



Original article

Impact of transport pathways on the time from symptom onset of ST-segment elevation myocardial infarction to door of coronary intervention facility



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ABSTRACT

Background: Reducing total ischemic time is important in achieving better outcome in ST-segment elevation myocardial infarction (STEMI). Although the onset-to-door (OTD) time accounts for a large portion of the total ischemic time, factors affecting prolongation of the OTD time are not established.

Purpose: The purpose of this study was to determine the impact of transport pathways on OTD time in patients with STEMI.

Methods and subjects: We retrospectively studied 416 STEMI patients who were divided into 4 groups according to their transport pathways; Group 1 ($n=41$): self-transportation to percutaneous coronary intervention (PCI) facility; Group 2 ($n=215$): emergency medical service (EMS) transportation to PCI facility; Group 3 ($n=103$): self-transportation to non-PCI facility; and Group 4 ($n=57$): EMS transportation to non-PCI facility. OTD time was compared among the 4 groups.

Essential results: Median OTD time for all groups combined was 113 (63–228.8) min [Group 1, 145 (70–256.5); Group 2, 71 (49–108); Group 3, 260 (142–433); and Group 4, 184 (130–256) min]. OTD time for EMS users (Groups 2 and 4) was 138 min shorter than non-EMS users (Groups 1 and 3). Inter-hospital transportation (Groups 3 and 4) prolonged OTD by a median of 132 min compared with direct transportation to PCI facility (Groups 1 and 2). Older age, history of myocardial infarction, prior PCI, shock at onset, high Killip classification, and high GRACE Risk Score were significantly more frequent in EMS users.

Principal conclusions: Self-transportation without EMS and inter-hospital transportation were significant factors causing prolongation of the OTD time. Approximately 35% of STEMI patients did not use EMS and 21% of patients were transported to non-PCI facilities even though they called EMS. Awareness in the community as well as among medical professionals to reduce total ischemic time of STEMI is necessary; this involves educating the general public and EMS crews.

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Introduction

ST-segment elevation myocardial infarction (STEMI) is a life-threatening disease necessitating immediate revascularization, since one third of patients die within the first 24 h after the onset of symptoms. Notably, STEMI has fatal complications within the first 1–2 h of onset [1,2]. Prompt restoration of the coronary flow has a valuable role in reduction of the size of infarcted tissue in

the myocardium and improvement in patient mortality [3–10]. Therefore, primary percutaneous coronary intervention (PCI) in acute coronary syndrome is recommended to be performed within 90 min between entering the door of PCI facilities and balloon inflation (DTB) [2].

The time from symptom onset to door of PCI facility (OTD) is noteworthy since the OTD time accounts for the greatest percentage of total ischemic duration [11,12]. A decrease in OTD time may be key to prevent sudden death in the acute phase or improvement of medium or long-term mortality by shortening the total ischemic time.

STEMI patients who experience acute symptoms visit a PCI facility through various transport pathways. Patients may visit a PCI facility directly by themselves or with an ambulance; alternatively,

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they may arrive at a PCI facility indirectly after first arriving at a non-PCI facility. Differences in the transit time between these routes to a PCI facility have a major impact on OTD [13–16].

In this study we determined the impact of the transport pathways on the OTD time in STEMI patients.

Materials and methods

Study population and study protocol

We retrospectively studied the medical records of 416 consecutive STEMI patients, who visited Tokai University School of Medicine within 24 h of the onset of symptoms from December 2005 to March 2011. Patients who developed onset symptoms of STEMI in the hospital were excluded from this study.

A total of 416 patients were enrolled. Patients were divided into 4 groups according to their transport pathways from onset of symptoms to the PCI facility at Tokai University School of Medicine, a tertiary hospital performing primary PCI: Group 1 (self to PCI), patients who transported themselves to the PCI facility directly; Group 2 (EMS to PCI), patients who were transported to the PCI facility directly by ambulance or helicopter emergency medical service (EMS); Group 3 (self to non-PCI), patients who transported themselves to a referral hospital without a PCI facility, from where they were transported to the PCI facility through inter-hospital transportation; and Group 4 (EMS to non-PCI), patients who were transported to a referral hospital by EMS, and then they were transported to the PCI facility through inter-hospital transportation (Fig. 1). The impact of the time difference in transport pathways, which is derived from EMS use or inter-hospital transportation, on OTD was assessed by comparing OTD and onset to first medical contact (OTF) among the 4 groups.

Definitions

Among patients who visited non-PCI facilities or PCI facilities due to acute onset and presented with electrocardiogram findings

consistent with STEMI, i.e. persistent ST-segment elevation > 1 mm in two contiguous leads, or new or presumed new left bundle branch block. Those with confirmed STEMI by emergency coronary angiography were enrolled [17].

All enrolled patients were evaluated for the time-points of “Onset”, “FMC”, “Arrival at first-visit-hospital”, and “Arrival at PCI facility door”. “Onset” was defined as the time-point when patients experienced acute symptoms of STEMI. “FMC” was defined as the time of first contact with any medical staff including EMS crews, this being the time of arrival at PCI facility in Group 1, the time of contact with EMS in Groups 2 and 4, and the time of arrival at the referral hospital in Group 3. “Arrival at first-visit-hospital” was defined as the time of arrival at the first-visit-hospital, PCI facility, or non-PCI facility (referral facility). The first-visit-hospital is the PCI facility in Groups 1 and 2, and the non-PCI facility (referral facility) in Groups 3 and 4. “Arrival at PCI facility door” was defined as the time of arrival at the PCI facility. Each of the following time intervals was calculated from the time records. “OTF” is the interval between “onset” and “FMC”. “OTD” is the interval between symptom onset and arrival at the PCI facility door (Fig. 1).

Statistical analysis

Numerical factors with skewed distribution are shown as median (interquartile range). Wilcoxon rank-sum test was used to determine statistically significant differences in clinical parameters between two different groups. Kruskal-Wallis one-way analysis of variance was used to compare more than three groups. If Kruskal-Wallis one-way analysis of variance showed a significant difference, differences between individual groups were estimated using Steel–Dwass multiple comparison. Fisher’s exact test was applied to determine the difference between categorical variables.

