Diagnosis of coronary artery rethrombosis after effective systemic thrombolytic therapy in patients with ST-segment elevation myocardial infarction

Valentin E Oleynikov,[1] Simon Matskeplishvili,[2] Ekaterina Shigotarova,[1] Alexey Kulyutsin,[1] Nadezhda Burko [1]

[1]Therapy Department, Penza State University, Penza, Russian Federation
[2]Cardiology Department, Lomonosov Moscow State University Clinic, Moscow, Russian Federation

Correspondence to
Dr Valentin E Oleynikov, Therapy Department, Penza State University, Penza 440026, Russian Federation; v.oleynikof@gmail.com

Accepted 7 December 2021

To cite: Oleynikov VE, Matskeplishvili S, Shigotarova E, *et al*. *J Investig Med* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/jim-2021-001945

ABSTRACT

The aim of the study was to evaluate the diagnostic significance of ST-segment re-elevation episodes registered with telemetric ECG monitoring in patients with ST-segment elevation myocardial infarction (STEMI) treated with thrombolytic therapy (TLT). The study included 117 patients with STEMI following effective TLT. The elective coronary angiography followed by percutaneous coronary interventions was performed in the interval from 3 to 24 hours after a successful systemic TLT. Before and after cardiac catheterization, the telemetric ECG monitoring was performed using AstroCard Telemetry system (Meditec, Russia). During the study, two groups of patients were formed. Group 1 included 85 patients (72.6%) without new ST-segment deviations on telemetry. 77 patients (90.6%) had no recurrent coronary artery thrombosis at angiography. Eight patients (9.4%) from group 1 were diagnosed with thrombosis of the infarct-related coronary artery. Group 2 included 32 patients (27.4%) who underwent TLT and then had ST-segment re-elevation episodes of 1 mV or more in the infarct-related leads, lasting for at least 1 minute. In group 2, in 27 of 32 patients (84.4%), thrombosis of the infarct-related coronary artery was confirmed ($p<0.01$ compared with group 1). In 71.9% cases, the recurrent ischemic episodes were asymptomatic ('painless myocardial ischemia') ($p<0.01$). Thus, in patients with STEMI and successful TLT, re-elevation of ST-segment during remote ECG monitoring is strongly related to angiographically documented coronary artery thrombotic reocclusion. The absence of chest pain during recurrent myocardial ischemia requires continuous ECG telemetry to select patients for the rescue percutaneous coronary interventions at an earlier stage.

Significance of this study

What is already known about this subject?

- According to a retrospective study from 243 patients with ST-segment elevation myocardial infarction (STEMI) who underwent 24-hour ECG monitoring after systemic thrombolytic therapy (TLT) (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) Studies), episodes of ST-segment deviation recorded within 6–24 hours after TLT are associated with an increase in 30-day mortality and 1-year death rate (Langer A, Krucoff MW, Klootwijk P, *et al*. Prognostic Significance of ST Segment Shift Early After Resolution of ST Elevation in Patients With Myocardial Infarction Treated With Thrombolytic Therapy: The GUSTO-I ST Segment Monitoring Substudy. *J Am Coll Cardiol* 1998;31:783–9).

INTRODUCTION

Diagnosis and treatment of acute myocardial infarction with ST-segment elevation (STEMI) is one of the most severe complications of coronary heart disease; it is an urgent problem of modern cardiology requiring immediate intervention.[1 2]

The hospital mortality for STEMI in countries represented in the European Society of Cardiology varies from 4% to 12%, and approximately 10% of patients die within 12 months after STEMI.[3]

Although the first myocardial reperfusion in STEMI with intracoronary injection of thrombolytics took place more than 40 years ago,[4] thrombolytic therapy (TLT) is being successfully used as a method to restore coronary artery blood flow. The transportation of patients to percutaneous coronary intervention (PCI) centers within 2 hours after the first medical contact is impossible in many countries, which necessitates implementing prehospital TLT. The relevance of TLT has increased dramatically due to the COVID-19 pandemic. The pandemic has led to restructuring of specialized clinics worldwide into hospitals caring for patients with the new coronavirus infection. It has significantly limited the availability of PCI. Despite the rapid delivery of patients who go on to receive

Significance of this study

What are the new findings?

- The present study has proven that episodes of ST-segment re-elevation, recorded during remote ECG monitoring in patients with STEMI who underwent systemic TLT, are asymptomatic in 71.9% of cases and are associated with the development of coronary artery thrombotic reocclusion.
- In some patients with STEMI (27.3%) who underwent systemic TLT, the ST-segment deviation episodes in the infarct-related leads, lasting for at least 1 minute, have been registered.
- These episodes of ST-segment re-elevation in 84.4% of cases indicated the development of a rethrombosis of an infarct-related coronary artery.
- Transient episodes of ST-segment re-elevation after TLT in most cases (71.9%) were asymptomatic, were not detected by standard bedside ECG monitoring and discrete ECG recording, which leads to a delay in the rescue percutaneous coronary intervention (PCI) in these patients.

