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More STEMI patients should receive thrombolytic therapy

PERSPECTIVES

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In patients with an ST-elevation myocardial infarction (STEMI) on ECG, the occluded coronary artery must be opened as quickly as possible. This can prevent myocardial damage, complications and death. Many patients in Norway are treated too late.

Many STEMI patients do not receive reperfusion therapy with primary percutaneous coronary intervention (PCI) or thrombolysis within the recommended time frame (1, 2) (Figure 1). We propose that primary PCI be performed if the patient can reach an invasive cardiology unit within 60 minutes of the STEMI diagnosis. If transport time is longer, thrombolytic therapy should be considered if the symptom duration is short (< 3 hours) and there are no contraindications. This approach involves increased use of prehospital thrombolysis and will help ensure that more patients receive reperfusion therapy within the recommended time frame.

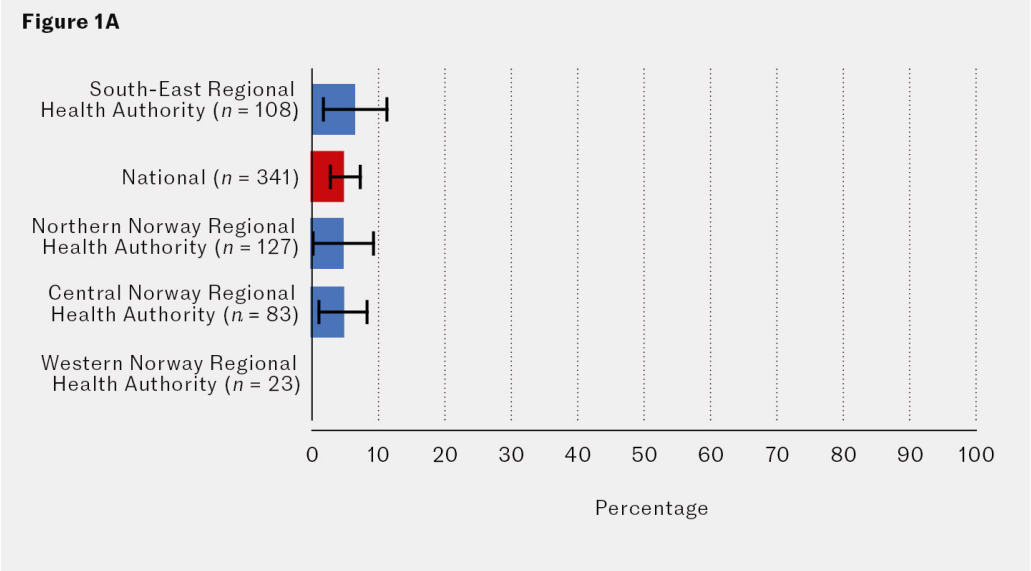

Figure 1A Thrombolytic therapy for STEMI. The proportion (95 % confidence interval) of patients who met the goal set in the ESC guidelines. The goal is administration of a bolus dose within ten minutes of an ECG showing STEMI. Source: Norwegian Myocardial Infarction Registry, 2023.

