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Treatment of ST-elevation myocardial infarction – an observational study

ORIGINAL ARTICLE

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BACKGROUND

ST-elevation myocardial infarction is treated with reperfusion, either in the form of primary percutaneous coronary intervention (PCI) or thrombolytic therapy. The choice of treatment depends on transport time to the nearest PCI centre. Norway's geography means that thrombolytic therapy will be appropriate for many patients. Irrespective of treatment choice, it is important to avoid delays. We wished to compare the outcomes of primary PCI and thrombolytic therapy in our healthcare region and to examine whether reperfusion therapy was administered within the recommended time window.

MATERIAL AND METHOD

Using registry data and patient medical records, we compared the outcomes of primary PCI and thrombolytic therapy in cases of ST-elevation myocardial infarction in the Central Norway Regional Health Authority in the period 2015–16. The outcomes analysed were 30-day mortality, ejection fraction measured by echocardiography during the hospital stay, incidence of bleeding complications, and time from diagnosis to start of treatment.

RESULTS

The study population comprised 648 patients with ST-elevation myocardial infarction. Of these, 382 were treated with primary PCI and 266 received thrombolytic therapy. The 30-day mortality was 5.5 % in the primary PCI group and 5.6 % in the thrombolysis group (p = 1.0). There were no significant differences in ejection fraction and no cases of serious bleeding. In 45 % of the total population, reperfusion therapy was started later than recommended in guidelines.

INTERPRETATION

There was no statistically significant difference in mortality or ejection fraction when comparing primary PCI and thrombolytic therapy in an unselected population with ST-elevation myocardial infarction. Many patients experienced delayed start of treatment . It is important to take action to reduce delays at all stages of the therapeutic chain. Thrombolytic therapy should be considered when it is unclear whether transport time to a PCI centre will exceed that recommended in guidelines.

Main points

In patients with ST-elevation myocardial infarction, there was no statistically significant difference in ejection fraction or 30-day mortality between those who received primary percutaneous coronary intervention (PCI) and those who received thrombolytic therapy.

In almost half of patients, reperfusion therapy was started later than recommended in guidelines.

Possible steps to reduce treatment delays should be considered at all stages of the therapeutic chain and, in cases where transport time to a PCI centre is uncertain, more patients should be considered for thrombolysis.

In myocardial infarction with ST-segment elevation, rapid reperfusion of the occluded coronary artery is important to reduce myocardial damage. The benefit of reperfusion therapy is greatest when it is administered within 2–3 hours of symptom onset (1, 2).

In Norway, the European Society of Cardiology guidelines are followed for the treatment of ST-elevation myocardial infarction. These guidelines were last revised in 2017 (3). Patients are treated with either primary percutaneous coronary intervention (PCI) or thrombolytic therapy, depending on transport time to the nearest PCI centre. For patients presenting within 12 hours of symptom onset, primary PCI is recommended if it can be performed within 120 minutes of diagnosis. If this time requirement cannot be met, thrombolytic therapy is recommended within ten minutes of diagnosis (3). During the study period (2015–16), the 2012 guidelines from the European Society of Cardiology were followed, which recommended thrombolytic therapy within 30 minutes (4).

The aim of our study was to compare timings and outcomes in patients receiving thrombolytic therapy or primary PCI for ST-elevation myocardial infarction in the Central Norway Regional Health Authority.

Material and method

Study design

The study is based on data collected by the Norwegian Myocardial Infarction Registry (NMIR) and the Norwegian Registry for Invasive Cardiology (NORIC) (5, 6), with any missing information obtained from patient medical records. The analysis is based partly on cross-sectional data and partly on prospective data, whereby patients were followed for 30 days from the time of myocardial infarction. According to Section 2–1 of the Cardiovascular Disease Registry Regulations, Norwegian hospitals are required to register patients treated for acute myocardial infarction in the NMIR, and patients who undergo coronary angiography and, if indicated, PCI in NORIC. Measured against the Norwegian Patient Registry, the NMIR had 93 % coverage of the Central Norway Regional Health Authority in 2016 (7). At St. Olavs Hospital in 2016, NORIC had 98 % coverage both for coronary angiography and for PCI (8).

