Original Article

Defective recovery of QT dispersion due to no-reflow following acute interventional therapy in patients with ST-segment elevation myocardial infarction

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Background: Previous studies have suggested that adequate myocardial reperfusion after percutaneous coronary intervention (PCI) can improve the inhomogeneity of myocardial repolarization. However, it remains unclear whether no-reflow (NR) following emergency PCI involves disadvantages related to ventricular repolarization indices. The present study aimed to determine the effect of NR on QT dispersion (QTd) in patients with ST-segment elevation myocardial infarction (STEMI) and to evaluate the prognostic value of the relative reduction of QTd on ventricular arrhythmia events (VAEs).

Methods: A prospective case-control study was conducted. According to the inclusion criteria, 275 patients with STEMI who underwent primary PCI treatment at the First People's Hospital of Anqing affiliated to Anhui Medical University from January 2020 to May 2023 were enrolled. According to whether NR occurred during PCI, these patients were divided into two groups: an NR group and a non-NR group. Subsequently, the QT intervals were measured before and at 12 hours after PCI. Afterward, the QTd, corrected QTd (QTcd), and the relative reduction of QTd and QTcd 12 hours pre- and postprocedure (ΔQTd-R and ΔQTcd-R, respectively) were calculated. Finally, multivariable logistic regression analysis was performed to predict the risk of VAE occurrence.

Results: In the non-NR group, there was a significant decrease from baseline in postprocedure QTd (48±17 *vs.* 73±22 ms; P=0.009) and QTcd (54±19 *vs.* 80±23 ms; P=0.01); in contrast, the NR group showed no significant difference in QTd (64±20 *vs.* 75±23 ms; P=0.58) or QTd (70±22 *vs.* 82±26 ms; P=0.45). Furthermore, the ΔQTd-R and ΔQTcd-R were both lower in the NR group than in the non-NR group (P<0.05); however, the rate of VAEs was higher in the NR group than in the non-NR group (15.2% *vs.* 6.2%; P=0.02). The multivariable logistic regression analysis results revealed that each increase of 12% in ΔQTcd-R was an independent predictor of VAEs (odds ratio: 0.547; 95% confidence interval: 0.228–0.976).

Conclusions: The NR phenomenon following primary PCI in patients with STEMI leads to the defective recovery of QTd and QTcd. Furthermore, ΔQTcd-R can be viewed as an effective indicator for evaluating the myocardial repolarization inhomogeneity, and short-term clinical outcomes.

Keywords: QT dispersion (QTd); no-reflow (NR); percutaneous coronary intervention (PCI); ST-segment elevation myocardial infarction (STEMI); ventricular arrhythmias events

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Introduction

Primary percutaneous coronary intervention (PCI) is a critical measure in treating ST-segment elevation myocardial infarction (STEMI) and can contribute to enhanced myocardial perfusion (1). However, over the past decade, studies have revealed that approximately 10–30% of patients with STEMI treated with PCI fail to reach optimal myocardial reperfusion (2). Perera *et al.* (3) indicated that approximately 27% of patients experience persistent ventricular arrhythmias after PCI. Moreover, the occurrence of no-reflow (NR) is evident in this patients, primarily manifesting in the patency of infarct-related arteries (IRAs) and microvascular obstruction (MVO) (4). It is currently speculated that NR can be attributed to the distal embolism or spasm of the coronary artery (5). NR can lead to left ventricular remodeling, malignant arrhythmias, decreased heart function, increased hospitalization, and high mortality rates (6). Therefore, there is a need to enhance our understanding and treatment of this condition. Common treatment methods include adenosine (7), calcium channel blockers, nitroprusside, platelet glycoprotein IIb/IIIa inhibitors (8), and nonpharmacological approaches such as thrombus aspiration (9), pressure-controlled intermittent coronary sinus occlusion (10), and hypothermic therapy (11). QT dispersion (QTd) is defined as the difference between the longest and shortest QT intervals in a simultaneously recorded 12-lead surface electrocardiogram (ECG). Corrected QT (QTc), which is corrected for heart rate, provides a more accurate assessment of myocardial repolarization. Both parameters serve as crucial indicators of repolarization heterogeneity, which is closely linked to malignant cardiac events (4,12). Although the review by Dahrab *et al.* (13) unequivocally established the association between QTd and reperfusion in patients with STEMI and demonstrated a substantial reduction in QTd, QTc, and corrected QT dispersion (QTcd) after the PCI procedure, it remains uncertain whether the NR following PCI adversely impacts ventricular repolarization. Our study thus aimed to assess the effects of NR during acute PCI on QTd in patients with STEMI and to evaluate the prognostic value of the relative reduction of QTd on postoperative ventricular arrhythmia events (VAEs) during hospitalization. We present this article in accordance with the STROBE reporting checklist (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-398/rc).

Highlight box

Key findings

- The no-reflow (NR) phenomenon following primary percutaneous coronary intervention (PCI) in patients with ST-segment elevation myocardial infarction leads to the defective recovery of QT dispersion (QTd) and corrected QTd (QTcd).

What is known and what is new?

- PCI can improve the inhomogeneity of myocardial repolarization.
- However, it remains unclear whether NR following emergency PCI involves disadvantages related to ventricular repolarization indices. We thus aimed to determine the correlation between these factors.

What is the implication, and what should change now?