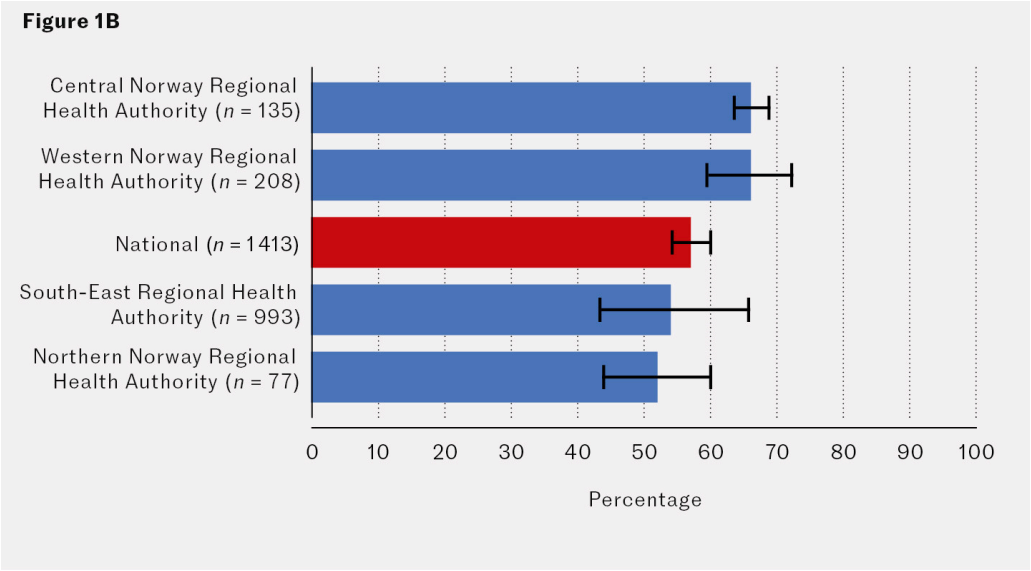

Figure 1B Primary PCI for STEMI. The proportion (95 % confidence interval) of patients who met the goal set in the ESC guidelines, by health region. The goal is wire crossing within 90 minutes of an ECG showing STEMI. Wire crossing is estimated as ten minutes after arterial puncture. Source: Norwegian Myocardial Infarction Registry, 2023.

> ***«We propose that primary PCI be performed if the patient can reach an invasive cardiology unit within 60 minutes of the STEMI diagnosis. If transport time is longer, thrombolytic therapy should be considered if the symptom duration is short and there are no contraindication»***

Early opening of an occluded coronary artery and reperfusion of ischemic myocardium is one of the greatest advances in modern cardiology (3). Reperfusion has the greatest potential to limit myocardial damage if the artery

is opened shortly after the onset of symptoms (4). Few issues in cardiology have been more intensely debated than what is the best strategy for opening the artery: PCI or thrombolysis.

PCI versus thrombolysis in older studies

Compared to thrombolysis, PCI performed without a significant delay was associated with lower mortality and a lower incidence of recurrent infarction and stroke in a meta-analysis of 23 randomised trials conducted in the 1980s and 90s (5). Many of the trials in the meta-analysis were small, and obsolete treatment regimens were used. Most patients were at a PCI-capable hospital at the time of randomisation, and the average delay for PCI compared to thrombolysis was just 39 minutes. However, current guidelines from the European Society of Cardiology (ESC) recommend primary PCI if the occluded artery can be opened with a guidewire within 120 minutes of an ECG (1). If PCI cannot be performed within 120 minutes, thrombolysis is recommended within ten minutes of the ECG. The ESC thus recommends primary PCI even if it is performed with a delay of up to 110–120 minutes after thrombolysis could have been administered.

Why 120 minutes?

There are no randomised trials on how long primary PCI can be delayed while still being more beneficial than thrombolysis. So where does the 120-minute time frame come from? It is based on three sources: the 23 studies in the meta-analysis mentioned above (5), a Danish study (6) and US registry data (7). These data sources have been analysed using different methods, and the results regarding the maximum acceptable PCI delay range from 60 minutes (8) to 120 minutes (7), with one study even suggesting that time is not a factor (9).

The varying estimates reflect shortcomings in both the studies and the analyses. In regression analyses of the 23 randomised studies, the analytic unit was the study, not the individual, which raises the risk of an ecological fallacy. The relationship between delay and outcome can obviously differ between the individual level and the group level. The Danish study has limited relevance because it used obsolete methods, and registry data must be interpreted with caution due to the risk of bias and confounding (10).

The old studies cited in the ESC guidelines therefore offer no clear support for primary PCI over thrombolysis when PCI is delayed by up to 120 minutes.

Thrombolytic therapy versus primary PCI

Four randomised trials compared primary PCI with prehospital thrombolysis followed by rapid transfer to a PCI-capable hospital for potential rescue PCI in the case of failed thrombolysis (a pharmacoinvasive strategy) (11–14). The trials included patients with a short symptom history for whom primary PCI could not be performed within one hour. None of the trials showed significantly better outcomes with primary PCI compared to thrombolysis, but they provided indirect support for a pharmacoinvasive strategy in STEMI patients with a short symptom history for whom primary PCI cannot be performed within one hour.

> ***«None of the trials showed significantly better outcomes with primary PCI compared to thrombolysis»***

In the largest trial, STREAM (Strategic Reperfusion Early after Myocardial Infarction), a numerically lower, but not statistically significant, incidence of the primary end point (death, cardiogenic shock, heart failure or reinfarction within 30 days) was found with the pharmacoinvasive strategy compared to primary PCI (13). After the thrombolysis dose was halved in older patients, the primary end point was 22 % lower with the pharmacoinvasive strategy than with primary PCI (13). While PCI performed with a delay of less than 55 minutes was associated with a somewhat better outcome than thrombolysis, there was a clear trend (p = 0.073) toward better outcomes with the pharmacoinvasive strategy for longer PCI delays (15). These findings are supported by two older trials that found lower mortality at 30 days and one year for the pharmacoinvasive strategy compared to primary PCI (11, 16).

