

Interhospital transfer due to failed prehospital diagnosis for primary percutaneous coronary intervention: an observational study on incidence, predictors, and clinical impact

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Abstract

Background: For patients with ST-elevation myocardial infarction (STEMI), guidelines recommend prehospital triage and direct referral to a percutaneous coronary intervention (PCI)-capable centre in order to minimize ischemic time. However, few have studied failed prehospital diagnosis. We assessed the incidence, predictors, and clinical impact of interhospital transfer for primary PCI after initial referral to a non-PCI-capable centre due to a failed prehospital STEMI diagnosis.

Methods: We studied 846 consecutive STEMI patients undergoing primary PCI between January 2008 and January 2010.

Results: We found that 609 patients (72%) were directly admitted through prehospital triage and 127 patients (15%) required interhospital transfer after failed prehospital diagnosis. Median first medical contact to treatment time was 88 min in the prehospital diagnosis group and 155 min in the interhospital transfer group ($p < 0.001$). In the interhospital transfer group, the first available electrocardiogram was diagnostic for STEMI in 77% of cases. Predictors of interhospital transfer were female gender, diabetes, prior myocardial infarction, and greater event location to PCI-capable centre distance. Interhospital transfer independently accounted for a 47% increase in ischemic time (95% CI 33 to 63%; $p < 0.001$). One-year mortality was higher in the interhospital transfer group (10 vs. 5.3%; $p = 0.030$).

Conclusions: Despite an often-diagnostic electrocardiogram, interhospital transfer after failed prehospital diagnosis occurred in 15% of STEMI patients undergoing primary PCI. Interhospital transfer was a major predictor of ischemic time and 1-year mortality was significantly higher. Continuing efforts to optimize prehospital triage are warranted, especially among patients at higher risk of failed prehospital diagnosis.

Keywords

Angioplasty, delay, emergency medical services, ischemic time, myocardial infarction, triage

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Introduction

In patients with ST-elevation myocardial infarction (STEMI), rapidly performed primary percutaneous coronary intervention (PCI) by an experienced team has shown to be a superior reperfusion strategy over fibrinolysis,¹ even if the patient is initially admitted to a non-PCI-capable centre.² As a longer time from symptom onset to reperfusion therapy (ischemic time) has been associated with

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decreased myocardial reperfusion and increased mortality,^{3,4} many efforts have been made in reducing it. Recently published European Society of Cardiology (ESC) guidelines recommend prehospital diagnosis and direct referral to a PCI-capable centre for primary PCI as the preferred strategy to minimize ischemic time in patients with STEMI.⁵ Whenever possible, non-PCI-capable centres should be bypassed. In addition, faster system performance is proposed with first medical contact to treatment time (system delay) ≤ 90 min and door-to-balloon time ≤ 60 min. Numerous studies document the implementation of regional 12-lead electrocardiogram (ECG)-based prehospital triage systems with subsequent reductions in door-to-balloon time and ischemic time.⁶⁻⁹ However, the proportion of STEMI patients diagnosed by these prehospital triage systems is often unclear. Thus, little is known about the occurrence and clinical impact of a failed prehospital diagnosis in a fully operational prehospital triage system. Our primary purpose was to study the incidence and predictors of interhospital transfer for primary PCI after initial referral to a non-PCI-capable centre due to failure of prehospital STEMI diagnosis and assess its impact on delay to reperfusion and mortality. Furthermore, we studied ECG characteristics of STEMI patients undergoing interhospital transfer due to failed prehospital diagnosis.

Methods

Study design and population

We currently studied the incidence, predictors, and clinical impact of interhospital transfer due to failed prehospital diagnosis. Failed prehospital diagnosis was defined as failure to activate the prehospital triage protocol for STEMI and initial referral of a STEMI patient to a non-PCI-capable centre, despite the regional agreement with emergency medical services (EMS) and referral centres and to directly refer STEMI patients for primary PCI. All consecutive patients with suspected STEMI undergoing acute coronary angiography between 1 January 2008 and 1 January 2010 were considered for this analysis. Among this group, we selected patients with STEMI who had undergone prehospital triage for primary PCI (prehospital diagnosis group) and patients with a failed prehospital diagnosis of STEMI and subsequent interhospital transfer for primary PCI (interhospital transfer group). STEMI was defined as chest pain suggestive of myocardial ischaemia, time from onset of symptoms of less than 12 hours, and an ECG diagnostic for STEMI with new or presumed-new ST-segment elevation in 2 or more contiguous leads of ≥ 0.2 mV in leads V2-V3 and/or ≥ 0.1 mV in other leads or left bundle branch block. Primary PCI was the preferred reperfusion strategy for all patients, and fibrinolytics were never administered. Importantly, we excluded all self-referrals, since these patients could not have been diagnosed in the prehospital

setting. We also excluded patients on mechanical ventilation, as this may have been a reason for an intermediate admission to the nearest non-PCI-capable centre despite a diagnosis of STEMI. Finally, we excluded patients admitted to our emergency department (ED) and patients with onset of STEMI during hospitalization for other conditions.

