 and Microsoft Excel 2010. Continuous variables were compared using the Mann–Whitney U test, while categorical variables were analyzed using the chi-square (χ^2) test. The McNemar test was applied to assess changes within groups over time. A p-value < 0.05 was considered statistically significant.

Results

The two study groups were comparable in terms of baseline clinical and demographic characteristics. No statistically significant differences were observed between the groups regarding age, sex, body mass index (BMI), MI localization, extent of coronary artery disease, or SYNTAX score (SS). Most patients had anterior MI and single-vessel coronary artery involvement. The average number of affected coronary vessels did not differ significantly between groups. LVEF was preserved in both groups, with no significant intergroup differences. Post-discharge pharmacotherapy was also similar between the groups and adhered to guideline-directed medical therapy protocols.

Among the assessed NIRFs for SCD, pathologically reduced HRV was the most prevalent, observed in 90% of the cohort. Ventricular extrasystole (VE), as defined by Bigger's criteria, was detected in approximately one-third of patients. Prolongation of the corrected QT interval (QTc) and abnormal HRT were each observed in about 20% of patients. Non-sustained ventricular tachycardia (NSVT) was the least frequently identified NIRF, found in only 6.4% of patients. Notably, 6.4% of the cohort exhibited no NIRFs. In total, over 90% of patients presented with between one and four NIRFs (Table 1).

Preliminary intergroup analysis revealed no statistically significant differences in the frequency or distribution of ventricular ectopy, the total number of NIRFs, or their individual occurrences. Additionally, echocardiographic parameters remained comparable between the early and late revascularization groups.

Table 1: Clinical and Demographic Characteristics of Patients

Parameters		Revascularization periods (days)			χ2	p
		Common group n=110	Median 68 [43,5;137,5] n=55	Median 580 [267; 1410] n=55		
Age, years		61 [54; 65]	60 [53; 65]	62 [56; 66]	0,20	0,658
Sex	Man Woman	93 (84,5%) 17 (15,5%)	48 (87,3%) 7 (12,7%)	45 (81,8%) 10 (18,2%)	3,147	0,207
BIM, kg/m2		28,3 [26;32]	27,4[25;31]	29,2 [27;33]	0,15	0,694
From acute MI to		145 [67,5; 566]	68	580	86,42	<0,0
examination, day			[43,5;137,5]	[266;1410]	3	1
Localization MI	Anterior posterior Circular	64 (58,2%) 41 (37,3%) 5 (4,5%)	29 (52,7%) 23 (41,8%) 3 (5,5%)	35 (63,6%) 18 (32,7%) 2 (1,7%)	1,303 0,960 0,943	0,521 0,619 0,624
amount DCA	1 artery 2 arteries 3 and more	57 (51,8%) 40 (36,4%) 13 (11,8%)	30 (54,5%) 20 (36,4%) 5 (9,1%)	27 (49,1%) 20 (36,4%) 8 (14,5%)	0,988 1,300 5,883	0,811 0,317 0,041
Average amount of DCA		1,63±0,70	1,57±0,67	1,69±0,72		0,865
LVEF, %		53,5 [47;59,8]	54,9 [50; 60]	52,1[45;59.7]		0,661
SS I		13,6 [8; 16,9]	14 [9; 17,5]	11 [7; 16,3]		0,132
iLVMM gr		109,3 [95;127,4]	106,1 [94,9; 123,7]	113,4 [96,6; 129,9]		0,05
Beta blocker, n		108 (98,2%)	55 (100%)	53 (96,4%)	0,144	0,916
ACF/ARA, n		65 (59,1%)	31 (56,4%)	34 (61,8%)	0,323	0,851
Ca channel antagonists, n		66 (60,0%)	32 (58,2%)	34 (61,8%)	0,234	0,880
ARNI, n		21 (19,1%)	10 (9,1%)	11 (10,0%)	0,383	0,790
Nytrates, n		29 (26,4%)	13 (23,6%)	16 (29,1%)	0,587	0,746
Amiodarone, n		11 (10,0%)	4 (3,6%)	7 (12,7%)	1,948	0,061
AMR, n		53 (48,2%)	30 (54,5%)	23 (41,2%)	1,453	0,096
Statins, n		108 (98,2%)	53 (96,4%)	55 (100%)	0,144	0,916
Aspirin, n		110 (100%)	55 (100%)	55 (100%)	0,00	1
Klopidogrel, n		100 (90,9%)	49 (89,1%)	51 (92,7%)	0,941	0,625

