Primary percutaneous coronary intervention delay for patients living in a peripheral area in Denmark

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ABSTRACT

INTRODUCTION: In patients with ST-elevation myocardial infarction (STEMI), timely primary percutaneous coronary intervention (PPCI) is superior to thrombolysis and it is the preferred treatment in Denmark. The prognosis depends on the time delay until coronary blood flow is re-established. The purpose of this registry study was to evaluate the PPCI treatment delay of the triage algorithm in a peripheral area in the Region of Central Jutland in the context of European guidelines.

MATERIAL AND METHODS: From 1 September 2009 through 31 August 2010, we included all PPCI-treated patients from the catchment area of Regional Hospital Herning (RHH) who were diagnosed with probable STEMI based on the first electrocardiography (ECG) wirelessly transmitted to the physician on call at RHH after symptom onset.

RESULTS: A total of 101 patients were included, 77% were males and their median age was 63.4 years. The median distance to the PCI centre was 120.3 (range 63.5-174.2) km. The 2008 European guidelines on transportation delay were fulfilled for 35 (35%) patients and the 2012 European guidelines for seven (7%) patients. Overall, 46% of the patients had a delay from first medical contact to PCI < 120 min., 9% a delay < 90 and none a delay < 60 min.

CONCLUSION: Our registry study showed that 35% and 7% of PPCI patients from a peripherally located area in Denmark met the 2008 and 2012 European guidelines for an acceptable transport delay to a PCI centre, respectively. Our current PPCI triage strategy therefore needs reconsideration.

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ST-elevation myocardial infarction (STEMI) is primarily caused by an acute thrombotic occlusion of a major coronary artery. The prognosis is closely related to the delay until re-establishment of the coronary artery blood flow [1], and timely performed primary percutaneous coronary intervention (PPCI) is the preferred treatment [2]. STEMI patients are therefore transferred to a percutaneous coronary intervention (PCI) centre as soon as possible after onset of symptoms [3, 4].

The clear relation between delay to reperfusion and mortality has formed the basis for several guidelines on acceptable PCI-related delays. Unfortunately, recommendations are not uniform. The American guidelines accept a delay from the patient's first medical contact

(FMC) to the coronary intervention of 90 min. If this is not possible, the recommended treatment is thrombolysis [5]. The 2008 European guidelines for the management of patients with STEMI recommend referral to a PCI centre if the expected delay from FMC to PCI is < 120 min., and < 90 min. in patients with large infarctions, low bleeding risk and a time from symptom onset to FMC < 2 h. Otherwise, thrombolytic treatment should be instituted [3]. In the 2012 European guidelines, the acceptable FMC-to-PCI delay is reduced by 30 min. to 90 min. with a further reduction to 60 min. in patients with time from symptom onset to FMC < 2 h and a large anterior infarction [4]. Danish guidelines from 2012, currently under revision, accept an unspecified transportation delay of 120 min. in all patients.

After the Danami II study, the treatment for STEMI in Denmark has been PPCI. Thrombolysis is obsolete [6]. We therefore assessed the PPCI treatment delays of our PPCI triage algorithm in a peripherally located area in the Region of Central Jutland, the catchment area of Regional Hospital Herning (RHH), and evaluated compliance with the 2008 and 2012 European guidelines for treatment of patients with STEMI.

MATERIAL AND METHODS
Patients

This registry study was performed in the western part of the Region of Central Jutland; the catchment area of the RHH with approximately 285,400 inhabitants (the municipalities of Herning, Ikast-Brande, Holstebro, Lemvig, Ringkøbing-Skjern and Struer).

From 1 September 2009 through 31 August 2010, we included all patients who 1) were living in the catchment area of the RHH, 2) had a probable STEMI diagnosed by the first electrocardiography (ECG) after symptom onset wirelessly transmitted (Tele ECG) to the physician on call at the RHH, 3) were directed to PPCI and 4) had a PPCI procedure. We included patients bypassing as well as patients transferred to PPCI via the local hospital. Results are given separately for these two subgroups.

The group of STEMI patients that should be considered for early PPCI is not well defined in the 2008 or 2012 ESC guidelines. Both guidelines do, however, refer to the work by Pinto and colleagues [7], who analysed data on 192,509 STEMI patients treated by thrombolysis or PPCI in a large registry study. They assessed the effect

of the PCI-related delay (door-to-balloon-time minus door-to-thrombolysis-time) on mortality in several subgroups. The survival advantage of PPCI was lost if the PCI-related delay was > 94 min. in patients presenting with a symptom duration < 2 h and > 71 min. in patients < 65 years when the effect of age and symptom duration was analysed independently. Based on this reference, we considered that patients who were both younger than 65 years and presented with a symptom duration < 2 h should have early PPCI. This may be regarded as a conservative approach. The infarct size was not estimated.

