RESEARCH LETTER

Treatment delays and in-hospital outcomes of patients with ST-segment elevation myocardial infarction treated at a tertiary center in Poland

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Introduction Treatment of myocardial infarction (MI) has evolved over the past 30 years.[1] Primary percutaneous coronary intervention (pPCI) is the preferred strategy in patients with ST-segment elevation MI (STEMI).[2] According to the European Society of Cardiology (ESC) guidelines,[2] timely reperfusion is a critical factor affecting mortality and clinical outcomes of patients. However, the potential benefits of pPCI are considerably limited by treatment delays.[3] Currently, the recommended optimal time from the first medical contact (FMC) to pPCI is less than 60 minutes for patients presenting to an emergency unit (EU) personally, and less than 90 minutes for those calling emergency medical services (EMS). Therefore, patients with STEMI should preferably report / be transported directly to a center that performs pPCI 7 days a week, around the clock. In addition, they should be referred directly to a catheterization laboratory, bypassing the EU.[2] After 12 hours from symptom onset, no additional advantages of urgent pPCI were reported.[4,5] No time restrictions regarding pPCI exist for patients with persistent symptoms, life-threatening rhythm disturbances, cardiogenic shock, or cardiac arrest.[6]

Thorough assessment of the quality-of-care rates is pivotal for providing every STEMI patient with the best possible treatment. The ESC guidelines underline the need to monitor whether pre- and in-hospital delays comply with the recommendations.[2] This approach is supported by several studies.[7-10] The most frequently assessed parameters are onset-to-door time (OTDT; time from the onset of symptoms to patient admission) and time from admission to wire crossing.

The aims of this study were to 1) evaluate the effectiveness of health care services provided to patients with acute coronary syndrome (ACS) in Tricity, Poland (an agglomeration of 3 cities: Gdańsk, Sopot, and Gdynia, with around 1 million inhabitants based on the data from Statistics Poland[11]), 2) assess the impact of treatment delays on in-hospital mortality, and 3) indicate the most significant factors contributing to particular delays.

Patients and methods This was a single-center, retrospective study including 331 patients (234 men [70.7%]) with an initial diagnosis of STEMI based on typical symptoms and specific electrocardiographic patterns. The mean (SD) age of the participants was 63 (12.2) years. The patients were admitted to the catheterization laboratory at the University Clinical Centre (UCC) in Gdańsk, Poland between January 1, 2015 and December 31, 2016. They presented to the UCC in one of the following ways: 1) were transported by EMS (n = 267 [81%]), 2) reported personally to the EU of the UCC (n = 50 [15%]), or 3) were referred from another ward (n = 14 [4%]). Each participant was subsequently treated with pPCI. The exclusion criteria were unknown OTDT and transportation by EMS from another hospital. To estimate the 6-month mortality risk in the patients with ACS, we used the GRACE 2.0 scale.[12] The medical data were collected from the patients' electronic documentation.

The study complies with the Declaration of Helsinki. The methods used in this analysis were reviewed and approved by the Institutional Review Board at the UCC (151/2020) and the Local Independent Bioethical Committee (NKBBM/379–176/2018). Informed consent was waived due to the retrospective design of the study.

Delays in pre- and in-hospital settings In accordance with the ESC guidelines,[2] the patients were divided into groups to analyze the following parameters: OTDT (≤12 hours, n = 222 vs >12 hours, n = 72), and time from patient admission to

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TABLE 1 Factors affecting prolongation of onset-to-door time and time from admission to wire crossing

Parameter	Onset-to-door time			Time from admission to wire crossing		
	≤12 h (n = 222)	>12 h (n = 72)	*P* value	<90 min (n = 159)	≥90 min (n = 172)	*P* value
Age, y	61.6 (12.3)	65.8 (12.7)	0.01	60.6 (11.5)	65.1 (12.6)	<0.001
Women, n / N (%)	57/222 (25.7)	27/71 (38)	0.045	38/158 (24.1)	58/171 (33.9)	0.045
Weight, kg	83 (75–95)	80 (69.5–94.5)	0.1	85 (78–96)	80 (70–95)	0.02
Height, cm	172 (165–177)	170 (160–175.5)	0.02	173 (165–178)	170 (160–176)	0.03
Hypertension, n / N (%)	141/220 (64.1)	49/70 (70)	0.37	93/154 (60.4)	121/167 (72.5)	0.02
Renal failure, n / N (%)	8/214 (3.7)	7/68 (10.3)	0.04	4/150 (2.7)	14/159 (8.8)	0.02
Dyslipidemia, n / N (%)	167/220 (76)	43/70 (61.4)	0.02	111/154 (72.1)	119/165 (72.1)	0.99
Insulin-treated diabetes, n / N (%)	8/216 (3.7)	5/69 (7.3)	0.22	4/148 (2.7)	10/164 (6.1)	0.15
Chronic lung disease, n / N (%)	9/216 (4.2)	3/71 (4.2)	0.98	3/150 (2)	11/167 (6.6)	0.047
Cardiac arrest, n / N (%)	26/222 (11.7)	6/72 (8.3)	0.42	33/157 (21)	20/167 (12)	0.042
Hemoglobin, g/dl	14.4 (13.3–15.5)	14.0 (12.7–15.3)	0.14	14.7 (13.4–15.5)	14.1 (13.1–15.3)	0.047
CK-MB, ng/ml	65.5 (17.4–147)	33.8 (7.7–83.7)	0.003	78.2 (22–161)	37.8 (9.4–98.3)	0.001
In-hospital GRACE 2.0 score, points	112 (96–138)	119 (104–148)	0.08	111.5 (99–141)	119.5 (101–146.5)	0.047
In-hospital mortality, n / N (%)	13/222 (5.86)	7/72 (9.72)	0.26	9/159 (5.66)	17/172 (9.88)	0.15
β-Blockers, n / N (%)	56/191 (29.3)	18/56 (32.1)	0.69	32/128 (25)	51/138 (37)	0.04

