Prehospital diagnosis in STEMI patients treated by primary PCI: the key to rapid reperfusion

R.P. Vermeulen, T. Jaarsma, F.G.A. Hanenburg, J.W. Nannenberg, G.A.J. Jessurun, F. Zijlstra

Background. Primary coronary intervention (PCI) for acute myocardial infarction should be performed as quickly as possible, with a door-to-balloon time of less than 90 minutes. However, in daily practice this cannot always be achieved. Prehospital diagnosis of ST-elevation myocardial infarction (STEMI) is of major importance in reducing time to treatment, in particular when patients can be transported directly to a centre with interventional capacities.

Objectives. The aim of the current study was to evaluate the time from prehospital diagnosis of STEMI to balloon inflation and identify factors related to treatment delay in patients directly referred to the catheterisation laboratory of the University Medical Centre of Groningen.

Methods. A cross-sectional descriptive design was used to collect data on patients treated with primary PCI after prehospital diagnosis of STEMI.

Results. Median prehospital diagnosis-to-balloon time was 64 minutes for patients directly admitted to the catheterisation laboratory and 75 minutes for patients initially admitted to the coronary care unit. A delay longer than 90 minutes was observed in 18 patients. Higher age was associated with longer delay times ($p=0.041$). Long delays were not associated with diabetes ($p=0.293$), time from

symptom onset to prehospital diagnosis ($p=0.87$) or time of day ($p=0.09$). Initial unavailability of the catheterisation laboratory due to running procedures contributed to longer delay times in ten cases.

Conclusion. Prehospital diagnosis of STEMI and direct referral to a catheterisation laboratory for primary PCI allows a prehospital diagnosis-to-balloon time of less than 90 minutes in 82% of patients. Older patients are at risk of longer delays. (*Neth Heart J* 2008;16:5-9.)

Keywords: prehospital diagnosis, myocardial infarction, ST-segment elevation, STEMI, percutaneous coronary intervention (primary), treatment delay

The 2005 Guidelines for Percutaneous Coronary Intervention (PCI) recommend that first medical contact or door-to-balloon time for patients with ST-segment elevation myocardial infarction (STEMI) should be as short as possible, preferably less than 90 minutes.^{1,2} Many reports have shown that first medical contact to balloon or even door-to-balloon times often exceed the recommended 90 minutes.³⁻⁵

From several studies it is evident that prehospital diagnosis of patients with STEMI is a major asset to reduce time to treatment, whether that treatment is mechanical through PCI or pharmacological through fibrinolysis.⁶⁻⁹ Time to treatment should be as short as possible to improve patient outcomes, such as more myocardial salvage, better left ventricular function, and reduced mortality.¹⁰⁻¹²

Most studies on delay times in STEMI patients concentrate on delay from door to balloon or randomisation to balloon. However, from a patient perspective, the period of myocardial ischaemia starts at onset of chest pain. From a medical perspective, the treatment delay begins when a clinical diagnosis of STEMI has been confirmed by electrocardiography. This treatment delay is in part susceptible to interventions that shorten the avoidable delay. Prehospital diagnosis and direct referral to an interventional centre are two of

R.P. Vermeulen
T. Jaarsma
F.G.A. Hanenburg
J.W. Nannenberg
G.A.J. Jessurun
F. Zijlstra

Department of Cardiology, Thoraxcentre, University Medical Centre Groningen, University of Groningen, Groningen, the Netherlands

Correspondence to: R.P. Vermeulen
Department of Cardiology, Thoraxcentre, University Medical Centre Groningen, University of Groningen, PO Box 30.001, 9700 RB Groningen, the Netherlands
E-mail: r.p.vermeulen@thorax.umcg.nl

Table 1. Recorded time intervals for patients with STEMI treated with primary PCI.