How might these results change the focus of research or clinical practice?

- The inclusion of telemetric ECG monitoring in the required set of diagnostic procedures in patients after fibrinolysis can be useful for detecting transient asymptomatic ST -segment deviation and timely selection of patients for rescue PCI.

excellent treatment, the currently available data indicate that in 12.5%–30% of cases, successful TLT is followed by the development of rethrombosis of infarct-related coronary arteries caused by residual stenosis.[5 6] To ensure a reliable revascularization after an effective TLT, a routine PCI is performed; and in case of coronary blood flow instability, a rescue PCI is performed. Note that the current methods of non-invasive rethrombosis diagnosis are imperfect, the development of rethrombosis is not always accompanied by typical clinical symptoms such as chest pain and shortness of breath due to an adequate analgesia and a number of protective pathophysiological mechanisms.[7 8]

ECG telemonitoring systems provide continuous automated ECG analysis in real-time concomitantly with rapid response to a number of diagnostically significant events, including ST-segment dynamics. It is necessary to make timely decisions regarding implementing emergency angioplasty, increasing the extent of myocardial salvage and the survival rate of patients.

Despite stent thrombosis in patients with STEMI being sufficiently described in detail in the literature, the number of reports regarding rethrombosis after TLT is scarce.

The first studies examining the effectiveness of ECG telemetry-assisted early detection of STEMI before and after TLT were published at the end of the 20th century. Krucoff *et al* described online ECG monitoring, underscoring the importance of accurate forecasting of ST-segment monitoring for assessing the effectiveness of TLT. These authors demonstrated a reduction of terms when diagnosing the effectiveness of coronary blood flow restoration and infarct-related coronary artery (CA) rethrombosis concomitantly with continuous assessment of ST-segment dynamics.[9 10]

In the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries Study, after systemic TLT the patients were subjected to daily continuous ECG monitoring, 30 minutes after the end of fibrinolysis. The study demonstrated that ST-segment deviation episodes, recorded after treatment, have negative prognostic significance and are associated with an increase in 30-day mortality.[11]

In this regard, it is important to study telemetric ECG monitoring as a method that potentially allows rapidly identifying high-risk patients requiring emergency PCI, thereby reducing the risks associated with rethrombosis.

The aim of this study was to evaluate the capabilities of ECG telemetric monitoring for diagnosing CA rethrombosis after TLT in STEMI.

MATERIALS AND METHODS

The research was conducted as a prospective observational study at the Department of Therapy of the Medical Institute of Penza State University of the Ministry of Education and Science of the Russian Federation on the basis of the Emergency Cardiology Department of Penza Regional Clinical hospital n.a. N.N. Burdenko (Penza, Russia). The study design is shown in figure 1.

Patients

The study included 117 patients with STEMI who were hospitalized on the first day after their anginal attack (persistent chest pain with or without radiation of pain to the neck, lower jaw, or left arm). All patients at the prehospital stage have undergone an effective TLT. The preference for TLT over PCI in all patients is due to the impossibility of performing PCI in less than 2 hours after the first medical contact. The effectiveness of TLT has been evaluated according to the ECG criteria, as follows: the ST-segment decreased to the isoline in the lead, with a maximum elevation of 50% or more from the baseline in 60–90 minutes after the start of TLT.[3] Due to effective therapy, chest pain has been relieved, and hemodynamics was stable.

The inclusion criteria for the study were as follows: written informed consent of the patient; physical and mental ability of the patient to participate in the study; acute STEMI; 24 hours from the onset of an anginal attack; successful TLT.

The exclusion criteria included: failure to sign an informed consent; conduction abnormalities that complicated the analysis of ST-segment deviation (including those due to post-infarction cardiosclerosis, previously performed heart valve replacement, persistent atrial fibrillation and atrial flutter, as well as an implanted artificial pacemaker); presence of chronic diseases in the terminal phase; acute violation of cerebral circulation; alcohol abuse and drug use.