Stepwise regression analysis was used in multivariable analysis. For selection of variables, a forward stepwise selection procedure was adopted in stepwise regression analysis to identify factors associated with OTD. The variable entered in the stepwise model was the variable that had the smallest p -value > 0.2. The analysis was stopped when no more variables could be justifiably entered from the stepwise model. Independent variable with multicollinearity for which the variance inflation factor was more than 10 between either variable was excluded. If the variance inflation factor between 2 or more independent variables was more than 10, these were regarded as multicollinear variables, and only one variable among them was used in stepwise regression analysis as the representative variable. OTD with skewed distribution was transformed into normally distributed model by raising to the 0.2th power.

A value of $p < 0.05$ was considered statistically significant. All statistical calculations were performed using JMP version 9 (SAS Institute, Inc., Cary, NC, USA).

Results

The percentage of enrolled patients in each group was as follows: Group 1, 9.9%; Group 2, 51.7%; Group 3, 24.8%; and Group 4, 13.7% (Fig. 2). Usage of EMS (Groups 2 and 4) accounted for 65.4% of the total, and patients who were transported from the referral hospital (Groups 3 and 4) accounted for 38.5%.

Baseline characteristics and clinical status on arrival at PCI facilities of all 416 enrolled patients are shown in Tables 1 and 2, respectively. Median age was 66 (57–76) years and 79.1% of patients were male. The differences between groups were shown in age, dyslipidemia, renal function, and brain natriuretic peptide on arrival. More critical patients with shock, high Killip classification, and high GRACE score were frequent in EMS users (Groups 2 and 4).

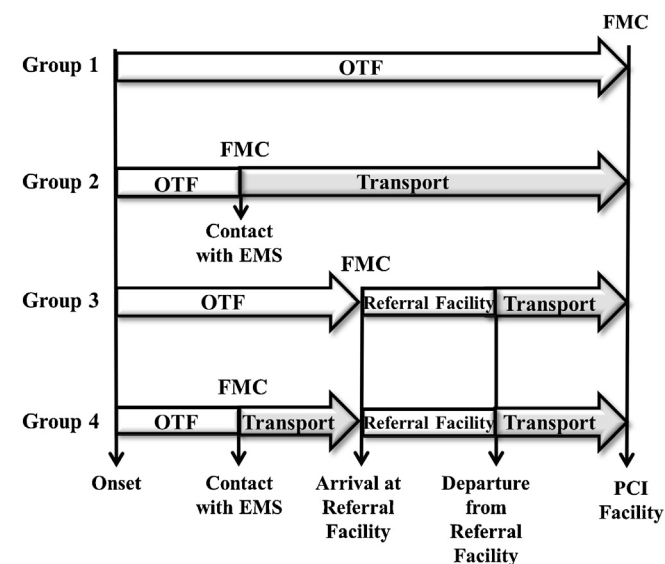


Fig. 1. The pathways to PCI facility. Group 1: Patients who themselves visited a PCI facility directly. Group 2: Patients who called the EMS, and then they were transported to PCI facility directly by EMS. Group 3: Patients who themselves visited a referral hospital by, and then they were transported to PCI facility through the inter-hospital transportation. Group 4: Patients who were transported to a referral hospital by EMS, and then they were transported to a PCI facility through the inter-hospital transportation. PCI, percutaneous coronary intervention; OTF, onset to first medical contact; FMC, first medical contact; EMS, emergency medical service.

	PCI Facility	Non PCI Facility	
Self Transporters	Group 1 n=41 (9.9%)	Group 3 n=103 (24.8%)	n=144 (34.6%)
EMS Transporters	Group 2 n=215 (51.7%)	Group 4 n=57 (13.7%)	n=272 (65.4%)
	n=256 (61.5%)	n=160 (38.5%)	

Fig. 2. Contingency table by transportation pathways. PCI, percutaneous coronary intervention.

Table 1
Baseline characteristics.

	All (n = 416)	Group 1 Self to PCI (n = 41)	Group 2 EMS to PCI (n = 215)	Group 3 Self to non-PCI (n = 103)	Group 4 EMS to non-PCI (n = 57)	p-Value
Age (years)	66 (57–76)	65 (56–73)	66 (59–76)	64 (52–74)	70 (61.5–81.5)	0.009
Male (n)	329 (79.1%)	33 (80.5%)	173 (80.5%)	79 (76.7%)	44 (77.2%)	0.855
Height (cm)	164 (157–168.1)	165 (159–169)	164 (157.2–168)	165 (157–170)	162.5 (155.4–167.5)	0.495
Weight (kg)	63 (55–72)	62.6 (54.8–71.5)	64 (55.5–71)	64 (55–74)	59 (50–65)	0.040
Current smoking (n)	274 (65.9%)	27 (65.9%)	147 (68.4%)	66 (64.1%)	34 (59.6%)	0.934
DM (n)	156 (37.5%)	19 (46.4%)	78 (36.3%)	38 (36.9%)	21 (36.8%)	0.285
Diet	91 (21.9%)	15 (36.6%)	41 (19.1%)	19 (18.4%)	16 (28.1%)	0.210
Medication	43 (10.3%)	2 (4.9%)	25 (11.6%)	13 (12.6%)	3 (5.3%)	
Insulin	22 (5.3%)	2 (4.9%)	12 (5.6%)	6 (5.8%)	2 (3.5%)	
Dyslipidemia (n)	294 (70.7%)	34 (82.9%)	159 (74.0%)	74 (71.84%)	27 (47.4%)	<0.001
Hypertension (n)	338 (81.3%)	35 (85.4%)	174 (80.9%)	83 (80.6%)	46 (80.7%)	0.916
Family history of MI (n)	65 (15.6%)	7 (17.1%)	33 (15.4%)	18 (17.5%)	7 (12.3%)	0.843
Old MI (n)	48 (11.5%)	1 (2.4%)	33 (15.4%)	4 (3.9%)	10 (15.7%)	0.049
Prior PCI (n)	48 (11.5%)	3 (7.3%)	28 (11.6%)	4 (3.9%)	4 (7.0%)	0.055
Prior CABG (n)	2 (0.5%)	0	2 (0.9%)	0	0	0.598
Prior stroke (n)	52 (12.5%)	5 (12.2%)	22 (10.2%)	14 (13.6%)	11 (19.3%)	0.316
Hemodialysis (n)	10 (2.40%)	1 (2.4%)	4 (1.9%)	2 (1.9%)	3 (5.3%)	0.664
DM	5 (1.2%)	1 (2.4%)	2 (0.9%)	1 (0.9%)	1 (1.8%)	0.721
Non-DM	5 (1.2%)	0	2 (0.9%)	1 (0.9%)	2 (1.8%)	
Hemoglobin (mg/dL)	14.3 (12.9–15.7)	14.6 (13.1–16.1)	14.4 (12.9–15.7)	14.4 (13.3–15.8)	13.7 (12–14.8)	0.050
Total cholesterol (mg/dL)	189 (160–222.3)	200.5 (175.3–230.8)	184 (159–219)	195.5 (161–225.3)	178 (157–206)	0.089
Triglyceride (mg/dL)	87 (53–145)	120 (91–161)	86 (51–155)	81.5 (54.5–137.3)	65 (46–106)	0.001
Serum Cr (mg/dL)	0.9 (0.7–1.1)	0.8 (0.7–1)	0.9 (0.8–1.2)	0.8 (0.7–1.0)	0.8 (0.7–1.4)	0.009
eGFR (ml/min/1.73 m ²)	64.6 (50.0–79.2)	66.8 (52.9–85.8)	61.4 (47.5–74.7)	70.0 (59.4–81.5)	65.4 (35.5–81.3)	0.004
BNP (pg/ml)	73 (24.6–232)	89.6 (23.4–337)	52.5 (18.1–178.7)	107.6 (32.8–235.9)	89.9 (30.8–423)	0.006