Clock time of diagnosis (T=0)
Start of procedure (when sterile draping touches patient, in minutes on stopwatch)
Sheath insertion completed (in minutes on stopwatch)
First balloon inflation or first thrombus aspiration (in minutes on stopwatch)
First angiogram with TIMI-3 flow in infarct-related vessel (in minutes on stopwatch)
End of procedure (X-ray off, in minutes on stopwatch) Arrival on CCU (in minutes on stopwatch) Clock time of arrival on CCU (in real time, for validation purposes)

these interventions. The aim of this study was to evaluate the time delay from prehospital diagnosis to balloon inflation in patients directly transported for primary PCI, and to identify patients at risk of delays longer than 90 minutes.

Patients and methods

STEMI logistics

The University Medical Centre of Groningen adopted a strategy of prehospital diagnosis and primary PCI in January 2004. The 12-lead electrocardiogram of a patient with symptoms compatible with myocardial infarction, not relieved by sublingual nitrates, is obtained in the ambulance and diagnosed by a pre-defined computer algorithm. If STEMI is confirmed by the algorithm, the paramedics notify the CCU of the coming arrival of a patient and send the ECG by fax to the hospital. When the paramedics are in doubt about the diagnosis by the algorithm, the CCU cardiologist is consulted by telephone. The CCU informs the catheterisation laboratory staff that a STEMI patient will be arriving.

During transport the ambulance nurse provides the CCU with the patient's personal data and estimated arrival time at the hospital. If the catheterisation laboratory is not ready at the time of arrival, the patient is initially admitted to the CCU. As premedication for PCI the paramedics administer heparin 5000 IU, acetylsalicylic acid (900 mg intravenously) and clopidogrel (600 mg orally).¹³

This protocol of direct transport to the interventional centre is followed by all ambulance services stationed within 90 minutes of transport time from the hospital. All noninterventional hospitals are therefore bypassed.

Study design

A cross-sectional descriptive design was used to obtain information on time intervals. Patients treated with primary PCI were included if STEMI had been diagnosed in the ambulance and the hospital had been notified of the coming arrival of the patient. No patients from referring hospitals or the emergency department were included.

In some cases thrombus aspiration was performed instead of balloon inflation. Therefore the term

'balloon inflation' in this article refers to either balloon inflation or thrombus aspiration.

Stopwatches were used to collect precise data on time between the various steps in the process. To validate time registration, clock times at the start and stop of data collection were recorded. Furthermore, time registration around therapeutic procedures took place routinely and retrospectively in a written report by the cardiologist.

The CCU nurse started recording time at the moment of STEMI diagnosis. From this moment, two routes were possible for the patient: preferably direct admission to the cath lab or, depending on the readiness of the cath lab and staff, initial admission to the CCU. Table 1 shows the time intervals that were recorded. If a patient was initially admitted to the CCU, no additional lytic or anticoagulant therapy was administered.

Demographical and clinical variables were collected from the patient charts and from the cath lab computer database, such as gender, age, distance to hospital, type and location of lesion, time of onset of chest pain, results from blood tests and blood gas analysis, and complications such as cardiopulmonary resuscitation, intubation, need for counterpulsation and concomitant pharmacological treatment.

Anatomical obstacles and coronary abnormalities were recorded by the nurse when encountered during the procedure. The localisation of sheath insertion was recorded, as well as the number of wires, balloons or suction catheters used before first inflation or thrombus aspiration.

Statistical analysis

All data were analysed in SPSS, version 12.0.1. Where appropriate, Fisher's exact test, Mann-Whitney U, χ^2 , ANOVA and binary logistic regression were used to calculate p values. A p value of ≤ 0.05 was considered statistically significant.

Results

Patient characteristics

From 1 December 2005 to 5 May 2006 a total of 255 patients with STEMI were treated with primary PCI. Of these 255 patients, 136 had a prehospital diagnosis

Table 2. Patient characteristics.