Telemetric ECG monitoring

Since the inclusion criterion was successful TLT, all patients underwent coronary angiography (CAG) between 3 and 24 hours after the initial presentation. The effectiveness

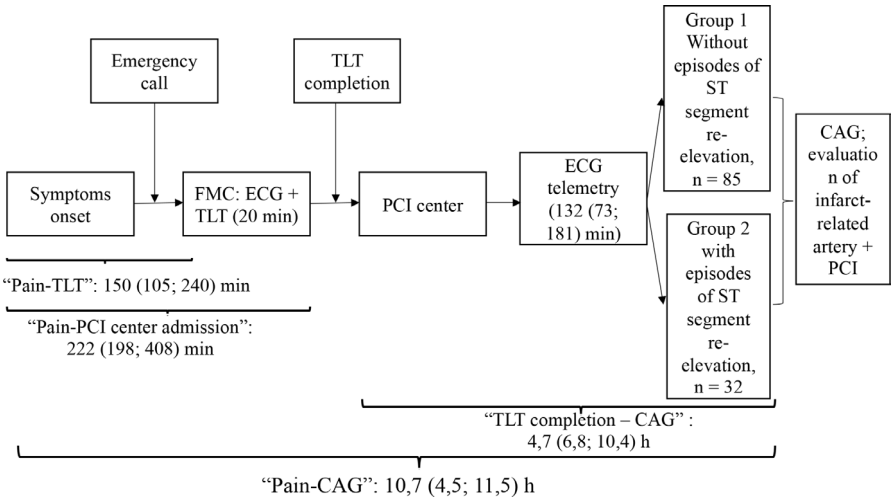

Figure 1 Study design. CAG, coronary angiography; FMC, first medical contact; PCI, percutaneous coronary intervention; TLT, thrombolytic therapy.

of coronary blood flow restoration after TLT was assessed according to the Thrombolysis in Myocardial Infarction (TIMI) guidelines.[12] Coronary thrombus was defined according to the Academic Research Consortium definition.[13]

In the interval between TLT and PCI, all patients underwent ECG monitoring via telemetric ECG recording using the AstroCard-Telemetry complex (ZAO Meditek, Russia). The duration of telemetric monitoring was 132 (73–181) minutes from the patient's admission to the hospital until PCI was performed. The dynamics of the ST-segment were analyzed using 12 leads in the automatic mode with subsequent manual verification. The appearance of a transient elevation of the ST-segment in leads, reflecting the zone of myocardial damage, with an amplitude of 1 mm or more and lasting not less than 1 minute, was considered an episode of ST-segment re-elevation. The ST-segment elevation amplitude was evaluated after 80 ms from the J point. Each episode was classified to be a separate event with intervals between them exceeding 1 minute.

According to some studies, such as Hirudin for Improvement of Thrombolysis 4 and TIMI 14 substudy, ST-segment elevation reflects the degree of CA thrombotic occlusion.[12 14] Bearing this in mind, we came to the conclusion that re-elevation of ST-segment episodes, recorded via telemetric monitoring, may indicate that coronary rethrombosis is developing after a previously recognized effective TLT.

According to the presence or absence of ST-segment re-elevation episodes, two groups of patients were formed to study the diagnostic importance of transient ST-segment re-elevation.

Group 1 included 85 patients (72.6%) with no transient re-elevation of the ST-segment recorder within the telemetric monitoring.

Group 2 included 32 patients (27.4%) with registered episodes of ST-segment re-elevation according to the criteria described earlier.

For an in-depth analysis of the effect of stability restoration of coronary blood flow both on the development of rhythm and conduction abnormalities, and on long-term results, an 'Absence of Rethrombosis' Group (RT(–), n=84, including patients with effective TLT, confirmed by CAG results), and 'Presence of Rethrombosis' Group (RT(+), n=33, including patients with diagnosed rethrombosis of infarct-related CA), were retrospectively formed.

In order to evaluate the long-term results, a comparative assessment of lethality and new cardiovascular events (acute coronary syndrome and acute cerebrovascular accident) has been carried out in a month and 12-month period after inclusion.

Long-term results were assessed in 115 out of 117 patients involved in the study (98.3%) 30±2 days later: 82 (97.6%) patients of the RT(–) group and 33 people (100%) of the RT(+) group. Two patients were not contacted.

Long-term results were analyzed in 86.3% of patients (101 people) in 12 months; 12 of them denied visiting the doctor, but agreed to answer the doctor's questions on phone. The primary endpoints were established in 13 patients according to the database of the Federal Hospital Management System. The data of 16 patients are unknown. Thus, data of 72 patients (85.7%) of the RT(–) group and of 29 patients (87.9%) of the RT(+) group were analyzed.

Statistical analysis

The results were statistically processed using the Statistica V.6.0 software package of StatSoft (USA). For a normal distribution, the data were denoted as M, and an SD was denoted as S. Student's t-test was used for both related and unrelated groups. For an asymmetric distribution, the data were presented as the number of observations (n), the median (Me), and the IQR (Q 25%; Q 75%). The Mann-Whitney test for related groups and the Wilcoxon test for unrelated groups were also used. To compare the qualitative variables, the X^2 test was applied with Yates' correction for continuity. The level of statistical significance was $p<0.05$.

RESULTS

Patient characteristics and ECG telemetry

Men prevailed in the study group (97 (82.9%)); the mean age of the patients was 59 years (range, 52–64 years).