- The relative reduction of pre- and post-procedural 12 hours on QTcd can aid in assessing the effectiveness of ventricular repolarization.
- Relatedly, the ability to actively predict the occurrence of NR after PCI may have clinical significance.

Methods

Patient selection and study design

A prospective case-control study was conducted, in which the eligible consecutive patients with STEMI who underwent primary PCI between January 2020 and May 2023 at the First People's Hospital of Anqing affiliated to Anhui Medical University were enrolled. The final cohort included 275 cases, with 66 in the NR group and 209 in the non-NR group (*Figure 1*). The inclusion criteria were as follows: (I) the diagnosis of STEMI consisting of at least a twofold elevation in troponin I level, a typical chest pain duration of >30 minutes, and an ST-segment elevation of ≥2 mv in adjacent leads on an admission ECG; (II) an onset of STEMI at 12 hours, including ischemic symptoms that continued for 12–24 hours and administration of acute PCI within 2 hours after admission; and (III) <20% residual stenosis and thrombolysis in myocardial infarction (TIMI) blood flow of grade 3 in IRAs confirmed by final angiography. The exclusion criteria were as follows: delayed PCI of >12 hours from onset, history of coronary artery bypass graft, hemorrhagic diseases, and severe hypertension (>180/100 mmHg). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee for Clinical Research of the First People's Hospital of Anqing affiliated to Anhui Medical University (No. AQYY--YXLL--KJXM--24-02) and informed consent was provided by all

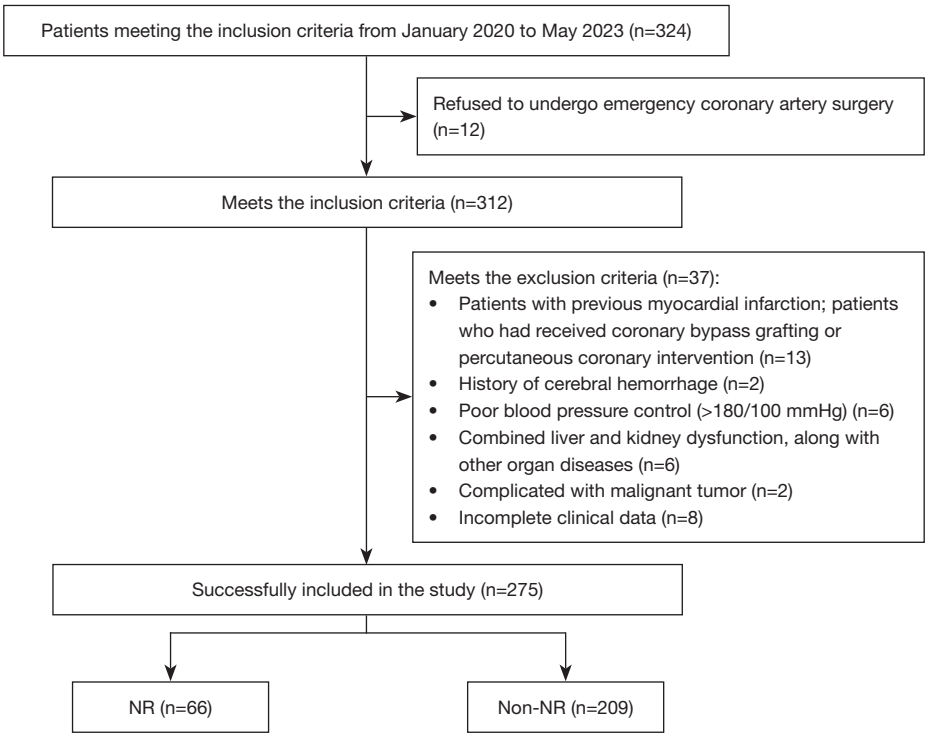

Figure 1 Flowchart of participant inclusion. NR, no-reflow.

the patients.

Primary PCI procedure and evaluation of NR

All patients were treated with an oral loading dose of 300 mg of aspirin and 600 mg of clopidogrel on admission, along with 120 U/kg of intravenous unfractionated heparin (UFH) before the coronary angiography. Intracoronary bolus tirofiban was administered at the discretion of the operator. Based on the extent of the thrombus burden, thrombus aspiration was performed to achieve the optimal TIMI grade (usually TIMI grades 2–3), without any debris. Balloon predilation was implemented when the stenosis was ≥90% in the IRAs, or direct stent implantation was attempted when deemed possible. After surgery, dual antiplatelet therapy with aspirin and clopidogrel was administered based on the patient's perioperative bleeding status. For patients with concomitant atrial fibrillation, addition of rivaroxaban to the dual therapy was considered.

The TIMI flow grading system was employed to determine the occurrence of the NR phenomenon. The patients with 275 STEMI were divided into two groups according to whether NR occurred during PCI: the NR group and the non-NR group. NR is a condition in which the epicardial coronary artery, after successful recanalization through thrombolysis or emergency intervention, with the elimination of factors such as vasospasm or dissection, the distal antegrade blood flow fails to fully recover, and the TIMI grading remains at 0–1. In this study, the observation of blood flow during the initial PCI allowed for the identification of NR. The individuals evaluating the NR phenomenon were experienced senior physicians with a wealth of interventional surgical experience and systematic training. For patients experiencing NR, the administration of intracoronary diltiazem and/or nitroprusside can restore flow to TIMI grade 3, indicating treatment efficacy.