	All included (n=100)	Cath lab route (n=59)	CCU route (n=41)	Not included (n=36)	P
Male (%)	78	78	78	75	
Age (years)	61±11.7	60±12	62±11	64±15.8	0.16
Anterior infarction (%)	39 (39)	21 (36)	18 (44)	11 (31)	0.42
Heart rate (beats/min)	80±18	83±17	75±17	82±22	0.59
Systolic blood pressure (mmHg)	134±23	137±26	129±19	129±27	0.43
BMI	26.7±3.7	27.4±4.1	25.9±3.3	27.2±3.5	0.54
Transport time to hospital by ambulance (minutes)	28±12.2	30±12.1	25±11.8	27±12.3	0.69
Diabetes (%)	9 (9)	5 (9)	4 (10)	7 (19)	0.09
Hypercholesterolaemia (%)	20 (20)	18 (31)	2 (5)	8 (22)	0.78
Family history of CAD (%)	40 (40)	25 (42)	15 (37)	8 (22)	0.06
Smoking (%)	44 (44)	25 (42)	19 (47)	16 (44)	0.79
- Yes	40 (40)	25 (42)	15 (37)	12 (33)	
- Stopped	4 (4)	0	4 (10)	4 (11)	
Hypertension (%)	29 (29)	18 (31)	11 (27)	15 (42)	0.17
Previous PCI (%)	11 (11)	7 (12)	4 (10)	3 (8)	0.60
Elevated troponin levels at admission (%)	70 (70)	41 (70)	29 (71)	25 (69)	0.95

BMI=body mass index, CAD=coronary artery disease, PCI=percutaneous coronary intervention; p value calculated comparing all included with not included patients.

established with direct transport to the hospital. The other patients were referred from other hospitals (n=102) or the emergency department of the UMCG (n=17). Of the 136 potential candidates, complete evaluable time data were obtained in 100 patients (74%). Baseline characteristics of the 36 patients not included in this study were similar to the 100 included patients (table 2). On hospital arrival, 59 patients were admitted directly to the cath lab, 41 were initially admitted to the CCU.

Overall, anterior infarction was present in 39 patients. TIMI-3 flow in the infarct-related vessel was present in 31 patients on first angiogram. Most patients (n=70) had elevated troponin levels. All procedures were performed via the right femoral artery. One patient died of cardiogenic shock due to anterior infarction.

From the 100 patient sample, median time from pre-hospital diagnosis to balloon inflation was 70 minutes, with an interquartile range (IQR) from 60 to 78. This

is well within recommended guidelines. Patients directly admitted to the cath lab were on average ten minutes faster than patients who were first admitted to the CCU (64 vs. 74 minutes) (table 3).

In total 18 patients did not receive first balloon inflation within 90 minutes after first medical contact. For these 18 patients, median medical contact to balloon time was 102 minutes (IQR 97-136). Patients undergoing a delay of more than 90 minutes to balloon inflation were on average older, had longer procedure times and more often had diabetes. Binary logistic regression analysis was performed, with age and diabetes as co-variables. Procedure time was ignored. After regression analysis, age was associated with longer delay times (p=0.041), diabetes was not (p=0.293).

Of the 18 patients with diagnosis-to-balloon time >90 minutes, 13 patients had to wait on the CCU on arrival at the hospital. Ten of these patients presented during office hours but, due to elective procedures, a catheter-

Table 3. Median delay times (Q25-Q75)

	All included (n=100)	Cath lab route (n=59)	CCU route (n=41)	Not included (n=36)	P
Median time from symptom onset to call (patient delay)	89 (10-613)	91 (24-397)	81 (10-613)	118 (20-445)	0.11
Median diagnosis-to-balloon time	70 (60-78)	64 (55-73)	74 (70-97)	75 (60-90)	0.87

P value comparing all included to not included patients.

Table 4. Clinical characteristics and prehospital diagnosis-to-balloon delay.

	Prehospital diagnosis-to-balloon delay <90 min (n=82)	Prehospital diagnosis-to-balloon delay ≥90 min (n=18)	P
Age (mean)	58.6	68	0.001*
Distance to hospital (km, mean)	32.6	33.5	0.87
Patient delay (median)	90	95	0.87
Anterior infarction (%)	32 (42)	7 (39)	0.84
Cath lab not available (%)	5 (6)	10 (56)	<0.001
Team not available	17 (21)	0	<0.001
Presentation during office hours	26 (32)	10 (56)	0.09
Procedure time (median)	33	38	0.04
Diabetes I and II	5 (6)	4 (22)	0.04*
BMI ≥30	18 (22)	2 (11)	0.47

* Entered as covariates in binary logistic regression analysis. BMI=body mass index.

isation room was not immediately available. In four of the 18 patients, two STEMI patients presented almost simultaneously outside office hours. Using ANOVA to determine the relation between interventionalist and long delay, no significant difference was found ($p=0.584$). Furthermore, there was no relationship between long delay and time from symptom onset to patient call or anterior infarction ($p=0.426$ and 0.836) (table 4).