Table 2: Comparative Results of Initial Noninvasive Risk Factors in the group

Parameters		Revascularization periods (days)			
		Median 68 [43,5;137,5] n=55	Median 580 [267; 1410] n=55	χ2	p
SS I		14 [9; 17,5]	11 [7; 16,3]		0,132
Density of VE		0,16 [0,01; 4,72]	0,28 [0,04; 8,4]		0,300
PLTVE, n		27 (49,1%)	28 (50,9%)		0,632
Bigger VA, n		19 (34,5%)	20 (36,4%)		0,700
Maximal registered	0 I	15 (27,3%) 15 (27.3%)	11 (20%) 13 (23,6%)	0,337 0,115	0,562 0,735
VE class (Lown-Wolf), n (%)	III IV A IV B	13 (23,6%) 10 (18,2%) 4 (7,3%)	7 (12,7%) 18 (32,7%) 3 (5,5%)	1,589 4,105 0,043	0,207 0,043 0,836
NIRF HRV, n		50 (90,9%)	52 (94,5%)	1,569	0,210
NIRF HRT, n		9 (16,4%)	13 (23,6%)	1,412	0,235
QT interval, ms		11 (20%)	14 (25,5%)	1,257	0,262
Averaged amount of NIRF		2,15±1,33	2,37±1,43	-	0,655
Amount of NIRF	0 1 2 3 4 5 6	4 (7,3%) 20 (36,4%) 10 (18,2%) 10 (18,2%) 9 (16,4%) 2 (3,6%) 0 (0%)	3 (5,5%) 17 (30,9%) 14 (25,4%) 8 (14,6%) 12 (21,8%) 0 (0%) 1 (1,8%)	0,013 1,626 1,375 0,293 0,508 - -	0,910 0,195 0,241 0,589 0,476 - -
SDNN, ms		41,9 [32,9; 50,3]	42,3 [36,4; 49,8]	-	0,746
QT, ms		384 [359; 404]	388 [367,5; 406]	--	0,367
QTc, ms		412 [398,5; 432,5]	415 [398,5; 437,5]		0,618

One-Year Follow-Up Findings: at one-year follow-up, patients in the late revascularization group exhibited a 30% higher incidence of PLTVE —a key NIRF for SCD—compared to those in the early stenting group ($p = 0.055$). Additionally, the prevalence of high-grade ventricular ectopy (VE), classified as Lown-Wolf class IVA, was 25% lower in the early group than in the late group ($p = 0.026$).

Although individual comparisons of the six NIRFs did not reach statistical significance in most cases, the total frequency of NIRFs was 16% lower in the early revascularization group ($p = 0.045$). Furthermore, the co-occurrence of four concurrent NIRFs was nearly twice as common in the late stenting group, suggesting a higher cumulative arrhythmic burden in patients with delayed intervention.

There were no significant differences between groups in terms of quantitative NIRF parameters or echocardiographic findings at follow-up. The dynamic evaluation of NIRF trends over time revealed little change in the

late revascularization group. However, although not statistically significant, the total number of NIRFs in the late group remained approximately 30% higher than in the early revascularization group (Table 3).

Notably, analysis of NIRFs that regressed over time demonstrated significant improvement in the early revascularization group. Specifically, the prevalence of PLTVE (p = 0.043) and VE (according to Bigger's criteria) (p = 0.038) decreased by more than two-fold compared to the late group. Other NIRFs—including newly detected abnormalities in HRV, HRT, NSVT, and QTc interval prolongation—did not show significant differences between the groups.