ECG measurement

The standard 12-lead ECG was recorded before and at 12 hours after PCI in a quiet environment, with 25 mm/sec of paper speed and 10 mm/mv of amplitude. The ECG results were manually assessed by two cardiologists; the indicators measured are detailed in the following sections.

QT interval and QTd

The QT intervals were measured from the starting point of the QRS complex to the end of the T wave. The end point

of the T wave was partly determined by the intersection of the wave declining branch and TP isoelectric line; in case this was not obvious, the nadir of the curve between the T and U waves when a U wave was present was considered. The QT maximum (QT_{max}) and QT minimum (QT_{min}) intervals before and at 12 hours after PCI were measured, and the QTd values were calculated using the following formula: $QTd = QT_{max} - QT_{min}$.

QTc and QTcd

The QTc intervals were calculated based on Bazett's formula ($QTc = QT/RR^{1/2}$) (14). The QTcd values were obtained using the difference between QTc_{max} and QTc_{min}.

ΔQTd-R and ΔQTcd-R

ΔQTd-R was defined as the relative reduction of QTd and calculated using the following formula: ΔQTd-R = [(QTd pre-PCI – QTd post-PCI)/QTd pre-PCI] × 100%. ΔQTcd-R was defined in a similar fashion and calculated as follows: ΔQTcd-R = [(QTcd pre-PCI – QTcd post PCI)/QTcd pre-PCI] × 100%.

Postprocedure VAEs during hospitalization

The VAEs included nonsustained monomorphic ventricular tachycardia (NSMVT), sustained monomorphic ventricular tachycardia (SMVT), polymorphic ventricular tachycardia (PMVT), ventricular flutter, or ventricular fibrillation. All postoperative VAEs of all patients were recorded during hospitalization. If two or more ventricular arrhythmias occurred in the same patient, only the most severe ventricular arrhythmia was considered as an event.

Statistical analysis

Statistical analysis was conducted using SPSS version 20.0 (IBM Corp.). Normally distributed continuous variables are expressed as the mean ± standard deviation, and group differences were compared using the two independent samples *t*-test. Nonnormally distributed continuous data are expressed as the median and interquartile range (IQR), and Mann-Whitney test was applied to analyze the group differences. Categorical variables are expressed in absolute numbers and percentages, and two groups were compared using the χ^2 test or Fisher exact test. Multivariable logistic regression analysis was performed to predict the risk of VAEs. A P value of <0.05 was considered statistically significant.

Results

Patient characteristics

Among the 275 patients who had an adequate TIMI grade of 3 at the final angiogram for IRAs after PCI, 66 patients who had NR during PCI were assigned to the NR group, while 209 patients who did not have NR were assigned to the non-NR group. Among these patients, 102 patients were male, and 173 patients were female, and the mean age of these patients was 64.6±8.5 years old. Approximately two-thirds of the procedures in this study, 184 cases, were conducted at night. Approximately 90% of surgeries were performed through the conventional approach, namely, via the radial artery. No statistically significant differences were observed between the two groups in terms of the application proportion of thrombus aspiration (58.4% *vs.* 66.7%; P=0.23) or drug-eluting stents (94.7% *vs.* 95.5%; P=0.82). Moreover, there was no significant difference in the occurrence rate of common perioperative complications between the two groups. However, the NR group had a higher rate of balloon predilation when compared to the non-NR group (77.3% *vs.* 61.2%; P=0.02). Furthermore, the usage rate of intracoronary tirofiban reached up to 65.2% in the NR group and up to 48.3% in the non-NR group (P=0.02). Moreover, intracoronary diltiazem or nitroprusside was administered to manage the NR phenomenon in the NR group, but this was not administered for the non-NR group. There were no significant differences in gender, age, body mass index (BMI), smoking status, hypercholesterolemia, hypertension, random blood glucose, serum creatinine, left ventricular ejection fraction (LVEF), or left ventricular end diastolic diameter (LVEDD) between the two groups. Similarly, there was no statistical significance in the COVID-19 incidence rate and whether the surgery was performed at night between the two patient groups. However, patients in the NR group, when compared to patients in the non-NR group, had higher rates of diabetes mellitus (28.8% *vs.* 17.2%, P=0.04) and Killip classification III (39.4% *vs.* 29.7%; P=0.02), along with longer reperfusion times (7.8±2.6 *vs.* 5.6±2.3 hours; P=0.03) (*Table 1*).

Effects of acute PCI on the QTd and QTcd indices

A total of 253 patients, which accounted for 92.0% of all participants, had a remarkable reduction in QTd or QTcd at 12 hours postprocedure. No statistically significant differences were found between the NR group and non-NR

Table 1 Clinical characteristics and angiographic findings for the study population