Patients

All patients diagnosed with ST-elevation myocardial infarction in the Central Norway Regional Health Authority between 1 January 2015 and 31 December 2016, and registered in the NMIR (N = 965), were considered for inclusion. Patients were excluded if they presented more than 12 hours after symptom onset (n = 94), received reperfusion therapy more than 12 hours after diagnostic ECG (n = 34) or not at all (n = 184), had symptom onset abroad (n = 2) or were erroneously registered in the NMIR as having ST-elevation myocardial infarction (n = 3). A total of 648 patients were included in the study. Four patients were admitted twice with ST-elevation myocardial infarction during the study period, giving a total of 644 unique patients.

In cases of missing or inconsistent information in the NMIR and NORIC, supplementary information was obtained from the patient medical records. Ambulance patient records were used to ascertain the time of first medical contact when this was missing.

The time of prehospital ECG showing ST elevation was used as the time of diagnosis. First medical contact was defined as the time at which an ambulance reached the patient or the patient arrived at a general practice, Accident and Emergency department or hospital.

Patient delay was defined as the time from symptom onset to diagnostic ECG. Treatment delay was defined as the time from diagnostic ECG to the start of reperfusion therapy (administration of tenecteplase or arterial puncture in primary PCI). The timing of arterial puncture was used because this is recorded in NORIC. Total delay was defined as the time from symptom onset to the start of reperfusion therapy.

Information about the time from diagnosis to reperfusion therapy, from symptom onset to diagnosis, and from symptom onset to treatment was missing for 5, 12 and 16 patients, respectively.

Treatment

Thrombolytic therapy was administered at a local hospital or in the ambulance or air ambulance prior to hospital arrival. Tenecteplase was used exclusively, and was given as a weight-adjusted bolus. Patients in whom thrombolytic therapy was unsuccessful, as indicated by ongoing pain or lack of resolution of ECG changes, underwent rescue PCI. Patients showing signs of successful thrombolytic therapy underwent coronary angiography after 3–24 hours.

Date of death was obtained by linking to the National Population Registry. The primary endpoint was 30-day all-cause mortality. Secondary endpoints were the peak measured troponin T value, ejection fraction measured by echocardiography during the hospital stay and severe bleeding during the hospital stay. Less severe bleeding was defined as type 2 bleeding and severe bleeding as type 3–5 bleeding according to the Bleeding Academic Research Consortium (BARC) criteria (9).

Statistical analyses

Data were analysed using the SPSS statistics programme, versions 24 and 25. For categorical data, group differences were tested for statistical significance with Fisher's exact test or Pearson's chi-squared test depending on the number of cells. Continuous, normally distributed data were tested with a two-sample t-test, while continuous, non-normally distributed data were tested with a Mann-Whitney U-test. No corrections were made for multiple testing. P-values <0.05 were considered statistically significant.

Ethics

The study has been approved by the Regional Committee for Medical and Health Research Ethics (REC) (reference 2017/960).

Results

In all, 59 % of patients were treated with primary PCI, whereas 41 % received thrombolytic therapy (Table 1). There were no significant differences between the groups in age, sex, smoking habits or prior disease history (Table 1).

Table 1

Characteristics of 648 patients with ST-elevation myocardial infarction who underwent primary percutaneous coronary intervention (PCI) or thrombolytic therapy in the Central Norway Regional Health Authority in 2015–16. Number (%) unless otherwise specified.