EMS, emergency medical service; PCI, percutaneous coronary intervention; DM, diabetes mellitus; MI, myocardial infarction; CABG, coronary artery bypass grafting; eGFR, estimated glomerular filtration rate; BNP, brain natriuretic peptide.

Table 2
Clinical status on arrival.

	All (n = 416)	Group 1 Self to PCI (n = 41)	Group 2 EMS to PCI (n = 215)	Group 3 Self to non-PCI (n = 103)	Group 4 EMS to non-PCI (n = 57)	p-Value
Symptom at onset (n)						
Chest pain	348 (83.7%)	38 (92.7%)	168 (78.1%)	98 (95.1%)	44 (77.2%)	<0.001
Syncope/disturbed consciousness	24 (5.8%)	0	21 (9.8%)	1 (0.9%)	2 (3.5%)	0.003
Dyspnea	22 (5.3%)	2 (4.9%)	13 (6.1%)	0	7 (12.28%)	0.009
Nausea/vomiting	16 (3.8%)	1 (2.4%)	10 (4.7%)	3 (2.9%)	2 (3.5%)	0.836
Cardiopulmonary arrest	8 (1.9%)	0	6 (2.8%)	0	2 (3.5%)	0.218
Others	1 (0.2%)	0	0	0	1 (1.75%)	0.236
Systolic blood pressure (mmHg)	130 (108.3–150)	142 (120.5–162.5)	124 (100–150)	138 (120–160)	130 (108.5–146.5)	<0.001
Diastolic blood pressure (mmHg)	80 (60–90)	84 (71–98)	72 (52–90)	80 (70–94)	74 (59.5–90)	<0.001
Shock on arrival (n)	81 (19.5%)	4 (9.8%)	54 (25.1%)	10 (9.7%)	13 (22.8%)	0.004
Heart rate (beats/min)	76 (61–92)	79 (64.5–93)	71 (56–89)	80 (70–92)	82 (68.5–100.5)	0.003
Killip classification (n)						
Killip I	197 (47.4%)	27 (65.9%)	95 (44.2%)	60 (58.3%)	15 (26.3%)	<0.001
Killip II	96 (23.1%)	8 (19.5%)	45 (20.9%)	28 (27.2%)	15 (26.3%)	
Killip III	42 (10.1%)	2 (4.9%)	21 (9.8%)	5 (4.9%)	14 (24.6%)	
Killip IV	81 (19.5%)	4 (9.8%)	54 (25.1%)	10 (9.7%)	13 (22.8%)	
GRACE Risk Score	165 (132.3–203)	145 (123.5–167.5)	170 (144–209)	150 (123–182)	200 (163–235)	<0.001

EMS, emergency medical service; PCI, percutaneous coronary intervention.

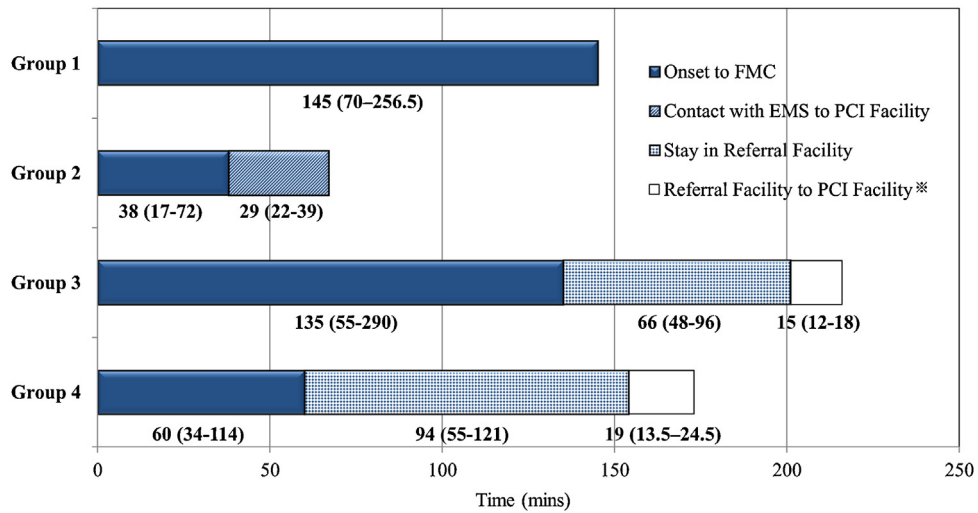


Fig. 3. Time from symptom onset to PCI facility door among the 4 groups. Comparison of time from symptom onset to PCI facility door (OTD) among the 4 groups is presented. Median time from onset to first medical contact (OTF) was 60.0 min, and mean OTF was 127.6 min. Median time of onset to door (OTD) was 113.5 min and mean time was 186.5 min. Patients who achieved OTF within 30 min accounted for 28.8% of the total, within 60 min 57.4%, and within 90 min 62.7%. Group 2 had significantly shorter OTD than the other 3 groups ($p < 0.01$). Groups 1 and 4 had significantly shorter OTD time than Group 3 ($p < 0.01$), but there were no significant differences between Groups 1 and 4. **Stay in Referral Facility” in Group 4 includes the transportation time of first medical contact to referral facility.