Setting

This study was conducted at the University Medical Center Groningen, The Netherlands. With five non-PCI-capable referral hospitals, this centre provides 24/7 emergency care in a region with 750,000 inhabitants. It is the only PCI-capable centre in this region and provides on-site cardiothoracic surgical support. Our EMS consists of ambulances staffed by a driver trained at a paramedic level and a nurse trained at an intensive care level who is experienced in ECG interpretation. In rare occasions, a helicopter staffed by an anaesthesiologist, a nurse, and a pilot is used for complex situations or remote locations. As a national benchmark, EMSs are required to arrive at the scene within 15 min of activation.

Prehospital triage route

In the prehospital setting, EMS staff performed a 12-lead ECG in all patients presenting with symptoms suggestive of acute myocardial infarction. A computerized algorithm aided EMS nursing staff in their assessment of whether the patient was likely to have a STEMI. Subsequent activation of the prehospital triage protocol by contacting the coronary care unit (CCU) of our centre was at the discretion of the EMS nurse. In case of an unclear diagnosis, the EMS nurse was allowed to contact the cardiologist on duty and send the ECG by fax. Once the prehospital triage protocol was activated, near non-PCI-capable centres and the ED of our centre were bypassed. The patient was transported directly to the catheterization laboratory or, less frequently, to the CCU if the catheterization laboratory was not yet available. A bed at the CCU was kept available at all times for emergency procedures. During transportation, the EMS nurse notified the CCU of the oncoming arrival of a STEMI patient and provided the CCU with the patient's data and estimated time of arrival. Antiplatelet and antithrombin therapy were usually started in the ambulance and consisted of aspirin (500 mg), heparin (5000 IU), and clopidogrel (600 mg), administered by the EMS nurse. During regular hours, the catheterization team was present in our centre and could be activated by the CCU using a pager system. During off-hours, the CCU activated the catheterization team by having the central phone operator call the catheterization team on duty. The catheterization laboratory kept a room ready and equipped during off-hours. The above prehospital triage protocol was the preferred route of

admission for patients with STEMI. After its implementation in January 2004, it was followed by all EMS within a range of 90 min of our centre.

Interhospital transfer route

Interhospital transfer for primary PCI was required in case of a failed prehospital diagnosis of STEMI and referral to a non-PCI-capable centre by EMS. Furthermore, EMS staff may refer patients requiring mechanical ventilation to the closest centre for initial stabilization, despite a prehospital diagnosis of STEMI. These patients were transferred for primary PCI after stabilization. All five referral centres were within a range of 60 km and patients were transferred by ambulance. All patients with STEMI were transferred to our centre for primary PCI, and aspirin (500 mg), heparin (5000 IU), and clopidogrel (600 mg) were usually started at the referral centre.

Methods of measurement

Baseline and procedural measures of all patients undergoing primary PCI were documented upon admission and were prospectively collected in a dedicated database. For the interhospital transfer group, the first available ECG was collected by audits to the referring centres and assessed by an experienced cardiologist (BS) blinded to other patient data. EMS time intervals and geographical event location were obtained from EMS registries. Time of first medical contact was defined as EMS arrival at the scene. The time of EMS arrival at the first centre was deemed the 'door' time. For patients undergoing interhospital transfer, door-in to door-out time was defined as the interval between arrival and departure at the non-PCI-capable centre. System delay was defined as time of first medical contact to initial intracoronary therapy by means of thrombus aspiration or balloon inflation of the infarct related coronary artery. Ischemic time was defined as time from symptom onset to initial intracoronary therapy. Other time intervals were calculated accordingly. All time-to-reperfusion data were available in >90% of patients except for door-in to door-out time (87%). TIMI flow and myocardial blush grade were scored by the operator during the PCI procedure as previously described and validated.^{10,11} All-cause mortality was collected using municipal civil registries. These registries provide completeness of follow up regarding mortality in >99% of patients admitted to our department.

Statistical analysis

Continuous variables were summarized as mean±standard deviation or median and interquartile range. Discrete variables were presented as counts and percentages. To compare groups, we used Student's t-test for normally distributed continuous variables, Mann-Whitney *U*-test for

nonparametric continuous variables, Pearson's χ^2 test for categorical variables, and the linear trend test for ordinal variables. Time-to-treatment intervals and all-cause mortality were analysed and plotted using the Kaplan-Meier method and group differences were tested with the log-rank test. For all analyses, $p<0.05$ (two-tailed) was considered statistically significant.