Variable	Non-NR group (n=209)	NR group (n=66)	t/χ^2	P value
Male/female (n)	73/136	29/37	1.746	0.19
Age (years)	64.2±8.7	64.8±8.2	0.061	0.32
BMI (kg/m^2)	26.6±5.4	26.8±5.5	3.253	0.08
Current smoker	40 (19.1)	18 (27.3)	1.994	0.16
Hypercholesterolemia	54 (25.8)	22 (33.3)	1.409	0.24
Hypertension	66 (31.6)	25 (37.9)	0.899	0.34
Diabetes mellitus	36 (17.2)	19 (28.8)	4.192	0.04
Random blood glucose (mmol/L)	8.7±3.5	9.4±3.7	0.265	0.15
Serum creatinine (μmol/L)	82.3±14.4	84.5±14.8	3.637	0.53
LVEF (%)	48.3±7.0	47.8±6.7	2.325	0.44
LVEDD (mm)	49.2±6.3	49.5±6.4	1.863	0.25
Killip classification III	62 (29.7)	26 (39.4)	5.617	0.02
Prevalence of COVID-19			0.041	0.84
Positive	70 (33.5)	23 (34.8)		
Negative	139 (66.5)	43 (65.2)		
Night surgery	139 (66.5)	45 (68.2)	0.064	0.80
Reperfusion time (hours)	5.6±2.3	7.8±2.6	2.463	0.03
IRAs			0.455	0.80
LAD	84 (40.2)	29 (43.9)	0.291	0.59
LCX	46 (22.0)	15 (22.7)	0.015	0.90
RCA	79 (37.8)	22 (33.3)	0.430	0.51
Thrombus aspiration	122 (58.4)	44 (66.7)	0.1442	0.23
Balloon predilation	128 (61.2)	51 (77.3)	5.671	0.02
Drug-eluting stent	198 (94.7)	63 (95.5)	0.053	0.82
Administration of drugs				
Tirofiban	101 (48.3)	43 (65.2)	5.693	0.02
Diltiazem	0	66 (100.0)	275.000	0.001
Nitroprusside	0	58 (87.9)	232.757	0.001
Perioperative complications				
Bleeding	2 (1.0)	3 (4.5)	1.887	0.17
CAP	0	2 (3.0)	2.873	0.09
Peripheral vascular damage	2 (1.0)	3 (4.5)	1.887	0.17
PSA	1 (0.5)	3 (4.5)	3.299	0.07

Data are presented as the mean ± standard deviation and n (%). NR, no-reflow; BMI, body mass index; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end diastolic diameter; IRA, infarct-related artery; LAD, left anterior descending artery; LCX, left circumflex coronary artery; RCA, right coronary artery; CAP, coronary artery perforation; PSA, pseudoaneurysm.

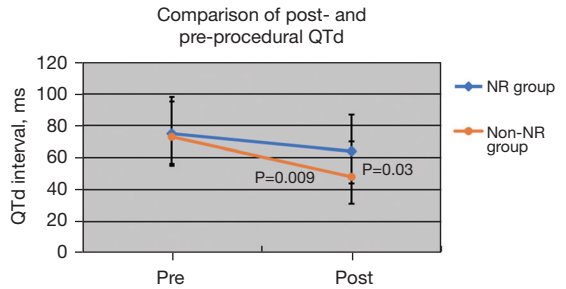

Figure 2 Comparison of post- and preprocedure QTd. Postprocedure QTd in the non-NR group significantly decreased from baseline (P=0.009). The postprocedure QTd was higher in the NR group than in the non-NR group (P=0.03). QTd, QT dispersion; NR, no-reflow.

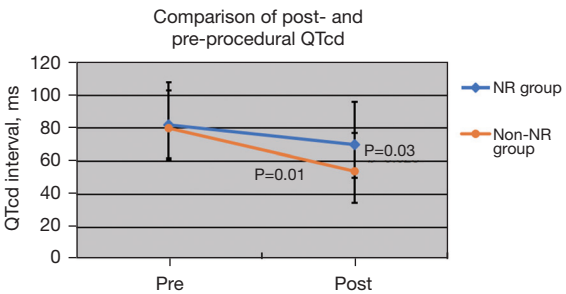

Figure 3 Comparison of post- and preprocedure QTcd. The postprocedure QTcd in the non-NR group was significantly decreased from baseline (P=0.01). The postprocedure QTcd was higher in the NR group than in the non-NR group (P=0.03). QTcd, corrected QT dispersion; NR, no-reflow.

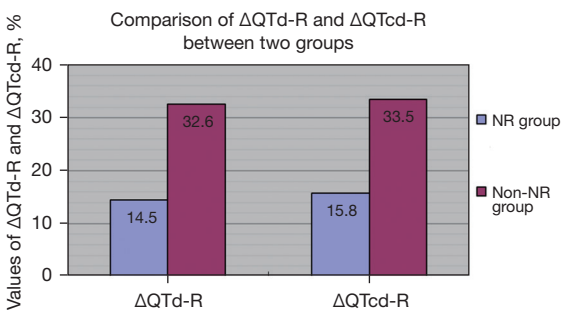

Figure 4 Comparison of the ΔQTd-R and ΔQTcd-R between the NR group and non-NR group. The ΔQTd-R and ΔQTcd-R values were higher in the NR group than in the non-NR group (P<0.05). NR, no-reflow; QTd, QT dispersion; ΔQTd-R, the relative reduction of pre- and post-procedural 12 hours on QTd. ΔQTcd-R, the relative reduction of pre- and post-procedural 12 hours on QTcd.