Table 1 Comparative characteristics of the patients in groups 1 and 2

Parameter	Group 1, n=85	Group 2, n=32
Mean age (y)	59.6±10.4	60.1±8.7
Men, n (%)	68 (80)	29 (90.6%)*
Body mass index, kg/m^2	27.7±2.3	27.7±2.6
Family history of coronary artery disease, n (%)	32 (37.6)	21 (65.6)**
Smoking, n (%)	49 (57.6)	25 (78.1)*
Dyslipidemia, n (%)	58 (68.2)	22 (68.6)
History of myocardial infarction, n (%)	7 (8.2)	4 (12.5)
History of hypertension, n (%)	68 (80)	23 (71.9)
Diabetes mellitus type 2, n (%)	9 (10.6)	5 (15.6)
Previous antiplatelet intake, n (%)	21 (24.7)	7 (21.9)
Mean level of troponin, ng/mL	23.7 (0.3; 3.9)	16 (0.4; 27.9)
Localization of myocardial infarction		
Myocardial infarction of the anterior wall of LV, n (%)	45 (52.9)	16 (50)
Myocardial infarction of the inferior wall of LV, n (%)	36 (42.4)	14 (43.8)
Circumferential myocardial infarction, n (%)	4 (4.7)	2 (6.2)
Characteristics of TLT		
'Pain-TLT' interval, min (Me (Q 25%; Q 75%))	180 (120; 240)	120 (90; 180)
TLT with alteplase, n (%)	35 (41.2)	12 (37.5)
TLT with tenecteplase, n (%)	15 (17.6)	6 (18.8)
TLT with pro-urokinase, n (%)	35 (41.2)	14 (43.7)
Class of heart failure according to the Killip classification		
1, n (%)	69 (81.2)	24 (75)
2, n (%)	7 (8.2)	2 (6.3)
3, n (%)	4 (4.7)	3 (9.4)
4, n (%)	5 (5.9)	3 (9.4)

Hereafter, significant differences are indicated as follows: *p<0.05; **p<0.01.
LV, left ventricle; Me, median; TLT, thrombolytic therapy.

Twenty-eight (23.9%) patients included in the study with a history of coronary artery disease and diabetes mellitus had been taking acetylsalicylic acid at a dose of 75–100 mg/day for a month or more. None of the patients has previously taken either P2Y12-receptor inhibitors or oral anticoagulants.

The median time period between pain onset and prehospital TLT was 2.5 hours (range, 1.75–4 hours). The 'pain-TLT' interval was determined by the time of medical resource utilization of a patient. In all cases, the choice of TLT as the first stage of revascularization was caused by the estimated 'diagnosis-conductor' time exceeding 120 minutes.[3] One of the drugs indicated in table 1 was used as a fibrinolytic agent, according to its availability for the emergency medical service personnel. Systemic bleeding disorders, intracranial hemorrhage, and puncture site bleeding were not found in the patients included in the study. The median time period between the onset of pain and the patient's arrival at the hospital was 3.7 hours (range, 3.3–6.8 hours). In the interval from 3 to 24 hours after a successful systemic TLT, the patients underwent CAG. The median time period between pain onset and CAG was 10.7 hours (range, 4.95–11.5 hours).

Telemetric ECG monitoring and cardiac catheterization results

The interval between the end of thrombolysis and the beginning of CAG was 6.8 hours (range, 3.2–10.4 hours). In some patients, ECG telemonitoring performed during this period revealed transient elevations of the ST-segment with an amplitude exceeding 1 mm, which were itemized above. Based on the absence or presence of such episodes, 117 patients were divided into 2 groups: group 1 included 85 people without episodes, and group 2 included 32 patients with ST-segment elevation episodes.

In group 2, male patients prevailed (p=0.04), and patients with a family history of heart problems and tobacco dependence (p<0.01 and p=0.04, respectively) (table 1).

In group 2, only 1 (1–2) episode of transient re-elevation of the ST-segment within the period of 132 minutes (range, 73–181 minutes) of telemetric ECG monitoring has been recorded. The total duration of the episodes was from 1.5 to 71 minutes, with an average duration of 18.9 (5.5–32.3) minutes.

CA stenosis was assessed by an operator via measuring the area of the proper and residual vessel lumen. Stenoses of the left CA trunk of 50% or more and other CA by 75% or more were considered to be significant.[3] The data presented in table 2 indicate that in group 2, the lesions in the circumflex artery (p=0.01) and significant stenosis of 1 (in all cases infarct related) of the CAs (p<0.01) were more common.

An operator visually assessed the blood flow of the infarct-related CA according to the TIMI classification[3] before and after angioplasty.