Data were drawn from the Western Danish Heart Registry, the medical emergency care unit (MECU) database, and these data were supplemented with registrations from hospital records, if necessary.

Organization
For individuals in the RHH catchment area who needed acute medical attention, various options were available. 1) Contact to the RHH. 2) Contact to own general practitioner (GP) or the GP on call. 3) Contact to the Medical Emergency Service (a 112 phone call). A 112 call was forwarded to the Central of the Emergency Medical Service (EMS). Also, a GP contact could be referred to the EMS. If the EMS suspected a heart attack, a MECU was sent to the scene. The MECU was staffed by an emergency medical technician and a critical care nurse or a specialist in anaesthesiology. If one of the telemedicine criteria was fulfilled (on-going chest pain lasting > 15 min., recent chest pain > 15 min. within the past 12 h, new onset dyspnoea within 12 h without known lung disease, clinical suspicion of an acute coronary syndrome), a 12-lead ECG was transmitted to the RHH. The doctor on-call at the department of medicine assessed the ECG and received clinical information from the MECU staff. The on-call doctor could also speak directly with the patient. If a STEMI diagnosis was established and the patient was haemodynamically stable, the patient was transferred directly to the Cardiac Catheterisation Laboratory at Aarhus University Hospital. Patients with haemodynamic instability were transported to the local hospital, or a rendezvous was arranged with a specialist in anaesthesiology for stabilization before further triage. The MECU registered if a STEMI was diagnosed within 5 min. after ECG transmission. The ECG criteria for STEMI were; presence of a (presumably) new left bundle branch block or ST-elevation in two adjacent leads (0.2 mV for men and 0.15 mV for women) in V2-V3 or 0.1 mV in other leads for both genders.

Data registration and definitions
Data for time delay registration were entered prospectively into the MECU database by the critical care nurse in the MECU. Time for catheterization and first interven-

tion was drawn from the Western Denmark Heart Registry. In case of missing values, data were retrieved from hospital files at Aarhus University Hospital, Skejby or from the RHH.

First medical contact (FMC): Time of MECU arrival at the scene. According to the European guidelines, the FMC is the place (ambulance or hospital) where thrombolytic therapy can be instituted [3].

Patient delay: Time from onset of symptoms to FMC.

System delay: Delay from the Emergency Medical Service (EMS) activation to the first coronary intervention.

FMC-to-PCI delay: Time from arrival of the MECU at the scene to the first coronary intervention.

EMS dispatch delay: Delay from EMS activation to arrival of the MECU at the scene.

On-scene delay: Time from arrival to departure of the MECU at the scene.

Transportation delay: Time from MECU departure to arrival at the PCI centre.

In-door/out-door delay: Time from arrival at the local hospital to departure from the local hospital. Only relevant in patients who had contact to the local hospital on their way to the PCI centre.

Inter-hospital transport delay: Time from departure from the local hospital to arrival at the PCI centre.

Door-to-intervention delay: Time from arrival at the PCI centre to the first coronary intervention.

Transportation distance: The distance in km from the scene to the PCI centre was obtained from krak.dk.

Permissions
The project was approved by the Danish Data Protection Agency and the Danish Health and Medicines Authority.

Statistical analysis
Continuous data are given as medians and interquartile range. Correlations were tested by Spearman's rho and comparisons between groups by the Mann-Whitney U test. A two-sided p-value below 0.05 was considered statistically significant. Data analyses were done in SPSS v. 20.

Trial registration: not relevant.

RESULTS
During the study period, 138 patients living in the RHH catchment area had a PPCI treatment. We excluded ten patients with cardiac arrest for whom the Tele-ECG was non-existing [8] or did not show STEMI [1], and another 27 patients in whom the STEMI was diagnosed in-hospital (seven without Tele-ECG and 20 with a Tele-ECG not diagnosed as STEMI). Thus, our study cohort com-

prised 101 patients.

A total of 78 (77%) patients were males. The median age was 63.4 (55.7-72.0) years, and 56 (55%) patients were < 65 years old. Eight patients died during the first year after PPCI (7.9% (95% confidence interval (CI): 3-13%).

The median distance from the scene to the PCI centre was 120.3 km (range 63.5-174.2) km. The FMC-to-PCI delay correlated significantly with the distance from the scene to the PCI centre (Spearman's rho = 0.49, p < 0.000001).

The PPCI treatment delays are shown in **Table 1**. Information about the time from the ECG was sent to the RHH until the MECU received an answer was available for 68 patients. In 61 (90%) cases, the response time was < 5 min.

Seventy-three patients (73%) were transported directly to the PCI centre bypassing the local hospital. The FMC-to-PCI delay was significantly shorter in patients transferred directly to PPCI than in patients transferred to PPCI via the local hospital (median 118 versus 147 min., p < 0.0001).