group in terms of preprocedure QTd (75±23 *vs.* 73±22 ms; P=0.27) or QTcd (82±26 *vs.* 80±23 ms; P=0.33). In the non-NR group, there was a significant decrease from baseline in postprocedure QTd (48±17 *vs.* 73±22 ms; P=0.009) and QTcd (54±19 *vs.* 80±23 ms; P=0.01); meanwhile, in the NR group, there was no significant change in QTd (64±20 *vs.* 75±23 ms; P=0.58) or QTcd (70±22 *vs.* 82±26 ms; P=0.45). Compared to the non-NR group, the NR group had higher postprocedure QTd (64±20 *vs.* 48±17 ms; P=0.03) and QTcd (70±22 *vs.* 54±19 ms; P=0.03) (*Figures 2,3*). The median ΔQTd-R and ΔQTcd-R were 14.5% (IQR, 6.4–23.7%) and 15.8% (IQR, 7.2–28.4%), respectively, in the NR group, and 32.6% (IQR, 21.5–45.8%) and 33.5% (IQR, 22.1–46.2%), respectively, in the non-NR group. The ΔQTd-R and ΔQTcd-R values were lower in the NR group than in the non-NR group (P<0.05) (*Figure 4*).

Occurrence of postprocedure VAEs during hospitalization

During the hospitalization after PCI, a total of 13 VAEs were observed in the non-NR group, which included five cases of NSMVT, three cases of SMVT, two cases of PMVT, one case of ventricular flutter, and two cases of ventricular fibrillation. In the NR group, 10 VAEs were observed: three cases had NSMVT, two cases had SMVT, two cases had PMVT, one case had ventricular flutter, and two cases had ventricular fibrillation. The incidence of total VAEs was higher in the NR group than in the non-NR group (15.2% *vs.* 6.2%; P=0.02). The NR group had an increased tendency of cardiac death, but the difference was not statistically significant between the two groups (3.0% *vs.* 1.0%; P=0.24; *Table 2*).

Correlation between NR and QTd

The variables of NR, balloon predilation, reperfusion time, and diabetes mellitus were incorporated into a multifactorial linear regression equation. The results revealed statistically significant differences in the influence of NR on QTd (P<0.001), confirming the correlation between QTd and NR (*Table 3*).

Independent determinants of VAEs

The variables of diabetes mellitus, Killip classification III, reperfusion time ≥6 hours, an increase of 10% in ΔQTd-R, and an increase of 12% in ΔQTcd-R were incorporated into a multifactorial logistic regression equation. The

Table 2 Comparison of prognoses between the two groups during the follow-up period

Event	Non-NR group (n=209)	NR group (n=66)	P value
VAEs	13 (6.2)	10 (15.2)	0.02
NSMVT	5 (2.4)	3 (4.5)	0.63
SMVT	3 (1.4)	2 (3.0)	0.60
PMVT	2 (1.0)	2 (3.0)	0.24
Ventricular flutter	1 (0.5)	1 (1.5)	0.42
Ventricular fibrillation	2 (1.0)	2 (3.0)	0.24
Cardiac death	2 (1.0)	2 (3.0)	0.24

Data are presented as n (%). NR, no-reflow; VAE, ventricular arrhythmia event; NSMVT, nonsustained monomorphic ventricular tachycardia; SMVT, sustained monomorphic ventricular tachycardia; PMVT, polymorphic ventricular tachycardia.

multivariable logistic regression analysis revealed that an increase of 12% in ΔQTcd-R [odds ratio (OR): 0.547; 95% confidence interval (CI): 0.228–0.976] was an independent predictor of VAEs (*Table 4*).

Follow-up on discharge from hospital

Follow-up was conducted for all patients upon discharge, and the specific follow-up process is detailed in *Figure 5*. Among the patients, 57 in the NR group completed the follow-up, while 9 patients were lost to follow-up. Statistical analysis of the follow-up of patients in the NR group showed a significant improvement in QTd compared to postoperative values (70±21 *vs.* 64±20 ms; P=0.002) (*Figure 6*). Meanwhile, follow-up of medication-related complications for all patients indicated no statistically

Table 3 Linear regression analysis of QTd

Variables	Univariate linear regression			Multifactorial linear regression		
	β	*t*	P value	β	*t*	P value
NR	0.821	23.739	<0.001	0.778	17.676	<0.001
Age (years)	–0.052	–0.859	0.39	–	–	–
Male	0.041	0.678	0.50	–	–	–
Hypertension	0.037	0.606	0.55	–	–	–
Hypercholesterolemia	0.080	1.329	0.19	–	–	–
Diabetes mellitus	0.144	2.405	0.02	0.035	0.973	0.33
Current smoker	0.059	0.981	0.33	–	–	–
LVEF (%)	0.005	0.082	0.94	–	–	–
Killip classification III	0.040	0.655	0.51	–	–	–
IRAs						
LAD	0.013	0.222	0.82	–	–	–
LCX	–0.041	–0.685	0.49	–	–	–
RCA	–0.048	–0.792	0.43	–	–	–
Thrombus aspiration	0.050	0.820	0.41	–	–	–
Balloon predilation	0.124	2.069	0.04	0.012	0.334	0.73
Drug-eluting stent	0.025	0.410	0.68	–	–	–
Reperfusion time (hours)	0.545	10.738	0.004	0.060	1.342	0.18

QTd, QT dispersion; NR, no-reflow; LVEF, left ventricular ejection fraction; IRA, infarct-related artery; LAD, left anterior descending artery; LCX, left circumflex coronary artery; RCA, right coronary artery.