Seventy-seven patients (90.6%) in group 1 had significant stenoses of the infarct-related CA with no signs of thrombosis according to the CAG results; the distal blood flow was restored to the TIMI 2 level. However, 8 patients (9.4%) were diagnosed with thrombotic occlusion of the CA, the distal blood flow was TIMI level 1-0. According to the Academic Research Consortium definition, coronary thrombus was defined as spheric, ovoid, or irregular intraluminal filling defect or lucency surrounded on 3 sides by contrast medium seen just distal or within the coronary stenosis in multiple projections or a visible embolization of intraluminal material downstream.[14]

Twenty-five patients (78.1%) in group 2 had signs of thrombosis of the infarct-related CA (p<0.01) and distal blood flow was not detected (TIMI 1-0). In patients with a significant atherosclerotic lesion of 2 or more CAs, the localization of the thrombus correlated with the severity of stenosis.

Stenting of the infarct-related CA was conducted in 102 (87.2%) of cases; 15 (12.8%) patients underwent balloon angioplasty only.

After angioplasty in 82 patients (70.1%) in groups 1 and 2, the coronary blood flow was restored to TIMI 3 level; 24 patients (20.5%) had a slower filling of the distal site (TIMI 2). In 11 cases (9.4%), PCI was ineffective (TIMI 1-0) because the contrast did not get through the stent implantation site.

According to the study inclusion criteria in all 117 patients, TLT by standard ECG signs was considered to be effective. However, some patients who had undergone CAG had thrombotic occlusions of the infarct-related CA.

Table 2 CAG results in groups 1 and 2

Parameter	Group 1, n=85	Group 2, n=32
Perfusion type, n (%)		
Right	69 (81.2)	26 (81.3)
Left	4 (4.7)	–
Balanced	12 (14.1)	6 (18.7)
Localization of stenosis		
Stenosis of LA >50%, n (%)	8 (9.4)	4 (12.5)
Stenosis of LAD >75%, n (%)	61 (71. 8)	19 (59.4)
Stenosis of LCx >75%, n (%)	6 (0.1)	8 (25)**
Stenosis of RA >75%, n (%)	20 (23.5)	5 (15.,6)
Quantitative characterization of CA stenosis		
Stenosis of 1 CA, n (%)	33 (38.8)	21 (65.6)*
Stenosis of 2 CA, n (%)	22 (25.9)	4 (12.5)
Stenosis of 3 CA or lesion of LA, n (%)	30 (35.3)	7 (21.9)
Infarct-related arteries		
LA, n (%)	–	1 (3.1)
LAD, n (%)	49 (5.6)	17 (53.1)
LCx, n (%)	6 (7.1)	2 (6.3)
RA, n (%)	30 (35.3)	12 (37.5)
Stenting characteristics		
The number of patients who underwent stenting, n (%)	74 (87.1)	28 (87.5)
Blood flow restoration in the infarct-related artery after PCI		
TIMI 0	3 (3.5%)	2 (6.3%)
TIMI 1	5 (5.9%)	1 (3.1%)
TIMI 2	19 (22.4%)	5 (15.6%)
TIMI 3	58 (68.2%)	24 (75%)

Hereafter, significant differences are indicated as follows: *p<0.05; **p<0.01.
CA, coronary artery; CAG, coronary angiography; LA, left artery; LAD, left anterior descending artery; LCx, left circumflex artery; PCI, percutaneous coronary intervention; RA, right artery; TIMI, Thrombolysis in Myocardial Infarction.

Thus, we come to the conclusion that the thrombosis under consideration has developed after effective TLT, and therefore, it is a rethrombosis. The anatomical localization of coronary thrombosis corresponded to indirect signs of myocardial ischemia in all cases, in the form of ST-segment re-elevation in the infarct-related leads on the ECG.

The obtained data are clearly presented in figure 2.

Thus, the ST-segment re-elevation episodes detected after successful thrombolytic therapy during telemetric ECG monitoring with a sensitivity of 75.8% and a specificity of

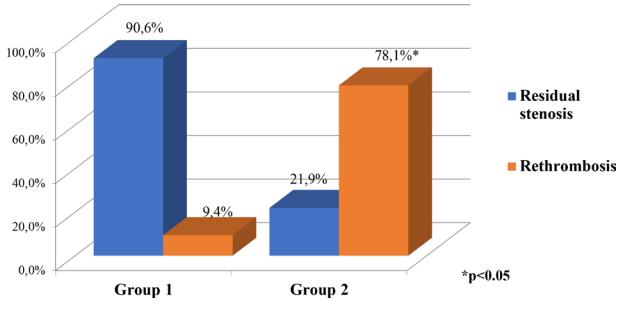

Figure 2 The frequency of coronary artery thrombosis diagnosed at coronary angiography.