Data are presented as mean (SD) or median (interquartile range) unless indicated otherwise.

P value <0.05 was considered significant.

SI conversion factors: to convert hemoglobin to g/l, multiply by 10; CK-MB to μkat/l, by 0.0167.

Abbreviations: CK-MB, creatine kinase–myoglobin binding; n, number of cases with analyzed variable; N, number of cases included in the analysis

the UCC to PCI-mediated reperfusion in the culprit lesion (<90 minutes, n = 159 vs ≥90 minutes, n = 172). The impact of prolonged times on short-term prognosis was assessed based on in-hospital mortality. We analyzed factors such as demographics, comorbidities, previous cardiac events, family history, laboratory test results, administered medications, and specific clinical scales to identify relevant predictors. Finally, we appraised the pre- and in-hospital delays in subgroups stratified by age (young: ≤65 years [n = 210; 63.4%] vs elderly: >65 years [n = 121; 36.6%]), sex (men [n = 234; 70.7%] vs women [n = 97; 29.3%]), and time of admission to the UCC (working hours: from 7 AM to 3 PM [n = 153; 46.2%] vs afternoon / night hours: from 3 PM to 7 AM [n = 178; 53.8%]).

Statistical analysis Descriptive statistics were used to summarize the characteristics of patients, including the baseline characteristics of the whole analyzed population and characteristics of the subgroups, depending on the specific parameter. Continuous variables are presented as mean (SD) or median with interquartile range (IQR), according to the data distribution. Dichotomous variables are presented as numbers with percentages. Normality of the data distribution and homogeneity of variance were determined with the Shapiro–Wilk and Levene tests, respectively. The *t* test or the Mann–Whitney test was used to compare continuous variables. Dichotomous variables were compared using the χ^2 test. *P* values below 0.05 were considered significant. Statistical analyses were performed using Statistica 13.3 (StatSoft, TIBCO Software Inc., Kraków, Poland).

Results Demographic and baseline characteristics of the study population are presented in Supplementary material, *Table S1*. The in-hospital mortality rate in the whole study population was 7.85% (26 out of 331). Mortality in subgroups stratified by occurrence of any delay was calculated after exclusion of patients with unknown OTDT and no systemic delay (because of uncertainty as to which group such patient should be included in), and reached 9.6% (18 out of 189 cases) in the group with any delay and 5.6% (7 out of 125 cases) in the group without any delay; however, the difference between the groups was not significant (*P* = 0.21). Moreover, in the subgroup with cardiac arrest or cardiogenic shock on admission, the in-hospital mortality rate was 27.3% (15 out 55 cases).

Onset-to-door time The median OTDT was 3 hours (IQR, 1.5–12), and it was prolonged (>12 hours) in 72 patients (21.8%; Supplementary material, *Figure S1*). The specific risk factors for OTDT prolongation are shown in TABLE 1. The patients with a prolonged OTDT were older and more likely to be women. They were also shorter, had a lower level of creatine kinase–myoglobin binding (CK-MB), lower prevalence of dyslipidemia, and higher prevalence of renal failure.

Time from admission to wire crossing The median time from admission to PCI-mediated reperfusion was 92 minutes (IQR, 65–187), and it was

prolonged (≥90 minutes) in 172 patients (52%; Supplementary material, *Figure S2*). The specific risk factors for time prolongation are shown in TABLE 1. In the group with a prolonged time, the patients were older and more often women. They were also shorter and had lower body weight than the patients without a treatment delay. The levels of hemoglobin and CK-MB were also lower in this group, as was the frequency of cardiac arrest occurrence, whereas the GRACE 2.0 score, frequency of β-blocker administration, and prevalence of hypertension, renal failure, and chronic lung disease were higher. In the group with a prolonged time from admission to wire crossing, OTDT was also longer (median, 3 hours [IQR, 1.5–11] vs 7.75 hours [IQR, 2–48]; P <0.001). The specific differences in times between the subgroups stratified by age, sex, and time of admission to the UCC are summarized in Supplementary material, *Table S2*.