Table 4 Logistic regression analysis of the independent predictors of VAEs

Variable	Univariate logistic regression			Multifactorial logistic regression		
	OR	95% CI	P value	OR	95% CI	P value
Age (years)	1.058	0.979–1.144	0.16	–	–	–
Male	2.343	1.020–5.380	0.06	–	–	–
Current smoker	0.929	0.333–2.592	0.89	–	–	–
Hypercholesterolemia	3.216	1.395–7.411	0.11	–	–	–
Hypertension	0.769	0.309–1.912	0.57	–	–	–
Diabetes mellitus	2.495	1.038–5.997	0.04	2.415	1.033–3.928	0.53
LVEF (%)	0.959	0.863–1.066	0.44	–	–	–
Killip classification III	2.806	1.187–6.629	0.02	2.839	1.525–4.274	0.84
Reperfusion time ≥6 hours	1.442	1.059–1.964	0.02	4.278	2.316–7.329	0.001
IRAs						
LAD	1.941	0.847–4.449	0.12	–	–	–
LCX	1.263	0.479–3.328	0.64	–	–	–
RCA	1.670	0.731–3.815	0.22	–	–	–
ΔQTd-R	0.017	0.000–2.888	0.02	0.564	0.275–1.053	0.004
ΔQTcd-R	0.372	0.002–7.287	0.02	0.547	0.228–0.976	0.001

VAE, ventricular arrhythmia event; OR, odds ratio; CI, confidence interval; LVEF, left ventricular ejection fraction; IRA, infarct-related artery; LAD, left anterior descending artery; LCX, left circumflex coronary artery; RCA, right coronary artery; QTd, QT dispersion; QTcd, corrected QT dispersion; ΔQTd-R, the relative reduction of pre- and post-procedural 12 hours on QTd; ΔQTcd-R, the relative reduction of pre- and post-procedural 12 hours on QTcd.

significant differences between the two groups in terms of bleeding (2.4% *vs.* 4.5%; P=0.63), gastrointestinal reactions (10.0% *vs.* 9.1%; P=0.82), hypotension (20.1% *vs.* 19.7%; P=0.94), or platelet reduction (1.4% *vs.* 3.0%; P=0.75; *Table 5*).

Discussion

This study revealed that the occurrence of NR during the procedure for primary PCI in patients with STEMI can lead to the defective recovery of QTd or QTcd. Furthermore, patients with NR were more likely to have a higher rate of VAEs during postoperative hospitalization when compared to non-NR patients. In addition, ΔQTcd-R was identified as an independent predictor of postprocedure VAEs.

In their study, Zimarino *et al.* (15) reported a decrease in QTcd in 343 out of 612 patients who underwent successful elective PCI. An abundance of studies have suggested that successful revascularization can provide an effective improvement in the inhomogeneity of myocardial repolarization (4,16,17). Earlier studies concluded that QTd or QTcd significantly decreases when TIMI reaches grades 2–3 (18). The methods for evaluating myocardial repolarization have been improved in recent years. However, challenges in achieving effective improvement in myocardial repolarization persist, even with TIMI flow grade 3, when myocardial blush grade (MBG) is less than 2 (19) and accompanied by an elevated corrected TIMI frame count (cTFC) (20) or when the ECG exhibits incomplete ST resolution (21,22), this has been reported in the research conducted by Fukushima *et al.* (23). Hence, the benefit of PCI on ventricular repolarization currently remains uncertain within the medical context.

In our study, the 253 patients, which accounted for 92.0% of all participants, had a remarkable reduction in QTd or QTcd at 12 hours postprocedure. In addition, we found that the non-NR group had a significant decrease in postoperative QTd and QTcd. However, in the NR group, these indices were not significantly different at 12 hours after PCI as compared to those before PCI. This suggests that the occurrence of NR during acute PCI in STEMI