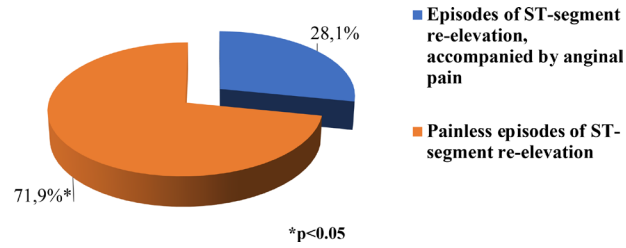

Figure 3 Clinical characteristics of ST-segment re-elevation episodes.

91.7% have indicated the instability of the coronary blood flow and the developing rethrombosis of the infarct-related CA. The forecasting value of a positive result was 78.1%; the forecasting value of a negative result was 90.6%; and the accuracy was 87.2%.

Acute painless myocardial ischemia

The analysis of the clinical picture that accompanied the ST-segment re-elevation showed that the episodes have been primarily painless (71.9%); and the term 'acute painless myocardial ischemia' for these episodes was proposed. ST-segment re-elevation episodes accompanied by the development of typical anginal attacks were found in only 9 patients (28.1%; p<0.01) (figure 3).

Thus, the presented data show that early identification of ST-segment re-elevation episodes, which in most cases are asymptomatic and point to the development of rethrombosis of the infarct-related CA, is possible only when telemetric ECG monitoring is used.

Depending on the presence or absence of rethrombosis of infarct-related coronary artery, RT(+) and RT(–) comparison groups were formed according to CAG. An analysis of rhythm and conduction abnormalities and of long-term results was carried out in the indicated groups.

It is interesting to note that patients with diabetes mellitus (p=0.02), burdened heredity (p<0.01), and tobacco addicts (p=0.02) were significantly more frequent among patients with developed rethrombosis.

In patients with developed CA rethrombosis, compared with patients with stable myocardial perfusion, life-threatening rhythm and conduction abnormalities, such as paroxysmal ventricular tachycardia (63.6% vs 44%), and episodes of third-degree atrioventricular (AV) block (12.1% vs 3.6%; p<0.05) occurred more often.

No significant difference in the frequency and nature of rhythm disturbances between the RT(+) and the RT(–) groups was detected during the telemetry period. However, after PCI life-threatening rhythm and conduction abnormalities, such as paroxysmal ventricular tachycardia (63.6% vs 44%), and episodes of third-degree AV block (12.1% vs 3.6%; p<0.05) were more often recorded in patients with rethrombosis.

The long-term results of treatment were assessed in patients with CA rethrombosis and with a stable course of coronary reperfusion. Within 30 days after the index event, no patients were hospitalized with exacerbation of CA disease, chronic heart failure, and other vascular events. Thirty-day mortality was 1.2% in the RT(–) group, and 6.1% in the RT(+) group (relative risk =4.97; CI (0.47

to 52.9)). It was found that mortality among patients with developed CA rethrombosis was significantly higher than that among patients with stable coronary perfusion (13.8% vs 1.4%; RR=9.9; CI (1.2 to 85.1)). Recurrent myocardial infarction developed more often in the group with CA rethrombosis (3.3% vs 20.8%).

DISCUSSION

The modern approach to diagnosis and treatment of STEMI, implying timely restoration of the coronary blood flow in the infarct-related artery, has led to decreased mortality caused by this disease, from 30%–35% to 4%–12%.[3] Of course, stenting as a method of choice has shown obvious advantages over TLT. However, there are only a few countries worldwide that have managed to completely abandon TLT.[3] In a number of countries, TLT remains one of the main approaches available for coronary blood flow restoration in relation to the territorial features, economic situation, or particular qualities of the healthcare system. Patients involved in the research have undergone pharmacoinvasive revascularization. The choice of the strategy for restoration of coronary blood flow has been caused by the peculiarities of medical resource utilization including the Penza region (the area of 43.4 thousand km^2 with a population of over 1,3 million people). The region has an angiographic laboratory that provides 7/24 care to patients with STEMI. The estimated 'diagnosis-conductor' timing has often exceeded the recommended 120 minutes.[3] In addition, there was patients' delay in medical resource utilization. Thus, the mean 'pain-TLT' interval was 150 minutes (range, 105–240 minutes), while the 'first medical contact-TLT' interval was less than 20 minutes.[3]

In pharmacological revascularization, the majority of deaths are due to initially extensive myocardial damage with a marked reduction of the left ventricular systolic function,[15] inefficiency of TLT[16] or rethrombosis of the infarct-related CA.[5 6 17 18] The TIMI I studies, the Western Washington study, as well as the data received by Ohman *et al* have convincingly demonstrated that the mortality rate among patients with rethrombosis after effective TLT was two times higher than in patients with stable coronary perfusion.[17 19 20] Any method of revascularization does not exclude the risk of repeated thrombosis. In particular, stent thrombosis was described in detail in a number of articles.[21] Much less attention, however, has been devoted to thrombosis that develops after TLT in 12.5%–30% of cases. Meanwhile, a high risk of rethrombosis is associated with preserving the morphological substrate of thrombosis—an unstable atherosclerotic plaque requiring angioplasty.[12 14 22 23] Therefore, studying ECG telemetry, as a method for dynamic assessment of the state of coronary blood flow and the quality of reperfusion, deserves close attention.