Overall for all groups combined, median and mean OTF were 60.0 (28.3–150) and 127.6 min, respectively, and median and mean OTD were 113.5 (63–228.8) and 186.5 min, respectively. A comparison of OTD and the components of OTD among the 4 groups are demonstrated in Fig. 3. The percentage of OTF relative to OTD in Groups 1 (self to PCI), 2 (EMS to PCI), 3 (self to non-PCI), and 4 (EMS to non-PCI) was 100%, 56.7%, 62.5%, and 34.7%, respectively. Group 2 had the shortest OTD time compared with the other groups ($p < 0.01$), and Groups 1 and 4 had shorter OTD time than Group 3 ($p < 0.01$). The difference between Groups 1 and 4 was not statistically significant. This similarity is regarded as inter-hospital transportation offset the EMS advantage in reducing the time delay of transit to PCI.

Fig. 4 shows a comparison of OTF and OTD among the 4 groups. Groups 2 and 4 had shorter OTF than Groups 1 and 3 [38 (17–72) and 60 (34–114) min, respectively, vs. 145 (70–256.5) and 135

(55–290) min, respectively; $p < 0.01$ for both], Group 2 had the shortest OTD compared with the other 3 groups [71 (49–108) min vs. 145 (70–256.5) [Group 1] vs. 260 (142–433) [Groups 3], and 184 (130–256) min [Group 4]; $p < 0.01$, respectively].

OTF time of EMS users (Groups 2 and 4) was significantly shorter (98.5 min) than self-transporters (Groups 1 and 3) (41.5 min vs. 140 min; $p < 0.01$, Fig. 5). OTD time was also significantly shorter in these groups (84.5 min vs. 222.5 min, $p < 0.01$). EMS users had 138 min shorter OTD than self-transporters. For patients with inter-hospital transportation (Groups 3 and 4) median OTD time was 207 (130.8–349.5) min and for direct transportation patients (Groups 1 and 2) it was 75.5 (51.3–135) min ($p < 0.01$), a median OTD time delay of approximately 132 min. Table 3 shows a comparison of baseline characteristics between EMS users and self-transporters. Older age, history of myocardial infarction, and prior PCI were significantly more frequent in EMS users. At onset of symptoms,

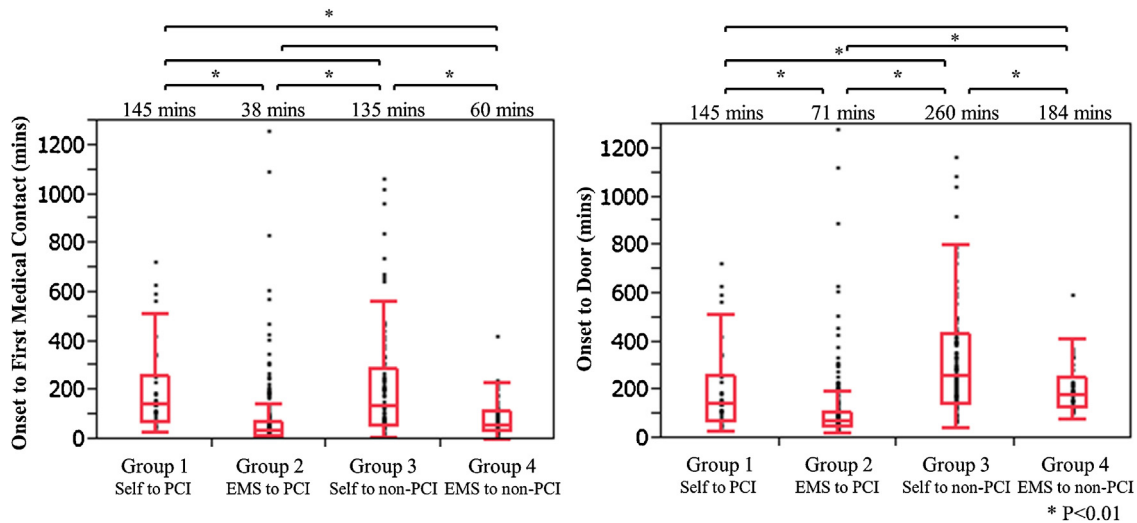


Fig. 4. Comparison of OTF and OTD among the 4 Groups. Left panel shows a comparison of onset to first medical contact (OTF) among the 4 groups. Groups 2 and 4, i.e. EMS users, had shorter OTF time than Groups 1 and 3, i.e. the self-transporters. There were no significant differences between Groups 2 and 4, or between Groups 1 and 3. Although the order of increase in symptom onset to PCI facility door (OTD) of the groups was similar to the order of increase in OTF of the groups (Group 3 > Group 1 > Group 4 > Group 2), inter-hospital transportation caused a significant delay in OTD compared with direct transportation (right panel). Thus, inter-hospital transportation resulted in Group 2 having the shortest OTD, and Group 3 the longest OTD. PCI, percutaneous coronary intervention; EMS, emergency medical service. * $P < 0.01$