Characteristic	Primary PCI (n = 382)	Thrombolytic therapy (n = 266)	Total (n = 648)
Male	274 (72)	199 (75)	473 (73)
Age, mean	63.5	64.6	64.0

Characteristic	Primary PCI (n = 382)	Thrombolytic therapy (n = 266)	Total (n = 648)
Smoker	150 (41)	109 (41)	259 (41)
Former smoker	105 (29)	88 (34)	193 (31)
Diabetes	53 (14)	18 (7)	87 (13)
Previous myocardial infarction	60 (16)	39 (15)	99 (15)
Previous cerebral insult	8 (2)	14 (5)	22 (3)
Previous PCI	51 (13)	27 (10)	78 (12)
Previous coronary artery bypass surgery	11 (3)	6 (2)	17 (3)
Previous peripheral vascular disease	27 (7)	18 (7)	45 (7)

The median time from symptom onset to diagnostic ECG was 73 minutes in both groups and the median time from first medical contact to ECG was 17 minutes. For patients in whom the time of ECG was missing (n = 147), the time of diagnosis was defined as the time of first medical contact plus 17 minutes. The median time from diagnosis to primary PCI was 100 minutes, and 64 % of the primary PCI group received treatment within the recommended time-window of 120 minutes. The median time from diagnosis to initiation of thrombolytic therapy was 34 minutes, and 42 % received treatment within the recommended time-window of 30 minutes.

The median time from symptom onset to start of reperfusion was 188 minutes for the primary PCI group and 105 minutes for the thrombolysis group. The PCI group thus received reperfusion therapy 83 minutes later than the thrombolysis group. The median time from diagnosis to angiography was 3.5 hours for the rescue PCI group and 19 hours for the group that received successful thrombolytic therapy. Overall 30-day mortality was 5.5 % for the primary PCI group and 5.6 % for the thrombolysis group (p = 1.00) (Table 2).

Table 2

Mortality, peak troponin T, ejection fraction and incidence of bleeding in 648 patients with ST-elevation myocardial infarction treated with primary PCI or thrombolysis in the Central Norway Regional Health Authority in 2015–16. Number (%) unless otherwise specified.

	Primary PCI (n = 382)	Thrombolytic therapy (n = 266)	Total (n = 648)	P-value
30-day mortality	21 (5.5)	15 (5.6)	36 (5.6)	1

	Primary PCI (n = 382)	Thrombolytic therapy (n = 266)	Total (n = 648)	P-value
Troponin T_{max} median (IQR)[1]	3 301 (6 016)	4 352 (7 291)	3 762 (6 310)	0.009
Ejection fraction				
≥50 %	169 (47)	102 (42)	271 (45)	
41–49 %	174 (48)	128 (53)	302 (50)	
≤30 %	21 (6)	12 (5)	33 (5)	0.47
Minor bleeding	6 (1.6)	4 (1.5)	10 (1.5)	1.000

[1]Troponin T level in ng/l

In both groups, more than 40 % of patients had a normal ejection fraction after myocardial infarction (Table 2). Median peak troponin was significantly higher in the thrombolysis group, and median troponin T_{max} was higher in the rescue PCI group than in the group that received successful thrombolytic therapy, 6 580 ng/l versus 3 762 ng/l ($p<0.001$). Only 31 % of patients in the rescue PCI group had an ejection fraction ≥50 %, compared to 46 % of patients with successful thrombolytic therapy (data not shown).

No serious bleeding was recorded in either group. The proportion of patients with minor bleeding was low in both groups (Table 2).

The main reasons for patients to be excluded from the study were because they had presented more than 12 hours after symptom onset (n = 94) or because they were considered unsuitable for acute reperfusion therapy, owing to comorbidities or other factors (n = 184). Patients in the latter group had an average age of 82.4 years and a 30-day mortality of 43 %.

Discussion

A comparison of primary PCI with thrombolytic therapy revealed similar and low mortality after 30 days, and no statistically significant difference in the incidence of reduced ejection fraction measured while in hospital. Reperfusion therapy was delayed for a large proportion of patients. No cases of serious bleeding were recorded.

Mortality and treatment selection

In 2003, Keeley et al. performed a meta-analysis of 7 739 patients, and found short-term mortality of 5 % for patients treated with primary PCI and 7 % for those treated with thrombolysis (10). The largest study included in the meta-analysis was the Danish DANAMI-2 trial with 1 572 patients, in which thrombolytic therapy was repeated if it initially proved unsuccessful (11). It has subsequently been shown that rescue PCI is superior to repeated thrombolysis in the event of failed thrombolytic therapy (12). In our study, 30-day mortality

in the thrombolysis group was lower than in Keeley's meta-analysis. This may be because rescue PCI and direct transfer to a PCI centre had not been established as a routine procedure in the earliest studies.