A multivariable logistic regression model and a multivariable Cox proportional hazards model were fitted to assess independent predictors of interhospital transfer and 1-year all-cause mortality, respectively. All baseline characteristics listed in Table 1 with $p<0.10$ in univariable analysis and interhospital transfer were considered for the models. To assess independent predictors of ischemic time, a multivariable linear regression model was fitted. All variables listed in Table 1 with $p<0.10$ in univariable analysis, interhospital transfer, and total distance travelled by EMS were considered. Ischemic time was first transformed logarithmically, to account for its skewed distribution. Parameter estimates and 95% confidence intervals (CI) were retransformed into meaningful units in the final model. For all multivariable models, a backward stepwise method was used. Predictors remained in the multivariable model if $p<0.05$. Data was presented as odds ratios (OR) and 95% CI or hazard ratios and 95% CI where appropriate. Statistical analyses were performed with SPSS version 18.0.3 (SPSS, Chicago, Illinois) and Stata version 11.0 (StataCorp, College Station, Texas).

Results

Study population and route of admission

A flowchart for our study population is shown in Figure 1. Between 1 January 2008 and 1 January 2010, prehospital ECGs were performed in 12,555 patients by the EMS, 1017 patients with suspected STEMI underwent acute coronary angiography, and 846 consecutive patients with STEMI underwent primary PCI. Of the latter, 609 patients (72%) were admitted through our prehospital triage protocol (prehospital diagnosis group) and 127 patients (15%) underwent interhospital transfer for primary PCI after failed prehospital diagnosis (interhospital transfer group). Other STEMI patients were emergency department admissions ($n=66$; 7.8%) and self-referrals ($n=44$; 5.2%). There were a total of 649 prehospital triage protocol activations of which 40 (6.2%) were false-positive.

Baseline characteristics of patients in the prehospital diagnosis group and interhospital transfer group are shown in Table 1. Patients in the interhospital transfer group were more likely to be female (39 vs. 28%; $p=0.014$) and have higher rates of diabetes (18 vs. 9.1%; $p=0.005$) and prior myocardial infarction (21 vs. 8.4%; $p<0.001$), when compared with patients in the prehospital diagnosis group. Furthermore, patients in the interhospital transfer group

Table 1. Baseline characteristics.

	Prehospital diagnosis (n=609)	Interhospital transfer (n=127)	p-value
Age (years)	65±13	66±13	0.287
Female	173/609 (28)	50/127 (39)	0.014
Body mass index (kg/m ²)	27±3.9	27±4.4	0.147
Systolic blood pressure			
mmHg	128±27	129±28	0.706
≤90 mmHg	48/603 (8.0)	10/124 (8.1)	0.969
Heart rate			
bpm	77±19	79±18	0.197
>100 bpm	61/600 (10)	14/124 (11)	0.709
Hypertension	243/599 (41)	59/123 (48)	0.130
Diabetes	55/606 (9.1)	22/125 (18)	0.005
Hypercholesterolaemia	146/540 (27)	38/110 (35)	0.111
Current smoking	300/604 (50)	53/124 (43)	0.160
Positive family history	258/594 (43)	56/116 (48)	0.337
Prior MI	51/606 (8.4)	26/125 (21)	<0.001
Prior PCI	48/606 (7.9)	13/127 (10)	0.390
Prior CABG	11/605 (1.8)	3/127 (2.4)	0.684
Prior admission to our department	101/609 (17)	25/127 (20)	0.399
Anterior MI	280/608 (46)	65/127 (51)	0.292
Event location to PCI-capable centre distance (km)	27 (16–38)	32 (22–44)	0.004
Helicopter transport	2 (0.3)	0 (0)	

Values are n/N (%), mean±SD, or median (interquartile range).

CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention.

were at greater median distance from the PCI-capable centre when they experienced their event (32 vs. 27 km; $p=0.004$). Remarkably, the number of patients with any prior inpatient or outpatient admission to our department did not differ between the interhospital transfer and prehospital diagnosis groups (20 vs. 17%; $p=0.399$).

Time-to-treatment intervals and procedural characteristics

Time-to-treatment intervals are shown in Table 2. No differences were seen in call to first medical contact time (Figure 2A), and median first medical contact to first door time was slightly shorter in patients in the interhospital transfer group (34 vs. 44 min; $p<0.001$). However, patients in the interhospital transfer group experienced additional delays due to door-in to door-out time at the non-PCI-capable centre (median 52 min) and interhospital transportation time (median 29 min). Consequently, substantially longer system delay (median 155 vs. 88 min; $p<0.001$; Figure 2B) and door-to-balloon time (median 116 vs. 43 min; $p<0.001$; Figure 2C) were seen in the interhospital transfer group. System delay ≤90 min was achieved in 2.7% of patients in the interhospital transfer group compared with 54% in the prehospital diagnosis group ($p<0.001$). These rates were 16 and 90% for system delay ≤120 min ($p<0.001$). Door-to-balloon time ≤60 min was achieved in 2.7 and 79% of patients in the interhospital transfer and prehospital diagnosis group, respectively. Median

ischemic time was 263 min for patients in the interhospital transfer group and 165 min for patients in the prehospital diagnosis group ($p<0.001$; Figure 2D).