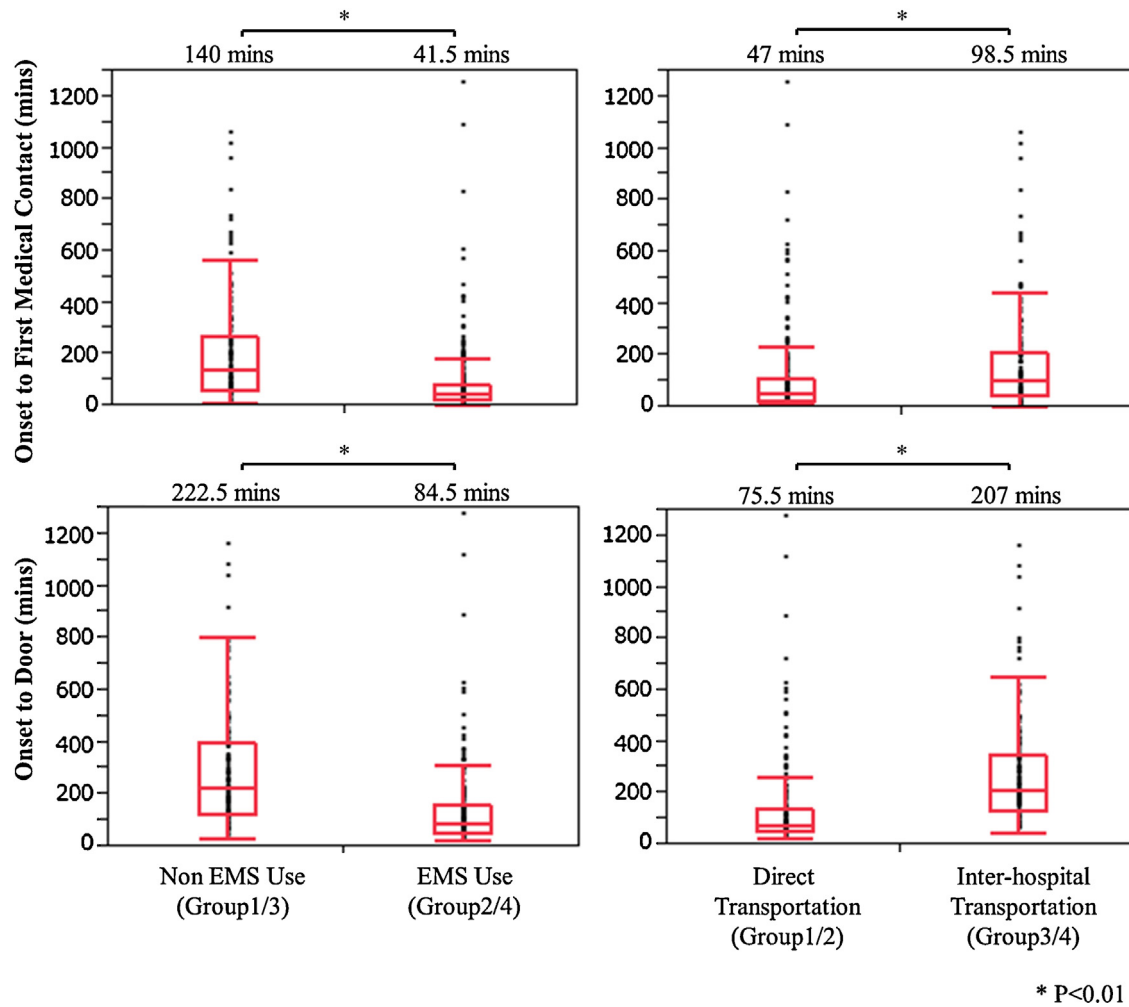


Fig. 5. Comparison of OTF and OTD in EMS users or non-EMS users with and without inter-hospital transportation. The left upper panel shows a comparison of onset to first medical contact (OTF) time between self-transporters (Groups 1 and 3) and EMS users (Groups 2 and 4). EMS users had on 98.5 min shorter OTF than self-transporters and the difference was statistically significant. Similarly, onset to door (OTD) was on 138 min shorter in EMS users and the difference was statistically significant (left lower panel). The right upper panel shows a comparison of OTF time between direct transporters and inter-hospital transporters. Direct transporters had 51.5 min shorter OTF than inter-hospital transporters and the difference was statistically significant. Similarly, OTD was 131.5 min shorter in direct transporters and the difference was statistically significant (right lower panel). EMS, emergency medical service.

syncope and disturbed consciousness were significantly more frequent in EMS users, while chest pain was significantly more frequent in non-EMS users. Patients with severe symptoms such as shock at onset, high Killip classification, and high GRACE Risk Score were significantly more frequent in EMS users.

Table 4 shows the comparison of EMS users between transportation to PCI facility (Group 2) and non-PCI facility (Group 4). This comparison could not show the factors that EMS crews used to judge that STEMI patients were transported to a non-PCI facility.

Stepwise regression analysis was performed to extract the clinical factors associated with OTD. Gender, age, prior PCI, hemodialysis, syncope/disturbed consciousness at onset, cardiopulmonary arrest at onset, and shock on arrival were included as independent variables. Prior PCI ($\beta -0.138$, 95%CI -42.7 to -8.4 , $p < 0.01$), syncope/disturbed consciousness at onset ($\beta -0.190$, 95%CI -65.9 to -21.7 , $p < 0.01$), cardiopulmonary arrest at onset ($\beta -0.100$, 95%CI -76.3 to -1.9 , $p = 0.03$), and shock on arrival ($\beta -0.113$, 95%CI -28.6 to -2.0 , $p = 0.02$) were extracted as contributing factors to OTD.

Thirty days all-cause mortality was 8.9% of all 414 patients [4.9% (Group 1), 13.0% (Group 2), 1.9% (Group 3), and 8.8% (Group 4); $p < 0.01$, respectively].

Discussion

This study suggested two factors that were significant in causing delay in OTD time in patients with STEMI. One was patient self-transportation without EMS use and the other was transportation to a non-PCI facility. This suggests that EMS transportation may lose its advantage of saving time by transporting to a non-PCI facility, not to a PCI facility.

The American College of Cardiologists/American Heart Association guidelines recommend that DTB for primary PCI should be less than 90 min in STEMI [2]. In fact, however, the OTD time accounts for the greater proportion of the total ischemic time rather than DTB time [11,18], and sudden cardiac death due to myocardial infarction frequently occurs in the first 1–2 h after the onset of symptoms. Therefore, shortening the OTD time is the most important factor to reduce total ischemic time and to improve mortality of STEMI patients. We need to eliminate the causes of delay in OTD time.