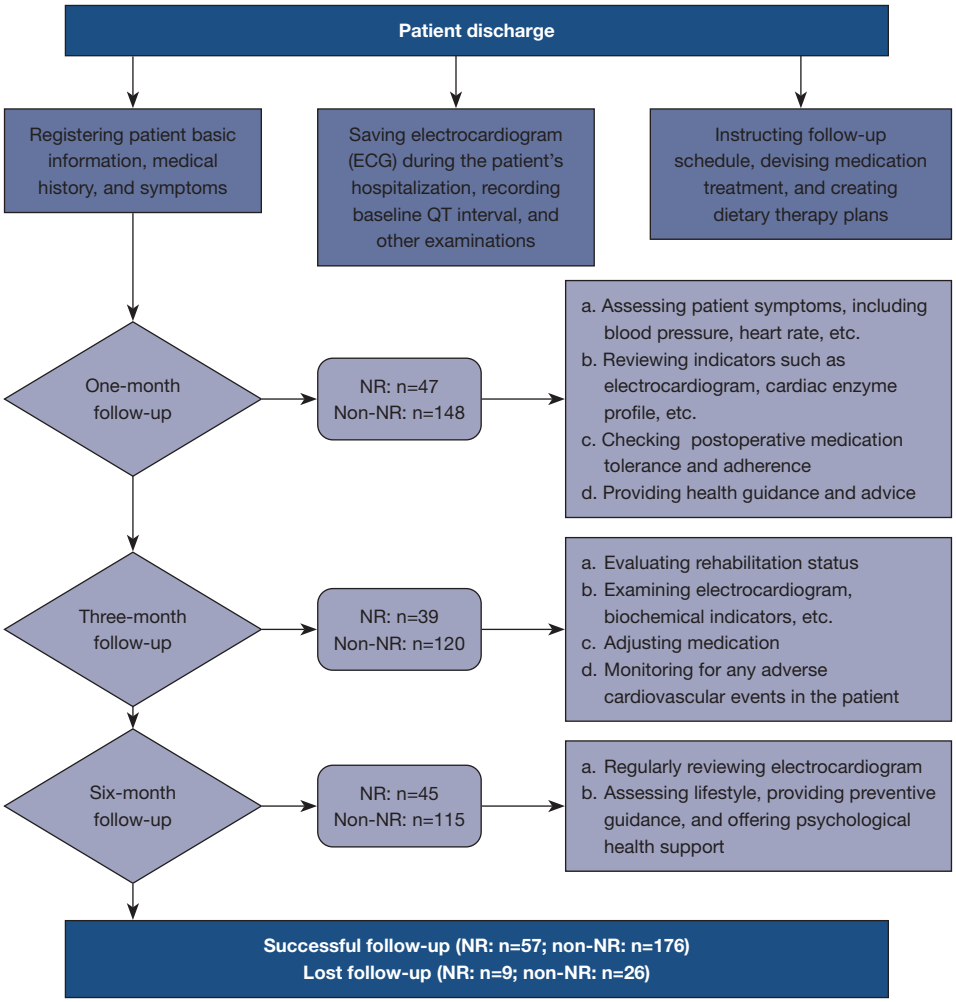

Figure 5 Diagram illustrating the patient follow-up process. NR, no-reflow.

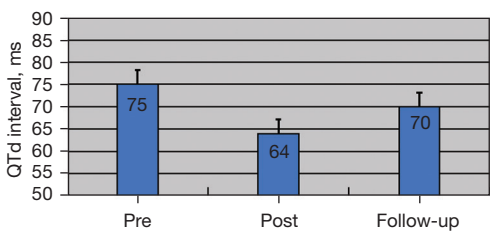

Figure 6 Changes in QTd at follow-up in the NR group. NR, no-reflow; QTd, QT dispersion.

may impact the enhancement of myocardial repolarization homogeneity.

QTd, which is defined as the maximum interlead variation in QT on the 12-lead ECG, is an indicator of ventricular depolarization (17). A number of previous studies have confirmed that STEMI increases the QT interval and QTd (24,25). This increase is accompanied by an elevated risk of severe cardiac arrhythmia and sudden death (4). A more reliable predictor for ventricular arrhythmias and

Table 5 Drug-related complications

Event	Non-NR group (n=209)	NR group (n=66)	χ^2	P value
Bleeding	5 (2.4)	3 (4.5)	0.237	0.63
Gastrointestinal reaction	21 (10.0)	6 (9.1)	0.052	0.82
Hypotension	42 (20.1)	13 (19.7)	0.005	0.94
Thrombocytopenia	3 (1.4)	2 (3.0)	0.101	0.75

Data are presented as n (%). NR, no-reflow.

cardiovascular mortality in patients with STEMI who have undergone PCI is the T peak-end interval and T peak-end/QT ratio, which specifically represents the transmural dispersion of repolarization from the epicardium to the endocardium (5,26). In contrast, the role of QTd and QTcd, as markers for predicting the risk of tachyarrhythmia events and cardiac mortality, remains controversial (27). There is presently less updated information on the timing and acute effects of the mechanical reperfusion of IRAs on QTc and QTd. Furthermore, only few studies have examined the changes in pre- and postprocedure QTd and QTcd, which may intuitively reflect the efficacy of revascularization. Abdelmegid *et al.* (28) reported that there was a significant reduction in QTd and QTcd from admission to 24 hours after reperfusion. They also indicated there to be an increase in minimum QTc interval (Δ=22.4±44.5 msec), which was accompanied by a decrease in QTc interval (Δ=5.1±47.8 msec). In another study, the ratio of QTd reduction at 1 hour postoperation was closely correlated to the percentage of the ST-segment elevation resolution in patients with STEMI who had undergone primary PCI (29). A recent study reported that the relative reduction in QTd was inversely correlated to infarct size (r=−0.506; P=0.001) and infarct transmurality (r=−0.415; P=0.001) in patients with acute non-STEMI (NSTEMI) and that this marker could be clinically applied to detect the successful reperfusion in NSTEMI (30). In our study, the ΔQTd-R and ΔQTcd-R levels were lower in the NR group than in the non-NR group. Furthermore, each increase of 12% in ΔQTcd-R was identified as an independent predictor for postoperative VAEs during hospitalization, which can be considered as a protective factor. Considering the above findings, we believe that ΔQTcd-R can be used as an effective indicator for evaluating the inhomogeneity of myocardial repolarization and the short-term clinical outcomes of patients with STEMI who have undergone primary PCI.