In the STREAM trial, there were initially more intracranial haemorrhages with the pharmacoinvasive strategy than with primary PCI, but after halving the thrombolysis dose in patients over 75 years, there was no difference in the incidence of severe bleeding (13).

The most recent of the four trials included patients over 60 years who received a half dose of thrombolysis (14). No difference was found between thrombolysis and primary PCI in the incidence of the primary end point.

In the STREAM 2 study, the incidence of intracranial bleeding in the pharmacoinvasive group was higher than expected, despite the reduced thrombolysis dose (1.5 % versus 0 % in the primary PCI group).

Compared with primary PCI, prehospital thrombolysis is associated with greater resolution of ST-segment elevation on ECG (14, 17). This may be due to less microvascular obstruction and better myocardial perfusion (17), and could explain why thrombolysis appears to be associated with a lower risk of cardiogenic shock and heart failure than PCI (18).

Recent observational studies

In several recent observational studies, modern prehospital pharmacoinvasive strategies have been associated with outcomes that are comparable to or better than those of delayed primary PCI (17, 19–21). In a Norwegian study, patients were divided into three groups in which PCI was performed 34 minutes, 92 minutes and 204 minutes after thrombolysis (21). There was no significant difference in the risk of death, myocardial infarction or stroke when PCI was delayed by 34 minutes. With a 92-minute delay, PCI was associated with a 20 % increased risk, and with a 204-minute delay, PCI was associated with a 40 % increased risk compared with thrombolysis.

Transport time of under 60 minutes for PCI

Randomised trials and recent observational studies thus both suggest that the maximum acceptable delay for primary PCI in relation to prehospital thrombolysis is shorter than 120 minutes, provided the patient has a short symptom history. The ESC guidelines acknowledge this, as they state that the goal for primary PCI is wire crossing within 90 minutes of diagnosis (1).

> ***«Transport time to a PCI-capable hospital should not exceed 60 minutes. We propose that this limit be applied in Norway»***

Data from randomised trials (12, 13) and the Norwegian Myocardial Infarction Registry for 2024 (Kiel, personal communication) show that the time from patient arrival at a PCI-capable hospital to wire crossing of the occluded coronary artery is approximately 30 minutes. To meet the ESC goal of 90 minutes from diagnosis, transport time to a PCI-capable hospital must not exceed 60 minutes. We propose that this limit be applied in Norway.

Less than half receive timely treatment

In 2023, just under 20 % of STEMI patients in Norway were treated with thrombolysis (2). The proportion receiving thrombolysis varied from 10 % in South-East Regional Health Authority and Western Norway Regional Health Authority to 45 % in Central Norway Regional Health Authority and Northern Norway Regional Health Authority (2). Less than half of patients in Norway were treated within the recommended time frame in the ESC guidelines. Fifty-seven per cent of patients who underwent primary PCI were treated within the recommended time frame, compared to just 5 % of those treated with thrombolysis (Figure 1).

Opting for primary PCI instead of prehospital thrombolysis is one of the main reasons why patients are treated too late. It often takes longer than expected to transport the patient to a PCI-capable hospital and to perform the procedure. Delayed thrombolysis is often due to delays related to ECG diagnosis and decisions on which strategy to employ (22).

> ***«Opting for primary PCI instead of prehospital thrombolysis is one of the main reasons why patients are treated too late»***

Thrombolysis is most effective in patients with a short symptom duration (3). In Norway, more than half of STEMI patients present to healthcare personnel less than one hour after symptom onset, and 85 % present less than three hours (2). Most patients therefore present within a time frame that offers great potential to salvage ischemic myocardium through early reperfusion. Prehospital thrombolysis will be a better option than a long journey to a PCI unit for many patients.

Faster reperfusion requires more thrombolysis

Many STEMI patients in Norway do not receive reperfusion therapy in time. We propose that primary PCI is performed if the patient can arrive at a PCI-capable hospital within 60 minutes of the STEMI diagnosis. For longer transport times, a pharmacoinvasive strategy should be considered if the symptom duration is short (< 3 hours) and there are no contraindications. This is in line with the aims of the ESC guidelines.

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