Our data showed the possibility that the EMS transportation made OTD time significantly shorter. EMS users had similar characteristics as reported in previous studies, such as high proportion of older age and a more critical condition (higher Killip scores, low blood pressure, shock, and higher GRACE risk scores) than self-transporters [14,15,19,20]. Patients with possible critical

Table 3
Comparison between EMS use and patient-self transportation.

	EMS use (n = 272)	Patient-self transportation (n = 144)	p-Value
Age (years)	67 (59–77)	65 (54–74)	0.009
Male (n)	217 (79.8%)	102 (70.8%)	0.051
Old MI (n)	43 (15.8%)	5 (3.5%)	<0.001
Prior PCI (n)	32 (11.8%)	7 (4.9%)	0.022
Prior CABG (n)	2 (0.7%)	0	0.546
Prior stroke (n)	33 (12.1%)	19 (13.2%)	0.757
Hemodialysis (n)	7 (2.6%)	3 (2.1%)	1.0
BNP (pg/ml)	59.1 (21.6–206)	101.2 (32.1–245.9)	0.674
Symptom at onset (n)			
Chest pain	212 (77.9%)	136 (94.4%)	<0.001
Syncope/disturbed consciousness	23 (8.5%)	1 (0.7%)	0.001
Dyspnea	20 (7.4%)	2 (1.4%)	0.010
Nausea/vomiting	12 (4.4%)	4 (2.8%)	0.410
Cardiopulmonary arrest	8 (2.9%)	0	0.055
Systolic blood pressure (mmHg)	126.5 (100–149.5)	140 (120–160)	<0.001
Diastolic blood pressure (mmHg)	72 (56–90)	80 (70–95.5)	<0.001
Shock on arrival (n)	67 (24.6%)	14 (9.7%)	<0.001
Heart rate (beats/min)	75 (58–91)	80 (68–92)	0.050
Killip classification (n)			
Killip I	110 (40.4%)	87 (60.4%)	<0.001
Killip II	60 (22.1%)	36 (25.0%)	
Killip III	35 (12.9%)	7 (4.9%)	
Killip IV	67 (24.6%)	14 (9.7%)	
GRACE Risk Score	176 (146–219)	147 (123.3–179)	<0.001

EMS, emergency medical service; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; BNP, brain natriuretic peptide.

symptoms, such as syncope, disturbed consciousness and dyspnea were frequently transported by EMS probably because bystanders can recognize the critical situation of these patients. By contrast, patients with chest pain as the initial symptom had a tendency not to call EMS. This may indicate that people in general are not aware of life-saving effects of prompt reperfusion in STEMI. On the other hand, patients with chest pain who had experienced prior myocardial infarction or prior PCI frequently used EMS. This suggests that these patients are likely to have knowledge of STEMI because of the prior experience of PCI. Education of the public about the natural course of STEMI and the role of primary PCI may be important. While some reports showed that males have a higher rate of EMS

use, our data did not show a significant gender difference in EMS use [19,21].

Patients who were transported to the PCI facility through inter-hospital transportation who visited a non-PCI facility as the first-visit-hospital (Groups 3 and 4), had 132 min of delay in the OTD time compared with patients who visited a PCI facility first (Groups 1 and 2) [20,22]. Moreover, Group 4 patients who were transported to non-PCI facilities despite calling EMS had a similar OTD time to Group 1 with self-transportation. This result suggests the possibility that EMS transportation to non-PCI facility loses the advantage of saving time by EMS. Thus, transport by EMS directly to a PCI facility (Group 2) is regarded as an ideal pre-hospital

Table 4
Comparison between EMS users.

	Group 2 EMS to PCI (n = 215)	Group 4 EMS to non-PCI (n = 57)	p-Value
Age (years)	66 (59–76)	70 (61.5–81.5)	0.1268
Male (n)	173 (80.5%)	44 (77.2%)	0.5479
Prior PCI (n)	28 (11.6%)	4 (7.0%)	0.2761
Prior CABG (n)	2 (0.9%)	0	1.0000
Prior stroke (n)	22 (10.2%)	11 (19.3%)	0.5486
Hemodialysis (n)	4 (1.9%)	3 (5.3%)	0.0728
Symptom at onset (n)			
Chest pain	168 (78.1%)	44 (77.2%)	0.1574
Syncope/disturbed consciousness	21 (9.8%)	2 (3.5%)	
Dyspnea	13 (6.1%)	7 (12.3%)	
Nausea/vomiting	10 (4.7%)	2 (3.5%)	
Cardiopulmonary arrest	6 (2.8%)	2 (3.5%)	
Others	0	1 (1.8%)	
Systolic blood pressure (mmHg)	124 (100–150)	130 (108.5–146.5)	0.6074
Diastolic blood pressure (mmHg)	72 (52–90)	74 (59.5–90)	0.8466
Shock on arrival (n)	54 (25.1%)	13 (22.8%)	0.8052
Heart rate (beats/min)	71 (56–89)	82 (68.5–100.5)	0.0644
Killip classification (n)			
Killip I	95 (44.2%)	15 (26.3%)	0.5763
Killip II	45 (20.9%)	15 (26.3%)	
Killip III	21 (9.8%)	14 (24.6%)	
Killip IV	54 (25.1%)	13 (22.8%)	
GRACE Risk Score	170 (144–209)	200 (163–235)	0.1318

EMS, emergency medical service; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

transportation. However, Group 2 comprised only 51.7% of the total because 34.6% of STEMI patients (Groups 1 and 3) did not use EMS and 21.0% of patients were transported to non-PCI facilities even though they called EMS. These results suggest the possibility that education aimed at reduction of these errors in judgment can have a major impact on improvement in OTD time and has a possibility to reduce the rate of sudden cardiac death. The target population of this education is not only the general public but also all pre-hospital providers.