In terms of overall regression, the early stenting group exhibited a 25.8% greater reduction in the total number of NIRFs compared to the late group. Among these, the most notable improvements were observed in VE (Bigger) and PLTVE. These findings suggest that early complete anatomical revascularization post-MI may lead to more favorable modification of the arrhythmogenic substrate, contributing to a more effective reduction in arrhythmic risk than delayed intervention (Table 4).

Table 3: Comparative Dynamics of Non-Invasive Risk Factors for Sudden Cardiac Death According to Timing of Revascularization after Myocardial Infarction

Parameters		**Revascularization periods (days)**			
		Median 68 [43,5;137,5] n=55	**Median 580 [267; 1410] n=55**	**$\chi 2$**	**p**
After 1 year NIRF (PLTVE), n		20 (36,4%)	26 (47,3%)	2,812	0,055
After 1 year NIRF (Bigger), n		13 (23,6%)	16 (29%)	0,201	0,79
After 1 year maximal registered VE class (Lown-Wolf), n (%)	**0** **I** **III** **IV A** **IV B**	17 (30,9%) 18 (32,7%) 11 (20%) 9 (16,4%) 1 (1,8%)	13 (23,6%) 15 (27,3%) 11 (20%) 12 (21.8%) 3 (5,5%)	2,415 0,724 1,041 4,945 2,528	0,135 0,395 0,308 0,026 0,112
After 1 year NIRF (HRV) , n		46 (83.6%)	48 (87,3%)	0,003	0,993
After 1 year NIRF (HRT) , n		5 (9,1%)	6 (10,9%)	0,122	0,826
After 1 year NIRF (QTc interval), n		7 (12,7%)	9 (16,4%)	0,957	0,328
After 1 year averaged amount of NIRF		1,61±1,12	1,91±1,37	3,256	0,045
After 1 year amount of NIRF	**0** **1** **2** **3** **4** **5** **6**	7 (12,7%) 26 (47,3%) 9 (16,4%) 11 (20%) 3 (5,5%) 0 (0%) 0 (0%)	4 (7,3%) 25 (45,5,%) 11 (20%) 9 (16,4%) 5 (9,1%) 1 (1,85) 0 (0%)	0,036 0,37 0,379 0,616 0,437 - -	0,851 0,543 0,538 0,431 0,848 - -
After 1 year LVEF, %		54,3 [49,5; 60]	53,9 [45,5; 61,8]	-	0,854
After 1 year iLVMM, gr		97,8[92,4; 107,6]	103,9[91,8; 117,3]	-	0,368
After 1 year SDNN, ms		47,1[38,9; 56,1]	45,3 [38,2; 53,0]	-	0,879
After 1 year QT, ms		400 [380; 407]	388,5[380; 407]	-	0,673
After 1 year QTc, ms		426[410; 439]	417,5[395; 436]	-	0,399

Table 4: Comparative Dynamics of Newly Manifested and Eliminated Non-Invasive Risk Factors Following Coronary Revascularization

Parameters	Revascularization periods (days)			
	Median 68 [43,5;137,5] n=55	Median 580 [267; 1410] n=55	χ2	p
New appeared pathological HRV, n	2 (3,6%)	3 (5,5%)	1,024	0,438
New appeared pathological HRT, n	2 (3,6%)	2 (3,6%)	0,000	0,990
New appeared PLTVE, n	1 (1,8%)	2 (3,6%)	0,616	0,431
New appeared Bigger as NIRF, n	2 (3,6%)	3 (5,5%)	1,024	0,438
New appeared NSVT, n	0 (0%)	1 (1,8%)	-	-
New appeared NIRF (prolonged QTc), n	2 (3,6%)	1 (1,5%)	0,503	0,478
Disappeared NIRF (HRV), n	7 (12,7%)	7 (12,7%)	0,000	0,991
Disappeared NIRF (HRT), n	6 (10,9%)	9 (16,4%)	1,035	0,309
Disappeared NIRF (PLTVE), n	8 (14,5%)	4 (7,3%)	3,412	0,043
Disappeared NIRF (Bigger), n	9 (16,4%)	4 (7,3%)	4,244	0,038
Disappeared NIRF (NSVT), n	3 (5,5%)	1 (1,8%)	1,150	0,223
Disappeared NIRF (prolonged QTc), n	6 (10,9%)	6 (10,9%)	0,015	0,915