European guidelines and system delay

A total of 31 patients were younger than 65 years and had a patient delay < 120 min. Two of these patients had an FMC-to-PCI delay < 90 min. Of the remaining 70 patients, 33 patients had an FMC-to-PCI delay < 120 min. Thus, the 2008 European guidelines for treatment delay criteria were met in 35 (2 + 33) out of 101 (34.7%, 95% CI: 25-44) patients. The 2008 guidelines recommendations were met in 30 (41.1%) of the 73 patients triaged directly to the PCI centre bypassing the local hospital and in 5 (17.9%) of the 28 patients transferred via the local hospital (**Table 2**).

Considering the 2012 European guidelines, none of the early presenters below the age of 65 years had an FMC-to-PPCI delay < 60 min. Of the remaining patients, seven had an FMC-to-PCI delay < 90 min. Thus, the 2012 European guidelines for treatment delay criteria were fulfilled in seven (0 + 7) out of 101 (6.9%, 95% CI: 1.9-12.0%) patients. For the patients bypassing the local hospital, seven (9.6%) fulfilled the guidelines, while no patients transferred via the local hospital met the recommendations (Table 2).

Overall, no patients had an FMC-to-PCI delay < 60 min., nine patients (8.9%, 95% CI: 3.3-14.6%) had an FMC-to-PCI delay < 90 min. and 46 patients (45.5%, 95% CI: 35.7-55.4%) an FMC-to-PCI delay < 120 min.

DISCUSSION

Our registry study showed that 35% of PPCI patients from this peripherally located area in Denmark met the 2008 European guidelines for timely triage to a PCI cen-

TABLE 1

Primary percutaneous coronary intervention treatment delays[a] in a peripherally located area in the Region of Central Jutland. The values are minutes, median (interquartile range).

Patient delay (n = 101)	115 (46-257)
EMS dispatch delay (n = 101)	12 (7-17)
On-scene delay (n = 101)	10 (7-16)
Transportation time	
All patients (n = 101)	75 (62-90)
Bypassed local hospital (n = 73)	70 (57-82)
Referral via local hospital (n = 28)	86 (76-105)
In-door/out-door delay (n = 28)	9 (5-34)
Interhospital transport delay (n = 28)	52 (50-59)
Door-to-intervention delay (n = 101)	28 (23-42)
System delay	
All patients (n = 101)	133 (117-163)
Bypassed local hospital (n = 73)	128 (114-147)
Referral via local hospital (n = 28)	154 (133-181)
FMC-to-PCI	
All patients (n = 101)	124 (106-149)
Bypassed local hospital (n = 73)	118 (103-133)
Referral via local hospital (n = 28)	147 (119-173)

EMS = Emergency Medical Service; FMC = first medical contact; PCI = percutaneous coronary intervention.
a) See Data registration and definitions.

TABLE 2

Fulfilment of European Society of Cardiology (ESC) guidelines for primary percutaneous coronary intervention treatment delay in a peripherally located area in the Region of Central Jutland. The values are n (%).

2008 ESC guidelines fulfilled	
By-passed local hospital (n = 73)	30 (41.1)
Referral via local hospital (n = 28)	5 (17.9)
All patients (n = 101)	35 (34.7)
2012 ESC guidelines fulfilled	
By-passed local hospital (n = 73)	7 (9.6)
Referral via local hospital (n = 28)	0 (0)
All patients (n = 101)	7 (6.9)

tre; 7% met the 2012 criteria. For patients bypassing the local hospital, 41% met the 2008 criteria; 10% met the 2012 criteria.

PPCI has been found to be superior to thrombolysis for the treatment of acute STEMI. However, time to reperfusion is a strong predictor of outcome both in PPCI and after thrombolytic treatment. In PPCI, system delay, the delay from contact to the health-care system to treatment, is a documented essential factor in reducing mortality [9] and morbidity [8] after STEMI. The time to reperfusion should therefore be reduced as much as possible by adopting a strategy that involves mechanical or pharmacological reperfusion. In both strategies, on-scene diagnosis is possible using a MECU. Thrombolysis

Medical emergency care unit with emergency medical technician and critical care nurse. Permission to publish the picture was obtained from both persons.

may be administered immediately on-scene, while a PPCI strategy requires transportation to a PCI centre. Thus, the distance to the PCI centre becomes critical, as shown in the present study and in two recent reports [10, 11] which documented a highly significant relationship between FMC-to-PCI or system delay and distance from the scene to the PCI centre.