Of note, prior studies have shown controversial results on the relationship between OTD and STEMI patients' mortality. Some studies failed to show an improvement in mortality despite the shorter OTD time [4–6,14,22,23]. There is a critical bias that EMS users would be more critical patients than non-EMS users [4,14,22,24–27]. The other reason is that OTD time does not always reflect total ischemic time. In some cases, occluded culprit arteries may spontaneously and repeatedly recanalize and re-occlude with changing severity of symptoms. Thus, the time from symptom onset to reperfusion is not equal to the actual ischemic time. Furthermore, it is difficult to identify with certainty the time of symptom onset in patients with floating symptoms [4,5]. Despite these prior paradoxical data, efforts to shorten the total ischemic time for STEMI patients could improve overall mortality rate. To achieve more prompt and accurate triage, various novel approaches such as pre-hospital electrocardiogram or pre-hospital troponin T testing have been attempted and their effects reported [28–35].

There are major limitations with this study as this is a retrospective study. Since this study did not include patients with sudden death caused by myocardial infarction before being confirmed by emergency coronary angiography, it might cause a gap with the real world. This study did not include the data about individual social background, personal physicians, or family structure. These factors might contribute to OTD. Though the initial treatment in a non-PCI facility is thought to contribute to OTD, the present study did not include these data. Thirty day mortality was higher in EMS users with short OTD. The reason might come from the fact that critical patients have shorter OTD and high frequency of EMS use. However, it was difficult to exclude these biases statistically. The present study is underpowered to draw the superiority of shorter OTD because of the small sample size of 30 days death. The present study did not include non-STEMI or unstable angina. These diseases have different characteristics from STEMI in respect to symptom onset or clinical course. If the present study had included these diseases, it might have led to different results.

In conclusion, this study suggested that EMS use makes OTD time shorter and inter-hospital transport makes it longer. Attempts should be made to educate the general public to call the EMS immediately when they observe the suspected symptoms of acute coronary syndrome in a patient, and educate EMS crews to exercise proper judgment in transporting the patients to a PCI facility.

References

- Boersma E, Mercado N, Poldermans D, Gardien M, Vos J, Simoons ML. Acute myocardial infarction. *Lancet* 2003;361:847–58.
- Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith Jr SC, 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:e82–292.
- Cannon CP. Time to treatment: a crucial factor in thrombolysis and primary angioplasty. *J Thromb Thrombolysis* 1996;3:249–55.
- Berger PB, Ellis SG, Holmes Jr DR, Granger CB, Criger DA, Betriu A, Topol EJ, Califf RM. Relationship between delay in performing direct coronary angioplasty and early clinical outcome in patients with acute myocardial infarction: results from the global use of strategies to open occluded arteries in Acute Coronary Syndromes (GUSTO-IIb) trial. *Circulation* 1999;100:14–20.
- Cannon CP, Gibson CM, Lambrew CT, Shoultz DA, Levy D, French WJ, Gore JM, Weaver WD, Rogers WJ, Tiefenbrunn AJ. Relationship of symptom-onset-to-balloon time and door-to-balloon time with mortality in patients undergoing angioplasty for acute myocardial infarction. *JAMA* 2000;283:2941–7.
- De Luca G, Suryapranata H, Zijlstra F, van't Hof AW, Hoorntje JC, Gosselink AT, Dambink JH, de Boer MJ, ZWOLLE Myocardial Infarction Study Group. Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. *J Am Coll Cardiol* 2003;42:991–7.
- Nallamothu BK, Bates ER. Percutaneous coronary intervention versus fibrinolytic therapy in acute myocardial infarction: is timing (almost) everything. *Am J Cardiol* 2003;92:824–6.
- De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. *Circulation* 2004;109:1223–5.
- Trzos E, Kurpesa M, Bednarkiewicz Z, Peruga J, Kasprzak J, Plewka M, Uznańska B, Krzemińska-Pakuła M. Impact of the time to reperfusion on early outcomes in patients with acute myocardial infarction undergoing primary angioplasty. *Kardiol Pol* 2007;65:1296–304.
- Kajija T, Agahari F, Wai KL, Tai BC, Lee CH, Chan KH, Teo SG, Richards AM, Tan HC, Low AF, Chan MY. A single-center experience of transitioning from a routine transfemoral to a transradial intervention approach in ST-elevation myocardial infarction: impact on door-to-balloon time and clinical outcomes. *J Cardiol* 2013;62:12–7.
- Luepker RV, Raczynski JM, Osganian S, Goldberg RJ, Finnegan Jr JR, Hedges JR, Goff Jr DC, Eisenberg MS, Zapka JG, Feldman HA, Labarthe DR, McGovern PG, Cornell CE, Proschan MA, Simons-Morton DG. Effect of a community intervention on patient delay and emergency medical service use in acute coronary heart disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. *JAMA* 2000;284:60–7.
- Nomura T, Tatsumi T, Sawada T, Kojima A, Urakabe Y, Enomoto-Uemura S, Nishikawa S, Keira N, Nakamura T, Matoba S, Yamada H, Matsumuro A, Shirayama T, Shiraishi J, Kohno Y, et al. Clinical manifestations and effects of primary percutaneous coronary intervention for patients with delayed pre-hospital time in acute myocardial infarction. *J Cardiol* 2010;56:204–10.
- Cabrita B, Bouyer-Daloz F, L'Huillier I, Dentan G, Zeller M, Laurent Y, Bril A, Jolak M, Janin-Manificat L, Beer JC, Yeguiayan JM, Cottin Y, Wolf JE, Freysz M. Beneficial effects of direct call to emergency medical services in acute myocardial infarction. *Eur J Emerg Med* 2004;11:12–8.
- So DY, Ha AC, Turek MA, Maloney JP, Higginson LA, Davies RF, Ryan S, Le May MR. Comparison of mortality patterns in patients with ST-elevation myocardial infarction arriving by emergency medical services versus self-transport (from the prospective Ottawa Hospital STEMI Registry). *Am J Cardiol* 2006;97:458–61.
- Song L, Hu DY, Yan HB, Yang JG, Sun YH, Li C, Liu SS, Wu D, Feng Q. Influence of ambulance use on early reperfusion therapies for acute myocardial infarction. *Chin Med J (Engl)* 2008;121:771–5.
- Clark CL, Berman AD, McHugh A, Roe EJ, Boura J, Swor RA. Hospital process intervals, not EMS time intervals, are the most important predictors of rapid reperfusion in EMS Patients with ST-segment elevation myocardial infarction. *Prehosp Emerg Care* 2012;16:115–20.
- Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Joint ESC/ACC/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, et al. Third universal definition of myocardial infarction. *Circulation* 2012;126:2020–35.
- Nakamura M, Yamagishi M, Ueno T, Hara K, Ishiwata S, Itoh T, Hamanaka I, Wakatsuki T, Sugano T, Kawai K, Kimura T. Current treatment of ST elevation acute myocardial infarction in Japan: door-to-balloon time and total ischemic time from the J-AMI registry. *Cardiovasc Interv Ther* 2013;28:30–6.
- Canto JG, Zalenski RJ, Ornato JP, Rogers WJ, Kiefe CI, Magid D, Shlipak MG, Frederick PD, Lambrew CG, Littrell KA, Barron HV, National Registry of Myocardial Infarction 2 Investigators. Use of emergency medical services in acute myocardial infarction and subsequent quality of care: observations from the National Registry of Myocardial Infarction 2. *Circulation* 2002;106:3018–23.
- Rodriguez-Leor O, Fernandez-Nofrerias E, Mauri F, Salvatella N, Carrillo X, Curós A, Serra J, Valle V, Bayes-Genis A. Analysis of reperfusion delay in patients with acute myocardial infarction treated with primary angioplasty based on first medical contact and time of presentation. *Rev Esp Cardiol* 2011;64:476–83.
- Zimmermann S, Ruthrof S, Nowak K, Alff A, Klinghammer L, Schneider R, Ludwig J, Pfahler AB, Daniel WG, Flachskampf FA. Short-term prognosis of contemporary interventional therapy of ST-elevation myocardial infarction: does gender matter. *Clin Res Cardiol* 2009;98:709–15.
- Brodie BR, Stuckey TD, Hansen CJ, VerSteeg D, Muncy D, Pulsipher M, Gupta N. Effect of treatment delay on outcomes in patients with acute myocardial infarction transferred from community hospitals for primary percutaneous coronary intervention. *Am J Cardiol* 2002;89:1243–7.
- Kruthkul K, Srimahachota S, Udayachalerm W, Budhari W, Charipromprasit J, Suithichayakul T, Sitthi-amorn C. Importance of delayed perfusion with primary angioplasty on short-term mortality in acute myocardial infarction patients. *J Med Assoc Thai* 2007;90:2587–96.
- Henry TD, Sharkey SW, Burke MN, Chavez IJ, Graham KJ, Henry CR, Lips DL, Madison JD, Messen KM, Mooney MR, Newell MC, Pedersen WR, Poulouse AK, Traverse JH, Unger BT, et al. A regional system to provide timely access