The 2013 STREAM trial showed that thrombolytic therapy was as effective as primary PCI in patients who presented shortly after symptom onset (13). In STREAM, 30-day mortality was 4.4 % in the PCI group and 4.6 % in the thrombolysis group. In our study, the corresponding figures for 30-day mortality were 5.5 % and 5.6 %. A recent meta-analysis by Roule et al. also found mortality to be similar after thrombolytic therapy and primary PCI in patients with ST-elevation myocardial infarction (14). These findings show the importance of thrombolytic therapy as a treatment option.

In our study, the patients who received treatment with primary PCI within 120 minutes were younger on average. This may be because the population of Trondheim, which has a PCI centre at St. Olavs Hospital, is younger on average than that of other parts of the Central Norway Regional Health Authority.

Bleeding

Thrombolytic therapy is associated with an increased risk of bleeding. In Keeley's meta-analysis, patients treated with thrombolysis had a 1 % risk of intracranial haemorrhage versus 0.05 % for patients treated with primary PCI (10). The STREAM trial reported similar findings, and during the study the dose of tenecteplase was reduced by 50 % for patients >75 years of age owing to the increased incidence of stroke in this age group. After the dose reduction, the risk of intracranial haemorrhage fell from 1 % to 0.5 %, with no reduction in the efficacy of reperfusion therapy (13). The revised European Society of Cardiology guidelines now recommend a half dose of tenecteplase for patients over 75 (3).

The patients in our study were treated with full-dose thrombolysis irrespective of age, in accordance with the 2012 guidelines (4).

Rescue PCI

In our study, 25 % of thrombolysis patients received rescue PCI. This is somewhat lower than in previous studies (13, 15). Higher troponin T levels and a lower ejection fraction in patients treated with rescue PCI indicate that myocardial damage is increased when thrombolytic therapy fails.

Timings

Thrombolytic therapy is most effective when administered within the first 2–3 hours of symptom onset (2, 3). We found that 45 % of patients did not receive reperfusion therapy within the recommended timeframes. Fifty-eight per cent of patients received thrombolytic therapy more than 30 minutes after symptom onset. Among patients who presented within two hours of symptom onset and who were treated with primary PCI, 32 % received treatment more than 120 minutes after symptom onset.

Gershlick et al. performed a supplementary analysis of the STREAM dataset in 2015. They found that thrombolytic therapy was superior to primary PCI if the PCI-related delay exceeded 50 minutes (16). Moreover, they found that the

benefits of thrombolytic therapy over primary PCI increased further with additional lengthening of the PCI-related delay.

Strengths and weaknesses

All patients in the Central Norway Regional Health Authority who, over a two-year period, received reperfusion therapy for ST-elevation myocardial infarction within 12 hours of symptom onset and who were registered in the NMIR, were included in this study.

The study has some limitations. The analyses are based on data from the NMIR, and data collection routines may vary between hospitals (17). The study is also an observational study covering a limited geographical area and a limited number of patients, and the findings must therefore be interpreted with caution.

Clinical significance

Reducing the time from symptom onset to reperfusion therapy is important when treating myocardial infarction with ST elevation. Efforts must be made to reduce delays at all stages of the therapeutic chain. Prompt interpretation of ECGs is key, along with clear procedures for prehospital thrombolytic therapy with checklists to identify contraindications. Increased awareness in the population of the symptoms of myocardial infarction and the importance of rapid treatment can reduce patient delay.

Conclusion

In this study, there was no statistically significant difference in mortality or ejection fraction between patients with ST-elevation myocardial infarction who received primary PCI or thrombolytic therapy. Reperfusion therapy was delayed in more than half of patients. Measures to reduce treatment delay should be considered throughout the therapeutic chain and, when transfer time to a PCI centre is uncertain, more patients should be considered for thrombolysis.

This article has been peer-reviewed.

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