Other reasons for a delay of more than 90 minutes were ventricular fibrillation prior to admission to the hospital ($n=2$), and abnormal anatomy of coronary origins ($n=2$). In one case, the interventionalist suspected a dissecting aorta, so a multisliced computed tomography was performed prior to coronary angiography.

Discussion

Direct transport to a catheterisation laboratory for primary PCI circumventing other hospitals or the emergency department reduces time from the first medical contact to balloon inflation or thrombus aspiration.^{3,14} In more than 80% of our STEMI patients, it is possible to perform an intervention within 90 minutes of prehospital diagnosis.

Patients transported directly to the cath lab obviously have the greatest benefit from reduction in treatment time. However, in this study a delay interval of less than 90 minutes was achieved in most cases, even in patients first admitted to the CCU of the UMCG. This is the result of agreements made between ambulance care, the CCU and the cath lab on fast transfer of patients with STEMI. The CCU keeps a bed available at all times for emergency procedures, and the cath lab always has a room ready and equipped for instant availability outside office hours.¹⁵

On the other hand, delays of more than 90 minutes were more frequent in patients admitted to the CCU prior to intervention. The reasons for this delay are not patient related or CCU related but are due to

limitations in cath lab capacity. One patient, whose diagnosis of STEMI was made within 30 minutes after symptom onset, had to wait on the CCU because another patient with a STEMI was admitted at the same time. This minimal interval between symptom onset and diagnosis is regrettably not standard. The median patient-related delay was almost 90 minutes for our study population, which is comparable with other studies.^{16,17} The long prediagnosis delay may account for the elevated troponin levels in 70% of patients on hospital admission. The fact that almost half of the STEMI patients (119 of 255) did not enter the UMCG with a prehospital diagnosis but through (the emergency department of) referring hospitals suggests that, on the one hand, public knowledge as to when to detect myocardial infarction is not yet at its optimum, but on the other hand maybe not all STEMI patients are correctly diagnosed in the ambulance.

When looking at patient characteristics, higher age is a risk factor for longer delays. A possible explanation might be that cardiologists are more conservative about treating elderly patients because of the higher risk of stroke and major bleeding in this patient category.¹⁸

Study limitations

For reasons of accuracy and the need for a uniform approach to time registration, we decided to measure time intervals by using stopwatches. However, giving a subject a stopwatch makes the subject more aware of the passing of time. This might result in a higher work pace and thus a positive colouring of the test results. On the other hand, CCU and cath lab staff are already fully aware that time is of essence when treating a patient with STEMI. So even if the stopwatch makes the staff more aware of time, they cannot act much faster than they already do.

The inclusion forms were filled in correctly in 100 of the 136 patients eligible for the study. This left us with

26% of the patients who had been diagnosed pre-hospitally, but for whom we did not have an accurate time measurement. Table 2 shows that baseline characteristics for the 36 patients who were not included were similar to the 100 included cases.

As stated earlier, time registration for the therapeutic procedures took place routinely and retrospectively in a report written by the cardiologist. We calculated that for the 100 included cases, on an individual level, the database time was unreliable, with differences between estimated and measured time ranging from minus 30 minutes to plus 20 minutes. However, we found on average little difference between stopwatch times and database times for the 100 included cases. This means that on a group level, delay times from diagnosis to balloon could be approximated for the 36 patients not included on the basis of the estimated data provided by the cardiologist. These delays were not different from the 100 included cases. Time between symptom onset and diagnosis was longer for excluded than for included patients (table 3). This difference is not significant ($p=0.11$) but the study may be underpowered to detect a significant difference. However, longer patient delay does not have an effect on the time registration procedure.