Discussion

The patients included in this study were admitted within the first few hours following acute MI but did not undergo immediate percutaneous coronary intervention (PCI) due to various clinical or logistical limitations. Revascularization procedures were subsequently performed at other medical centers following hemodynamic stabilization. While the benefits of emergency revascularization during the acute phase of MI are well documented—particularly in reducing mortality and improving long-term outcomes—the impact of delayed revascularization, particularly during the post-infarction remodeling period, on NIRFs for SCD remains less clearly defined.

Given the lack of universally accepted temporal classifications for myocardial remodeling phases in the international literature, and the heterogeneity in study designs, we divided the timing of revascularization into "early" and "late" categories based on the median time from MI to PCI within our cohort [8]. It is important to highlight that many experts regard the myocardial remodeling process as a dynamic and potentially lifelong phenomenon, which complicates the establishment of strict temporal boundaries [9].

Previous studies have shown that complete anatomical revascularization after MI can improve quality of life, prolong survival, and potentially mitigate the risk of ischemia-related major events [10,11]. Our study focused on patients with preserved or mildly reduced LVEF after 40 days post-MI, in accordance with literature suggesting that risk stratification using parameters such as HRV and HRT becomes more reliable after this point [12].

Our findings indicate that while individual NIRFs—such as non-sustained ventricular tachycardia (NSVT), abnormal HRT, or prolonged QTc—did not show statistically significant differences between the early and late revascularization groups, the overall burden of NIRFs was significantly lower in the early revascularization group. This was particularly notable for PLTVE and ventricular ectopy (VE), as defined by Bigger's criteria, both of which showed a more than two-fold reduction in the early PCI group.

Although patient groups in this study were categorized based on time from MI to stenting rather than strict remodeling phases, the significant difference in revascularization timing (median 67.5 vs. 580 days post-MI) provides clinically meaningful insight. Our

data suggest that earlier revascularization, even if not performed during the acute MI phase, may still offer protective benefits by positively influencing the post-infarction arrhythmogenic substrate and reducing the incidence of potentially fatal ventricular arrhythmias [12,13].

These results support the hypothesis that early complete anatomical revascularization may contribute to more favorable electrical remodeling and autonomic balance, thereby lowering the overall arrhythmic risk in post-MI patients with preserved or mildly reduced LVEF.

Limitations

This study has several limitations that warrant consideration. First, although all patients were followed for one year under standard pharmacological therapy, adherence levels—assessed using the Morisky-Green scale—were only moderate in both groups, which may have affected the observed clinical outcomes. Second, the classification of patients into early and late revascularization groups was based on the median time from MI to percutaneous coronary intervention (PCI), rather than predefined or clinically validated time intervals. This approach may have limited the temporal resolution of the analysis regarding remodeling phases. Finally, the relatively small sample size may have constrained the statistical power of the study, potentially obscuring significant differences in individual NIRFs for SCD.

In conclusion, this study provides evidence that early complete anatomical revascularization via stenting in post-MI patients with preserved or mildly reduced LVEF is associated with a significant reduction in the total burden of selected NIRFs for SCD. Compared to delayed revascularization, early intervention appears to facilitate the prompt resolution of ischemic changes, which may contribute to a more favorable arrhythmic risk profile during the post-infarction period.

Ethical Considerations

This study was conducted in accordance with ethical standards. The protocol was reviewed and approved by the Ethics Committee of the Republican Specialized Scientific and Practical Medical Center of Cardiology.

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