Patients in the interhospital transfer group and prehospital diagnosis group were equally likely to be treated during off-hours (44 vs. 45%; $p=0.871$; Table 2). The culprit coronary artery was significantly different between both groups ($p<0.001$). Patients in the interhospital transfer group had higher rates of circumflex artery infarctions (20 vs. 14%) and lower rates of right coronary artery infarctions (28 vs. 40%). The rate of left anterior descending artery infarctions was similar in both groups. Post PCI, epicardial and microvascular myocardial reperfusion as assessed by TIMI flow and myocardial blush grade trended towards poorer results in the interhospital transfer group ($p=0.085$) and ($p=0.071$), respectively (Table 2).

ECG characteristics

To gain further insight in the reasons for a failed prehospital diagnosis in the interhospital transfer group, the first available ECG was collected and assessed. ECG characteristics of the patients in the interhospital transfer group are shown in Table 3. Although this group of patients was not directly referred for primary PCI, only 14% of the first available ECGs showed ST-elevation <0.2 mV. The rate of patients with left bundle branch block was 6.9%. Overall, 77% of ECGs were diagnostic for STEMI.

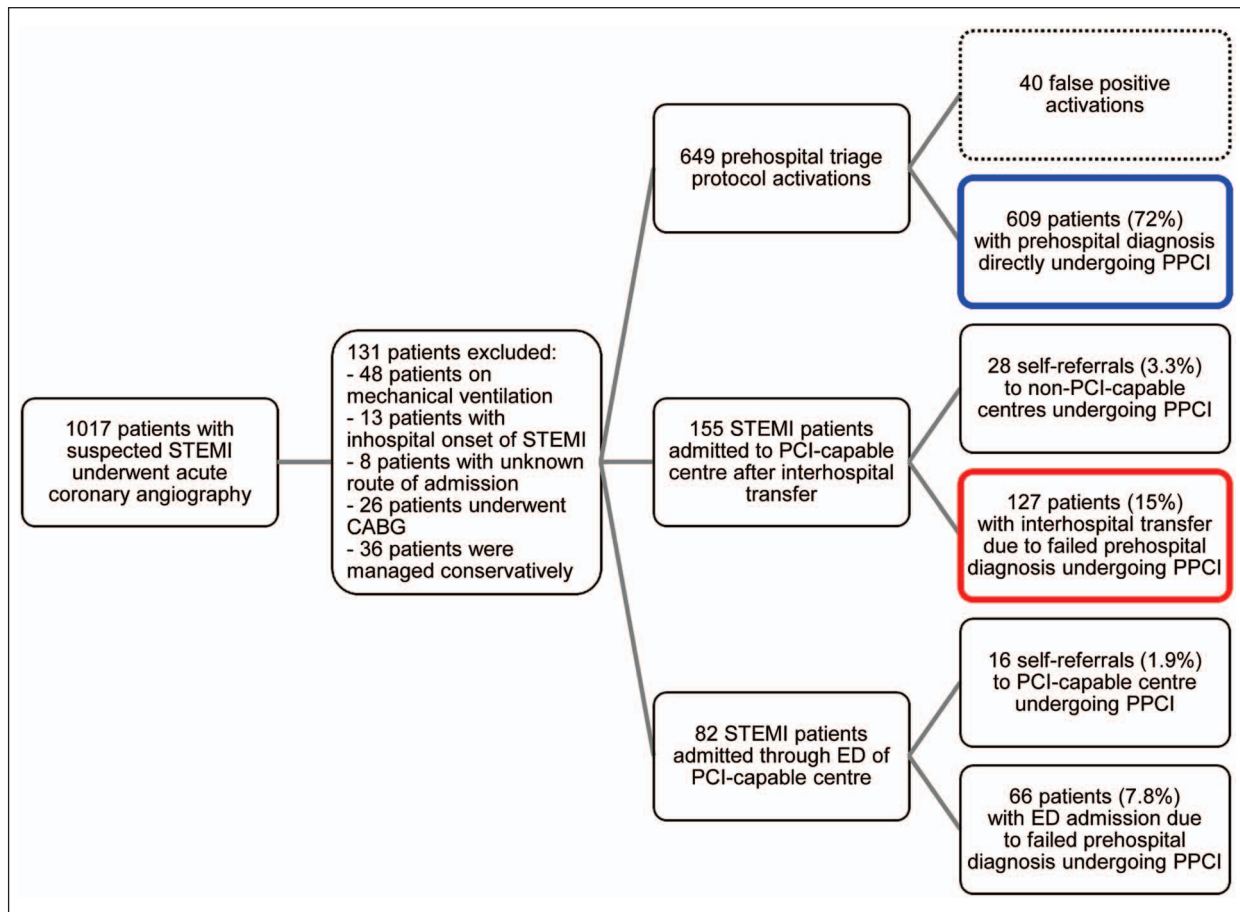


Figure 1. Flowchart for study design and route of admission of patients.