Implications

Regarding the finding that almost half of all STEMI patients from December 2005 to May 2006 were not diagnosed prehospitally but in other hospitals or in the emergency department, another study will be necessary to determine why not every STEMI patient is transported directly to the catheterisation laboratory or the CCU of an interventional centre.

Conclusion

Prehospital diagnosis and direct referral to an interventional centre for primary PCI enables a prehospital diagnosis to balloon time of less than 90 minutes in 82% of patients with STEMI. Older patients are at risk for longer delay. ■

References

- 1 Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *Circulation* 2004; **110**(9):e82-292.
- 2 Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update 2001 Guidelines for Percutaneous Coronary Intervention). *Circulation* 2006; **113**:e166-e286.
- 3 McNamara RL, Herrin J, Bradley EH, et al. Hospital improvement in time to reperfusion in patients with acute myocardial infarction, 1999 to 2002. *J Am Coll Cardiol* 2006; **47**:45-51.
- 4 Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NORMI)-3/4 analysis. *Circulation* 2005; **111**:761-7.
- 5 Pinto DS, Southard M, Ciaglo L, Gibson CM. Door-to-balloon delays with percutaneous coronary intervention in ST-elevation myocardial infarction. *Am Heart J* 2006; **151**(Suppl):S24-S29.
- 6 Curtis JP, Portnay EL, Wang Y, et al. The pre-hospital electrocardiogram and time to reperfusion in patients with acute myocardial infarction, 2000-2002: findings from the National Registry of Myocardial Infarction-4. *J Am Coll Cardiol* 2006; **47**:1544-52.
- 7 Bradley EH, Herrin J, Wang Y et al. Strategies for Reducing the Door-to-Balloon Time in Acute Myocardial Infarction. *N Engl J Med* 2006; **355**:2308-20.
- 8 Van Bavel H, Brenninkmeijer W, Van Ekelon D, et al. Regional implementation of the NVVC guideline on ST-elevation myocardial infarction. *Neth Heart J* 2005; **13**:401-7.
- 9 Firanescu C, Wilbers R, Meeder JG. Safety and feasibility of prehospital thrombolysis in combination with active rescue PCI strategy for acute ST-elevation myocardial infarction. *Neth Heart J* 2005; **13**:300-4.
- 10 Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. *Eur Heart J* 2006; **27**:779-88.
- 11 Brodie BR, Hansen C, Stuckey TD, et al. Door-to-balloon time with primary percutaneous coronary intervention for acute myocardial infarction impacts late cardiac mortality in high-risk patients and patients presenting early after the onset of symptoms. *J Am Coll Cardiol* 2006; **47**:289-95.
- 12 Ernst N, de Boer MJ, Zijlstra F, et al. Primary angioplasty: pre-procedural pharmacological therapy. *Neth Heart J* 2006; **14**:55-61.
- 13 Zijlstra F, Ernst N, de Boer MJ, et al. Influence of prehospital administration of aspirin and heparin on initial patency of the infarct-related artery in patients with acute ST elevation myocardial infarction. *J Am Coll Cardiol* 2002; **39**:1733-7.
- 14 Amit G, Cafri C, Gilutz H, Ilial R, Zahger D. Benefit of direct ambulance to coronary care unit admission of acute myocardial infarction patients undergoing primary percutaneous intervention. *Int J Cardiol* 2006; **119**:355-8.
- 15 Bradley EH, Roumanis SA, Radford MJ, et al. Achieving door-to-balloon times that meet quality guidelines: how do successful hospitals do it? *J Am Coll Cardiol* 2005; **46**(7):1236-41.
- 16 Terkelsen CJ, Lassen JF, Norgaard BL, et al. Reduction of treatment delay in patients with ST-elevation myocardial infarction: impact of pre-hospital diagnosis and direct referral to primary percutaneous coronary intervention. *Eur Heart J* 2005; **26**(8):770-7.
- 17 Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet* 2006; **367**:569-78.
- 18 Guagliumi G, Stone GW, Cox DA, et al. Outcome in elderly patients undergoing primary coronary intervention for acute myocardial infarction: results from the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial. *Circulation* 2004; **110**:1598-604.