In the studied cohort of patients, the coronary rethrombosis rate was 28.2%, which is consistent with published data. The present study shows that ST-segment re-elevation episodes with amplitude of 1 mm or more in the infarct-related leads, recorded during telemetric ECG monitoring for 12 channels, with a sensitivity of 75.8% and a specificity of 91.7%, indicate developing CA rethrombosis. This method allows the selection of patients for rescue PCI in critical circumstances.

In 79.1% of cases, the painless nature of the transient ST-segment re-elevation has been identified. Although painless myocardial ischemia has been the subject of numerous publications,[24 25] we have not found any reports in which this phenomenon on the first day of STEMI was described. At acute myocardial infarction, painless myocardial ischemia is probably caused by ischemic preconditioning. This phenomenon normally occurs under conditions of reperfusion followed by reocclusion of the CA. The complex pathogenesis of ischemic preconditioning, including the release of opioids,[26] with subsequent activation of δ-opioid receptors, induces a powerful analgesic effect.[8] A certain role is played by the physiological mechanism responsible for pain threshold, which increases after an intense pain attack, as well as the continuing effect of narcotic analgesics.

It is important to note that the detection of coronary blood flow instability in patients with STEMI indicates the rescue PCI group.[3] The present study has shown that applying telemetric ECG monitoring in patients after systemic TLT allows timely diagnosis of the developing rethrombosis of the infarct-related CA, which is important in patients with painless myocardial ischemia, since a typical clinic of a severe anginal attack is usually not observed.

CONCLUSION

In patients with STEMI and successful prehospital TLT, re-elevation of ST-segment during remote ECG monitoring indicates angiographically confirmed CA thrombotic reocclusion. The absence of chest pain during recurrent myocardial ischemia episodes necessitates continuous ECG telemetry to select patients requiring the rescue PCIs at an earlier stage.

STUDY LIMITATIONS

The number of patients included in the study was relatively small. We have not analyzed correlation of recurrent CA thrombosis rate with anti-thrombotic regimen applied at the prehospital period. The patients with recurrent myocardial infarction have been excluded from the study.

Contributors VEO has suggested to apply the telemetric ECG for the diagnosis of coronary artery rethrombosis after effective thrombolytic therapy in patients with STEMI, and organized study conduction and described the pathogenesis of painless ischemia in STEMI. SM has drafted the manuscript and provided general governance of the study. ES has conducted the recruitment of patients with STEMI who underwent effective systemic thrombolytic therapy and subsequent percutaneous coronary intervention. She has singled out the criteria for the infarct-related artery rethrombosis and described the pathogenesis of painless ischemia in STEMI. AK has analyzed the results of coronary angiography and percutaneous coronary intervention. NB has conducted an analysis of the clinical symptomatology of STEMI in patients with infarct-related artery rethrombosis, and prepared a literature review on the issue of rethrombosis in STEMI. VEO is responsible for the overall content as the guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval All patients gave their written informed consent and the study protocol was approved by the local ethics committee on human research of Penza State University (reference number 2014/101). The study was performed in accordance with ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplemental information. Deidentified participant data are available from the coauthor ES.