CABG, coronary artery bypass grafting; ED, emergency department; PPCI, primary percutaneous coronary intervention.

Predictors of interhospital transfer

In order to identify patient subgroups at higher risk of interhospital transfer, we assessed predictors of failed prehospital diagnosis (Table 4). After multivariable adjustment, female gender (OR 1.58, 95% CI 1.01–2.46; $p=0.046$), diabetes (OR 1.98, 95% CI 1.11–3.55; $p=0.022$), prior myocardial infarction (OR 2.86, 95% CI 1.62–5.08; $p<0.001$), and distance from event location to PCI-capable centre (OR 1.22 per 10 km, 95% CI 1.07–1.39; $p=0.002$) were independent predictors of interhospital transfer.

Predictors of ischemic time

Predictors of total ischemic time in multivariable analysis are shown in Table 5. Age and heart rate were independently associated with longer ischemic time. However, interhospital transfer was the most powerful predictor of ischemic time and was associated with an estimated 47% increase in ischemic time (95% CI 33 to 63%; $p<0.001$). Notably, the impact of interhospital transfer on ischemic

time was adjusted for total distance travelled by EMS (estimate +1.9% per 10 km, 95% CI –0.3 to 4.0%; $p=0.088$).

Clinical outcome

Follow up with regard to mortality at 30 days and 1 year was completed in all patients. Thirty-day mortality was 7.1% in the interhospital transfer group and 3.3% in the prehospital diagnosis group ($p=0.043$). This pattern was similar at 1-year follow up, with 10% mortality in the interhospital transfer group vs. 5.3% mortality in the prehospital diagnosis group ($p=0.030$; Figure 3). Independent predictors of mortality at 1-year follow up are shown in Table 6. After multivariable adjustment, an independent association between interhospital transfer and mortality could not be demonstrated (hazard ratio 1.42, 95% CI 0.70–2.88; $p=0.335$).

Discussion

We currently studied a comprehensive fully operational prehospital triage system with a single PCI-capable centre

Table 2. Time-to-treatment intervals and procedural characteristics.

	Prehospital diagnosis (n=609)	Interhospital transfer (n=127)	p-value
Symptom onset to call time (min)	62 (28–139)	76 (38–161)	0.156
Symptom onset to FMC time (min)	72 (37–150)	91 (47–171)	0.151
Call to FMC time (min)	9 (7–11)	9 (7–11)	0.937
FMC to door I time (min)	44 (37–52)	34 (27–43)	<0.001
Door-in to door-out time (min)	N/A	52 (31–85)	
Interhospital transportation time (min)	N/A	29 (19–34)	
Door-to-balloon time (min)	43 (32–56)	116 (102–166)	<0.001
Total system delay (min)	88 (78–103)	155 (132–198)	<0.001
Total ischemic time (min)	165 (125–242)	263 (202–380)	<0.001
Total distance travelled by EMS (km)	27 (16–38)	40 (25–53)	<0.001
Off-hour PCI ^a	272/606 (45)	56/127 (44)	0.871
Target coronary artery			<0.001
Right	240/608 (40)	35/127 (28)	
Left anterior descending	276/608 (45)	59/127 (47)	
Circumflex	85/608 (14)	25/127 (20)	
Left main	4/608 (0.7)	6/127 (4.7)	
Graft	3/608 (0.5)	2/127 (1.6)	
Preprocedural TIMI flow			0.224
0/1	360/609 (59)	69/127 (54)	
2	125/609 (21)	26/127 (21)	
3	124/609 (20)	32/127 (25)	
Post-procedural TIMI flow			0.085
0/1	14/607 (2.3)	2/127 (1.6)	
2	46/607 (7.6)	20/127 (16)	
3	547/607 (90)	105/127 (83)	
Post-procedural myocardial blush grade			0.071
0/1	147/583 (25)	37/115 (32)	
2	209/583 (36)	42/115 (37)	
3	227/583 (39)	36/115 (31)	
Glycoprotein IIb/IIIa inhibitor use	550/607 (91)	112/127 (88)	0.404

Values are n/N (%) or median (interquartile range).

^aBefore 08:00 hours or after 18:00 hours.

EMS, emergency medical systems; FMC, first medical contact; PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

and five non-PCI capable referral centres where the preferred reperfusion strategy for all patients with STEMI was primary PCI and self-referrals were excluded. Principal findings of our study were: (1) among patients with STEMI undergoing primary PCI, the incidence of interhospital transfer due to failed prehospital diagnosis was 15%; (2) in the interhospital transfer group, recommended system delay ≤ 90 min was seen in only 2.7% of patients, while this rate was 54% for patients in the prehospital diagnosis group; (3) despite a failed prehospital diagnosis, the first available ECG was diagnostic for STEMI in 77% of patients in the interhospital transfer group; (4) patients with onset of STEMI at greater distance from a PCI-capable centre were at higher risk of interhospital transfer, as were women, diabetics, and patients with prior myocardial infarction; (5) interhospital transfer was independently associated with an estimated 47% increase in ischemic time; and (6) mortality was significantly higher in the interhospital transfer group.