- to percutaneous coronary intervention for ST-elevation myocardial infarction. *Circulation* 2007;116:721–8.
- [25] Manari A, Ortolani P, Guastaroba P, Casella G, Vignali L, Varani E, Piovaccari G, Guiducci V, Percoco G, Tondi S, Passerini F, Santarelli A, Marzocchi A. Clinical impact of an inter-hospital transfer strategy in patients with ST-elevation myocardial infarction undergoing primary angioplasty: the Emilia-Romagna ST-segment elevation acute myocardial infarction network. *Eur Heart J* 2008;29:1834–42.
- [26] Brooks SC, Allan KS, Welsford M, Verbeek PR, Arntz HR, Morrison LJ. Prehospital triage and direct transport of patients with ST-elevation myocardial infarction to primary percutaneous coronary intervention centres: a systematic review and meta-analysis. *CJEM* 2009;11:481–92.
- [27] Wohrle J, Desaga M, Metzger C, Huber K, Suryapranata H, Guetta V, Guagliumi G, Witzendichler B, Parise H, Mehran R, Stone GW. Impact of transfer for primary percutaneous coronary intervention on survival and clinical outcomes (from the HORIZONS-AMI Trial). *Am J Cardiol* 2010;106:1218–24.
- [28] Schuchert A, Hamm C, Scholz J, Klimmeck S, Goldmann B, Meinertz T. Prehospital testing for troponin T in patients with suspected acute myocardial infarction. *Am Heart J* 1999;138:45–8.
- [29] Svensson L, Axelsson C, Nordlander R, Herlitz J. Elevation of biochemical markers for myocardial damage prior to hospital admission in patients with acute chest pain or other symptoms raising suspicion of acute coronary syndrome. *J Intern Med* 2003;253:311–9.
- [30] Curtis JP, Portnay EL, Wang Y, McNamara RL, Herrin J, Bradley EH, Magid DJ, Blaney ME, Canto JG, Krumholz HM, National Registry of Myocardial Infarction-4. 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.
- [31] Davis MT, Dukelow A, McLeod S, Rodriguez S, Lewell M. The utility of the prehospital electrocardiogram. *CJEM* 2011;13:372–7.
- [32] Nestler DM, White RD, Rihal CS, Myers LA, Bjerke CM, Lennon RJ, Schultz JL, Bell MR, Gersh BJ, Holmes Jr DR, Ting HH. Impact of prehospital electrocardiogram protocol and immediate catheterization team activation for patients with ST-elevation-myocardial infarction. *Circ Cardiovasc Qual Outcomes* 2011;4:640–6.
- [33] Drew BJ, Sommargren CE, Schindler DM, Benedict K, Zegre-Hemsey J, Glancy JP. A simple strategy improves prehospital electrocardiogram utilization and hospital treatment for patients with acute coronary syndrome (from the ST SMART Study). *Am J Cardiol* 2011;107:347–52.
- [34] Sorensen JT, Terkelsen CJ, Steengaard C, Lassen JF, Trautner S, Christensen EF, Nielsen TT, Bøtker HE, Andersen HR, Thygesen K. Prehospital troponin T testing in the diagnosis and triage of patients with suspected acute myocardial infarction. *Am J Cardiol* 2011;107:1436–40.
- [35] Zegre Hemsey JK, Dracup K, Fleischmann K, Sommargren CE, Drew BJ. Prehospital 12-lead ST-segment monitoring improves the early diagnosis of acute coronary syndrome. *J Electrocardiol* 2012;45:266–71.