NR can be diagnosed immediately after the conclusion of the initial PCI procedure. The considerably higher rate of VAEs during hospitalization in the NR group may be explained by the defective QTd or QTcd recovery at 12 hours after PCI. Therefore, more attention should be paid to NR patients, especially those exhibiting electrical instability. Patients with NR showed a tendency toward cardiovascular mortality, but the comparison between the two groups in this study lacked statistical significance, likely due to the relatively small number of included cases. The treatment for NR can be classified as pharmacologic (31,32) or nonpharmacologic (33,34) treatment. The European guidelines suggest that glycoprotein IIb/IIIa (GpIIb/IIIa) inhibitors may be used as a bailout therapy in the event of NR (9). Xu *et al.* (35) reported that the combined use of external therapeutic ultrasound and tirofiban can offer synergistic benefits for the treatment of myocardial NR. In addition, Okmen *et al.* (36) reported that intravenous tirofiban could improve the QTd at 24 hours postoperation as compared to heparin therapy but that this did not recover the increase in QTd at 6 hours postprocedure. In our study, the use rate of intracoronary tirofiban was higher in the NR group than in the non-NR group. Interestingly, the postprocedure QTd and QTcd were higher in the NR group. This suggests that the distal embolization attributable to thrombus and plaque debris may be a part of the complex and multifactorial pathogenesis of NR.

After the administration of diltiazem and/or nitroprusside, all 66 patients with NR achieved TIMI grade 3. However, the fact the non-NR group did not receive these interventions, might have influenced the clinical outcomes to some extent. In terms of baseline features, the NR group had a higher percentage of diabetes mellitus and Killip III classification and a longer reperfusion time, which aligns with the results of our previous study (37). As the present study was conducted during the COVID-19 pandemic, relevant investigations suggest (38) a global impact of the pandemic on major clinical outcomes in

patients with STEMI. Therefore, we incorporated the patients' COVID-19 status into our analysis. The research findings indicate no correlation between the occurrence of COVID-19 and reperfusion, which is consistent with Tokarek *et al.*'s (39) assertion that a COVID-19 diagnosis does not influence major endpoint events. The observed results may be attributed to the rigorous and effective disease diagnosis and prevention strategies implemented during the study. However, it is crucial to note that we employed a small-sample, single-center design, and stronger evidence would require further analyses and in-depth research. In addition, our investigation into the surgical timing and methods revealed that approximately two-thirds of emergency surgeries were conducted during the night, with around 90% completed through radial artery puncture. A similar study (40) conducted an analysis of the operative timing and operators, suggesting potential harm in performing surgeries on patients with STEMI during off hours. This consideration takes into account factors such as nighttime fatigue, the shortage of experienced operators during off hours, transit delay, and circadian variations in myocardial perfusion. Moreover, other research (41) suggests that emergency surgeries during off hours are often performed by operators with lower procedural volumes who lack surgical experience. However, regarding the perioperative complication rates in this study, no significant impact on the major outcomes of either group was observed. Moreover, there were no significant differences between the two groups in terms of common perioperative complications associated with PCI. The occurrence of complications was primarily correlated with patient factors of gender, age, underlying diseases, and the severity of vascular lesions, aligning with the findings reported by Rakowski *et al.* (42). As for whether off-hour surgeries had a deleterious impact on patient prognosis, this factor mainly manifested an effect of transit time. In this study, all operators underwent comprehensive intervention diagnostic and therapeutic training, obtaining qualifications for interventional procedures. The annual average of PCI procedures performed by each individual operator exceeded 200. Furthermore, the emergency surgeries at this center primarily address criminal vessels. For noncriminal vessels, elective surgeries are generally chosen. The proportion of criminal vessels with bifurcation lesions was less than 10%, and the occurrence rate of acute myocardial infarction on the basis of chronic occlusive diseases in criminal vessels was extremely low. Built upon these foundations, an improved referral system further would reduce the occurrence of surgical complications. Identifying high-risk clinical features may have potential for predicting the occurrence of NR after acute PCI. The deferred stenting strategy implemented at 4–16 hours after initial coronary reperfusion in high-risk patients can be conducive to reducing NR and increasing the myocardial salvage rate (43). Thus, preventing the occurrence of NR in patients undergoing primary angioplasty is essential.

Limitations

Some limitations to the present study should be acknowledged. The main limitation was the single-center design of the study, and the relatively small number of cases. Therefore, these present results should be further confirmed through prospective, multicenter studies with larger sample sizes. In addition, since the ECG was manually assessed without use of reliable automatic measurements, only the manual measurements of the QT interval, QTd, and other indices were available. Additionally, NR was mainly evaluated using the TIMI flow grade. However, the grade of myocardial perfusion was not validated through other quantitative methods, including MBG or myocardial contrast echocardiography. In addition, none of the pre- or postprocedure medications were systematically investigated, which might have partly influenced the corresponding indices of the surface ECG and the clinical outcomes.

Conclusions

In general, NR after primary PCI in patients with STEMI can lead to the defective recovery of QTd and QTcd, thus resulting in a higher risk of VAEs during postoperative hospitalization. In this study, ΔQTcd-R was identified as an independent predictor of postprocedure VAEs. It can be considered an effective index for evaluating the inhomogeneity of myocardial repolarization and the short-term clinical outcomes of patients with STEMI who have undergone emergency PCI.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-398/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://cdt.amegroups.com/article/view/10.21037/cdt-23-398/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics committee for Clinical Research of the First People's Hospital of Anqing affiliated to Anhui Medical University (No. AQYY--YXLL--KJXM--24-02) and informed consent was provided by all the patients.

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