ORCID iD
Nadezhda Burko http://orcid.org/0000-0002-4932-0000

REFERENCES

1 Claeys MJ, Sinnaeve PR, Convens C, *et al*. STEMI mortality in community hospitals versus PCI-capable hospitals: results from a nationwide STEMI network programme. *Eur Heart J Acute Cardiovasc Care* 2012;1:40–7.
2 Virani SS, Alonso A, Benjamin EJ, *et al*. Heart disease and stroke statistics – 2020 update: a report from the American heart association. *Circulation* 2020;141:e139–596.
3 Ibanez B, James S, Agewall S, *et al*. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J* 2018;39:119–77.
4 Chazov EI, Matveeva LS, Mazaev AV, *et al*. [Intracoronary administration of fibrinolysin in acute myocardial infarct]. *Ter Arkh* 1976;48:8–19.
5 Pinto DS, Kirtane AJ, Nallamothu BK, *et al*. Hospital delays in reperfusion for ST-elevation myocardial infarction: implications when selecting a reperfusion strategy. *Circulation* 2006;114:2019–25.
6 Gibson CM, Karha J, Murphy SA, *et al*. Early and long-term clinical outcomes associated with reinfarction following fibrinolytic administration in the thrombolysis in myocardial infarction trials. *J Am Coll Cardiol* 2003;42:7–16.
7 Depre C, Vatner SF, Vatner Depre SF. Cardioprotection in stunned and hibernating myocardium. *Heart Fail Rev* 2007;12:307–17.
8 Shlyakhto EV, Nifontov EM, Galagudza MM. Pre- and postconditioning as ways of cardioprotection: pathophysiological and clinical aspects. *J Heart Fail* 2008:1–10.
9 Krucoff MW, Croll MA, Pope JE, *et al*. Continuously updated 12-lead ST-segment recovery analysis for myocardial infarct artery patency assessment and its correlation with multiple simultaneous early angiographic observations. *Am J Cardiol* 1993;71:145–51.
10 Krucoff MW, Wagner NB, Pope JE, *et al*. The portable programmable microprocessor-driven real-time 12-lead electrocardiographic monitor: a preliminary report of a new device for the noninvasive detection of successful reperfusion or silent coronary reocclusion. *Am J Cardiol* 1990;65:143–8.
11 Langer A, Krucoff MW, Klootwijk P, *et al*. Prognostic significance of ST segment shift early after resolution of ST elevation in patients with myocardial infarction treated with thrombolytic therapy: the GUSTO-I ST segment monitoring substudy. *J Am Coll Cardiol* 1998;31:783–9.
12 de Lemos JA, Antman EM, Giugliano RP, *et al*. St-segment resolution and infarct-related artery patency and flow after thrombolytic therapy. *Am J Cardiol* 2000;85:299–304.
13 Campos CM, Costa F, Garcia-Garcia HM, *et al*. Anatomic characteristics and clinical implications of angiographic coronary thrombus: insights from a patient-level pooled analysis of SYNTAX, RESOLUTE, and leaders trials. *Circ Cardiovasc Interv* 2015;8:e002279.
14 Zeymer U, Schröder R, Tebbe U, *et al*. Non-invasive detection of early infarct vessel patency by resolution of ST-segment elevation in patients with thrombolysis for acute myocardial infarction; results of the angiographic substudy of the Hirudin for Improvement of Thrombolysis (HIT)-4 trial. *Eur Heart J* 2001;22:769–75.
15 Hochman JS, Sleeper LA, White HD, *et al*. One-year survival following early revascularization for cardiogenic shock. *JAMA* 2001;285:190–2.
16 Califf RM, Topol EJ, George BS, *et al*. Characteristics and outcome of patients in whom reperfusion with intravenous tissue-type plasminogen activator fails: results of the thrombolysis and angioplasty in myocardial infarction (TAMI) I trial. *Circulation* 1988;77:1090–9.
17 Ohman EM, Califf RM, Topol EJ, *et al*. Consequences of reocclusion after successful reperfusion therapy in acute myocardial infarction. TAMI Study Group. *Circulation* 1990;82:781–91.
18 Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) Investigators, Van De Werf F, Adgey J, *et al*. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. *Lancet* 1999;354:716–22.
19 Dalen JE, Gore JM, Braunwald E, *et al*. Six- and twelve-month follow-up of the phase I thrombolysis in myocardial infarction (TIMI) trial. *Am J Cardiol* 1988;62:179–85.
20 Kennedy JW, Ritchie JL, Davis KB, *et al*. The Western Washington randomized trial of intracoronary streptokinase in acute myocardial infarction. A 12-month follow-up report. *N Engl J Med* 1985;312:1073–8.
21 Gibson CM, Murphy SA, Rizzo MJ, *et al*. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. thrombolysis in myocardial infarction (TIMI) Study Group. *Circulation* 1999;99:1945–50.
22 Gibson CM, Cannon CP, Daley WL, *et al*. TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation* 1996;93:879–88.
23 Aitchison KA, Baxter GF, Awan MM, *et al*. Opposing effects on infarction of delta and kappa opioid receptor activation in the isolated rat heart: implications for ischemic preconditioning. *Basic Res Cardiol* 2000;95:1–10.
24 Ahmed AH, Shankar K, Eftekhari H, *et al*. Silent myocardial ischemia: current perspectives and future directions. *Exp Clin Cardiol* 2007;12:189–96.
25 Petretta M, Fiumara G, Petretta MP, *et al*. Detection of silent myocardial ischemia: is it clinically relevant? *J Nucl Cardiol* 2013;20:707–10.
26 Galagudza MM, Blokhin IO, Shmonin AA, *et al*. Reduction of myocardial ischemia-reperfusion injury with pre- and postconditioning: molecular mechanisms and therapeutic targets. *Cardiovasc Hematol Disord Drug Targets* 2008;8:47–65.