Because of the adverse effect associated with a long transportation time and the high efficiency of thrombolysis in patients with short symptom duration, the optimal reperfusion therapy may involve initial thrombolytic treatment followed by invasive diagnosis and catheter-based intervention, i.e. a pharmaco-invasive approach. This strategy has been extensively used in areas with low population density like the northern part of Scandinavia and large areas of the USA and Canada [12].

The pivotal Danami II trial documented that patients with acute STEMI should be transported to a PCI centre instead of receiving thrombolysis. After the Danami II inclusion period, PPCI became the recommended and, in reality, the only reperfusion therapy in Denmark. The Danami II trial compared transport for PPCI with thrombolysis at the local hospital. However, there is substantiated evidence that thrombolytic treatment can be administered safely on scene [12-14]. The transportation time to PPCI therefore becomes critical in these patients. Recent European guidelines recommend that PPCI should be performed with an FMC-to-PCI delay < 90 min. in patients with a symptom duration > 2 h and < 60 min. in patients with a symptom duration < 2 h [4]. In our study, only 7% of the patients met these criteria for transportation to a PCI centre for catheter-based reperfusion.

As a consequence of our data and recent reports on PPCI triage delays [10, 11, 15], our current reperfusion praxis may need reconsideration. From a practical clinical, logistical perspective, there seems to be several possibilities.

A pharmaco-invasive therapy with on-scene thrombolytic treatment combined with transportation to a PCI centre with angiography after three to 24 h, or earlier if

the patient is unstable [3-5, 16, 17], may be recommended for patients in whom triage times are expected to be long (> 120 min.) [12, 13, 15]. However, this approach has been challenged by a recent comparison of a combined thrombolysis and PCI versus primary PCI strategy in STEMI patients with symptom duration < 3 h who were unable to undergo primary PCI within 1 h. The composite of 30-day death, shock, congestive heart failure, or re-infarction occurred at similar rates in the study groups, while stroke was seen more frequently in patients receiving thrombolytic treatment [18].

Alternatively, the transportation time must be reduced. In principle, transportation time reduction may be achieved by improved ground transportation or airlifting of STEMI patients to existing PCI centres. Knudsen et al recently demonstrated that helicopter transportation reduced system delay in patients living more than 60 km from a PCI centre [10]. The median system delay in patients living 51-75 km and > 75 km from the PCI centre were 99 and 141 min., respectively. Thus, the 2012 ESC STEMI Guidelines was not fulfilled by the 22 helicopter transported patients in this study. However, final evaluation of the helicopter triage in our region needs a considerably larger patient cohort.

As documented in this paper and in earlier publications [15], it is mandatory to avoid contact to local hospitals, if possible.

The transportation time may also be reduced effectively by establishing new PCI centres, centrally located in a catchment area. Such decentralization of PCI treatment has been widely implemented in most Western World countries with good results [12, 19].

It was previously a concern to perform PCI at centres without cardiac surgery. However, comprehensive registry data and a large randomised clinical study have documented that PCI and PPCI can be performed safely and efficiently without surgical backup provided that there is sufficient centre and operator volume [20].

In our study, the median time from arrival at the PCI centre to reperfusion was 28 min. New PCI centres located centrally in the catchment area could therefore probably solve the system delay problem in the vast majority of patients, but it may still not be an acceptable solution for the most remotely living individuals. Here, upstream thrombolysis as part of a pharmaco-invasive therapy may be indicated.

When establishing new interventional centres, it should be borne in mind that there is a relationship between centre and operator volume and quality of the interventional treatment. An interventional centre should have a minimum annual work load of 400 PCI procedures and individual operators should perform > 70 annual interventions [5]. At the same time, we may recommend optimizing of the pre-hospital visitation. The

visitation needs to consider ground transportation or air-lifting to the nearest PCI team (time rather than distance) as well as up-stream thrombolytic treatment.

Limitations of the study

The study was performed before helicopter transportation became an option. This does reduce the actuality of our study. However, helicopter-transported patients rarely fulfill the 2012 ESC triage delay recommendations, and will probably not change significantly the percentage of patients transported in a timely fashion [10]. Future investigations are awaited concerning this topic. It is also a limitation that the study cohort was relatively small.

There is an ongoing debate as to which treatment delay should be used as the primary delay parameter, but in this registry study we have been loyal to the 2008 and 2012 ESC guidelines and used the FMC-to-PCI delay as intended in the guidelines.

Finally, it may be a limitation for the interpretation of our results that the 2012 ESC Guidelines are new and may still be subject to change when discussed in national cardiological societies. We hope that the present data may play a part in that discussion.

CONCLUSION

In conclusion, our registry study showed that only 35% and 7% of PPCI patients from a peripherally located area in Denmark met the 2008 and 2012 European guidelines on timely triage to a PCI centre, respectively. Therefore, our current PPCI triage strategy needs reconsideration.

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LITERATURE

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