Prior studies comparing patients admitted through prehospital triage and interhospital transfer have been performed, but were conducted during the implementation period of the prehospital triage protocol,⁸ did not use primary PCI as the preferred reperfusion strategy for all patients with STEMI,¹² or were limited by inclusion of self-referrals.^{13,14} Our study design lacked these limitations and allowed us to accurately estimate the rate of failed prehospital diagnosis and identify subgroups with higher risk of interhospital transfer. Moreover, our study includes the newly published ESC system performance measures, demonstrating that substantial improvement in first medical contact to treatment time is necessary for all STEMI patients despite relatively fast treatment times once the patient has arrived at the PCI-capable centre.

The incidence of interhospital transfer due to failed prehospital diagnosis was 15% in our study. This rate is similar to prior studies, reporting rates of 15 and 22%.^{8,12} Despite its relatively low incidence, interhospital transfer was

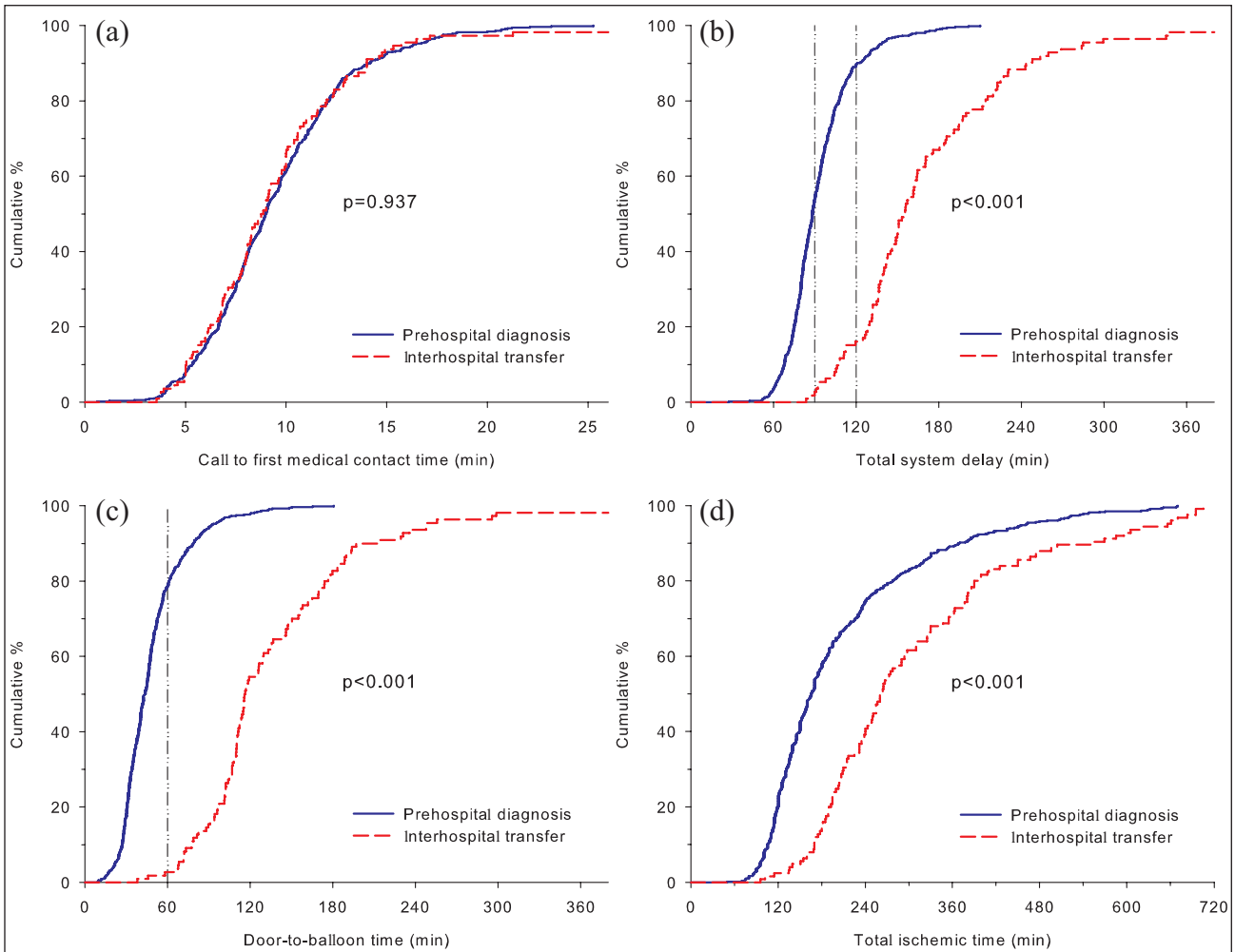


Figure 2. Time-to-treatment intervals: (a) call to first medical contact time; (b) total system delay with 90- and 120-minute reference lines; (c) door-to-balloon time with 60-minute reference line; (d) total ischemic time for patients in the prehospital diagnosis and interhospital transfer groups.

found to be a major predictor of ischemic time in our study. In a secondary analysis of the HORIZONS-AMI trial, interhospital transfer was also found to be associated with the greatest delay to reperfusion.¹⁵ Thus, considerable delay occurs in the group of patients not directly admitted to a PCI-capable centre and guideline recommended first medical contact to treatment time is not met. This finding is supported by most,^{13,14,16} but not all¹⁷ prior studies. Also, the finding that 72% of patients are directly referred for primary PCI after prehospital diagnosis closely resembles the rate of 73% recently reported in a small single-centre study.¹⁸ Remarkably, we found that distance travelled by EMS was not predictive of ischemic time in multivariable analysis. This suggests that, within our geographical context, distance travelled by EMS is of minor relevance for total ischemic time. For interhospital transfer patients, most time is lost as door-in to door-out time at the non-PCI-capable centre, rather than interhospital transportation time.

The minor impact of EMS transportation distance on total ischemic time was also underlined by a Danish study.⁸

We found that women and diabetics were at higher risk of interhospital transfer. This may relate to the phenomenon that symptom presentation in these subgroups is often atypical and without chest pain.^{19–21} Atypical clinical presentation in these subgroups may limit recognition of STEMI by EMS staff and increase the risk of interhospital transfer. Patients with prior myocardial infarction were also at greater risk of interhospital transfer. Although these patients are likely to recognize symptoms of myocardial infarction, ECG interpretation may be harder. Still, the first available ECG in the interhospital transfer group was retrospectively considered diagnostic for STEMI in 77% of cases.

The 1-year mortality we observed in interhospital transfer patients was approximately twice the rate of prehospital diagnosis patients. However, we could not demonstrate an

Table 3. ECG characteristics of interhospital transfer patients.

	Interhospital transfer (n=127)
ECG available	118
ECG not assessable ^a	2
ECG diagnostic for STEMI	91/118 (77)
Symptom onset to ECG time (min)	135 (72–228)
Left bundle branch block	8/116 (6.9)
Right bundle branch block	5/116 (4.3)
ST-segment	
Assessable	108
ST-elevation	
<0.2 mV	15/108 (14)
0.2–0.5 mV	42/108 (39)
0.6–1.0 mV	33/108 (31)
>1.0 mV	18/108 (17)
ST-deviation	
<0.2 mV	10/108 (9.3)
0.2–0.5 mV	28/108 (26)
0.6–1.0 mV	29/108 (27)
>1.0 mV	41/108 (38)

Values are n/N (%) or median (interquartile range)

^aDue to arrhythmia.

independent association between interhospital transfer and mortality. Part of the excess mortality in the interhospital transfer group may be explained by higher rates of high-risk subgroups, such as patients with prior myocardial infarction and diabetics. However, ischemic time was considerably longer in patients undergoing interhospital transfer and longer ischemic time and system delay have been clearly associated with decreased myocardial reperfusion, greater enzymatic infarct size, poorer left ventricular function, and higher mortality in prior studies, mostly with greater sample size.^{3,4,22} Therefore, we believe our study was not sufficiently powered to detect an independent association between interhospital transfer and mortality.

ESC guidelines recommend immediate fibrinolysis when expected system delay to primary PCI exceeds 120 min.⁵ In our study, 84% of patients in the interhospital transfer group and 10% of patients in the prehospital diagnosis group had a system delay >120 min. In some of these patients, fibrinolysis may be an alternative reperfusion strategy. However, we and others²³ believe that,

Table 4. Independent predictors of interhospital transfer by logistic regression.

	Odds ratio (95% CI)	p-value
Female gender	1.58 (1.01–2.46)	0.046
Diabetes	1.98 (1.11–3.55)	0.022
Prior MI	2.86 (1.62–5.08)	<0.001
Event location to PCI-capable centre distance (per 10 km)	1.22 (1.07–1.39)	0.002

CABG, coronary artery bypass grafting; MI, myocardial infarction.

in the context of STEMI networks with short transfer distances, further improvements in STEMI care are likely to come from efforts to improve prehospital triage and, if needed, efficient interhospital transfer in order to provide timely primary PCI rather than accepting delays and resorting to fibrinolysis. An important aspect in this process is discussing lessons from analyses as these with all regional STEMI care participants. Now that an increasing number of prehospital triage systems have been successfully implemented, future research should focus on optimization of operational prehospital triage systems by maximizing the percentage of STEMI patients included without an unacceptable rise in false-positive activations. Therefore, it is important to identify patient subgroups at risk of failed prehospital diagnosis and develop interventions aimed at reducing the rate of interhospital transfer in these patients. A greater distance from event location to a PCI-capable centre should not be a reason for an intermediate admission to a non-PCI-capable centre in a haemodynamically stable patient, since substantial delays occur as door-in to door-out time at a non-PCI-capable centre while greater distance travelled by EMS results in minor delays. Furthermore, EMS staff should be aware of the often-atypical symptom presentation in women and diabetics with STEMI. Transportation to a PCI-capable centre should be promptly performed in case of diagnostic uncertainty or difficulties with ECG interpretation in patients with prior myocardial infarction. Finally, physicians should be aware that patients with STEMI initially admitted to a non-PCI-capable centre mostly comprise a group of patients with higher mortality, rather than patients with minor ECG changes and a favourable outcome.

Table 5. Independent predictors of ischemic time by linear regression.

	Estimate (%)	95% CI	p-value
Age (per decade)	+7.5	4.8 to 10	<0.001
Heart rate (per 10 bpm)	+3.5	1.6 to 5.5	<0.001
Interhospital transfer	+47	33 to 63	<0.001
Distance travelled by EMS (per 10 km)	+1.9	-0.3 to 4.0	0.088

EMS, emergency medical systems.

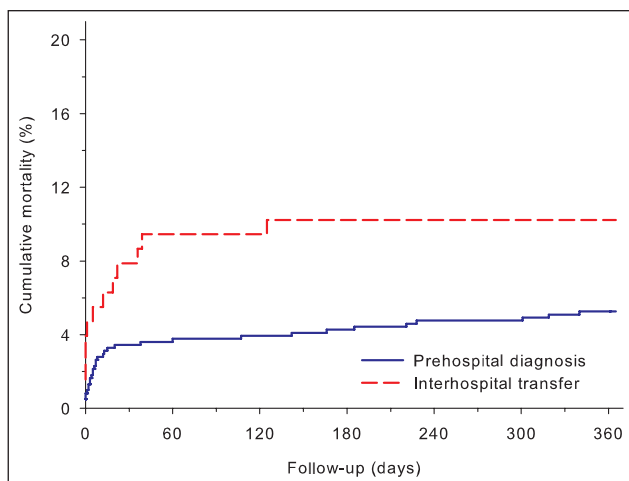


Figure 3. One-year mortality: 10% in the interhospital transfer group and 5.3% in the prehospital diagnosis group ($p=0.030$).

Study limitations

It is important to consider several limitations of our study. First, we studied all patients with suspected STEMI undergoing acute coronary angiography. Therefore, we may have missed patients eligible for primary PCI who died before admission, resulting in an underestimation of mortality. Second, we defined treatment time as time of initial intracoronary therapy (by thrombus aspiration or balloon inflation) which is slightly later than time of wire passage through the culprit lesion, used in the new ESC guidelines. Third, ECGs in patients undergoing interhospital transfer were retrospectively analysed by a single cardiologist. Although ECGs were reviewed independently of other patient data, this may have introduced a bias. Although we put much effort in obtaining the first ECG made by EMS, it is likely that some of the ECGs we assessed were not the first ECG. As studies have shown that an additional 15% of STEMI patients may be diagnosed by performing serial prehospital ECGs,²⁴ the rate of diagnostic ECGs we found in the interhospital transfer group (77%) may be an overestimate. Clearly, it is hard to prevent admission to a non-PCI-capable centre in patients who initially present with a non-diagnostic ECG. Finally, we did not study patients on mechanical ventilation, as this may have been a reason for an intermediate admission to the nearest non-PCI-capable centre despite a prehospital diagnosis of STEMI. Therefore, the results of our study should not be generalized to this complex subgroup of patients.

Conclusions

In a fully operational prehospital triage system, failed prehospital diagnosis and subsequent interhospital transfer occurred in 15% of STEMI patients undergoing primary PCI despite an often-diagnostic ECG. Interhospital transfer

Table 6. Independent predictors of mortality at 1-year follow up by Cox regression.

	Hazard ratio (95% CI)	<i>p</i> -value
Age (per decade)	4.35 (2.91–6.51)	<0.001
Systolic blood pressure (per 10 mmHg)	0.70 (0.63–0.79)	<0.001
Current smoking	2.14 (1.04–4.40)	0.038
Prior MI	2.39 (1.15–4.98)	0.020
Anterior MI	2.17 (1.13–4.16)	0.020
Interhospital transfer	1.42 (0.70–2.88)	0.335

MI, myocardial infarction.

was a major predictor of ischemic time and short-term and long-term mortality were higher. Continuing efforts to optimize prehospital triage and direct referral for primary PCI in patients with STEMI are warranted, especially for patients with onset of STEMI at greater distance from a PCI-capable centre, women, diabetics, and patients with prior myocardial infarction.

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Conflict of interest

The authors declare that there is no conflict of interest.

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