Discussion Measuring pre- and in-hospital treatment delays in patients with ACS is a simple and effective way of evaluating health care quality and social knowledge about basic symptoms of ACS.[2] Identification potential delays and their reasons is of key importance, as it may decrease mortality and improve patient quality of life.

An important parameter evaluated in our analysis was OTDT. It is affected by patient self-awareness and ability to recognize symptoms of MI. In a study by Park et al,[13] conducted in 20 hospitals in Korea, the median OTDT was 2 hours. In our study, it was 3 hours, which may be due to the fact that we included patients solely from the urban agglomeration of Tricity, where difficulties in reaching the PCI center within the recommended time frame may occur because of numerous calls to the EMS and heavy traffic. A study conducted in 16 metropolitan areas in the United States assessed the influence of implementing care protocol changes on time from FMC to inflation of the angioplasty balloon in the culprit lesion. In the centers that implemented the changes, the evaluated time decreased from 98 minutes to 88 minutes.[14] The outcomes of that study indicated that systemic improvements can result in a significant reduction of OTDT.

Cale et al[15] investigated patient-related delays in a population stratified by age, sex, and comorbidities. Elderly patients (≥75 years) and women experienced significantly longer delays. Our study also focused on the factors associated with OTDT prolongation. Older age, female sex, shorter height, renal failure, and a lack of dyslipidemia were identified as risk factors. Moreover, a lower plasma level of CK-MB was related to longer OTDT, which is a novel finding.

Another parameter evaluated in our study was the time from admission to wire crossing. In their study involving a group of 5243 patients, Park et al[12] reported a median door-to-balloon time of 59 minutes, and it was shorter than or equal to 90 minutes in 92.2% of the study population. In an analysis conducted in 18 Portuguese cardiology centers, the median systemic delay (defined as time from FMC to coronary reperfusion) was 125 minutes, with 58.1% of the patients experiencing a delay of more than 90 minutes.[15] In our study, the median time from admission to wire crossing was 92 minutes, and 52% of the patients experienced time prolongation. The reasons for such a high percentage of patients with in-hospital delay is a lack of an early notification system and internal procedures designed for patients with STEMI, and the necessity for patient transportation from the EU and to the catheterization laboratory. Currently, these problems have been eliminated in the UCC, which will probably lower the number of patients with systemic delays in the future. Blankenship et al[16] showed that improvements in the transport system and medical procedures implemented in a single center in Pennsylvania, United States, allowed for shortening the systemic delay to less than 90 minutes—from a mean of 189 minutes in 2004 to 88 minutes in 2008. In a study by Terkelsen et al,[17] the cumulative mortality increased from 23.3% in patients experiencing a delay of 61 to 120 minutes to 28.1% in those experiencing a delay of 121 to 180 minutes. In our study, in-hospital mortality was 5.6% in the patients without any delay and 9.6% in the group with a delay (P = 0.15).

Evidence from the literature indicates that critical factors associated with treatment delays are patient age, sex, and comorbidities.[15] In a study by Cale et al,[15] the median OTDT for the whole population was 105 minutes, whereas for elderly patients it was 133 minutes. Regarding the time from admission to wire crossing, the respective values were 125 minutes and 160 minutes. Moreover, only 43.6% of the elderly patients received PCI-mediated reperfusion therapy within the time frame recommended in the ESC guidelines, as compared with 58.1% of the whole population.[15] Another study comparing systemic delays between young (<65 years) and elderly (≥65 years) patients revealed longer median door-to-balloon time in the elderly group (73 minutes vs 64 minutes).[18] Our results showed that the median OTDT (3 hours vs 4 hours; P = 0.007) and time from admission to wire crossing (85.5 minutes vs 113 minutes; P = 0.067) were also longer in the elderly patients. This may result from communication issues and atypical symptoms in this group.

Bugiardini et al[19] evaluated differences in delays according to sex, and showed that the time from symptom onset to treatment was longer in women than in men (270 minutes vs 240 minutes, respectively; P <0.001), which translated into increased 30-day mortality in women. Cale et al[15] reported that both OTDT and time from admission to wire crossing were longer in women than in men (median, 117 minutes vs 103 minutes; P = 0.061 and median 145 minutes vs 120 minutes; P <0.001, respectively). Our results also showed significant differences between the sexes. Atypical symptoms of MI and more complicated diagnostic procedures in women are the possible

reasons. Cenko et al[20] reported a higher mortality rate among women, as compared with men (11.6% vs 6%). Our findings support these observations, as the in-hospital mortality rate in women was markedly higher than in men (14.58% vs 4.7%).

Another group exposed to longer delays are patients with coexisting diseases. While both OTDT and time from admission to wire crossing were shorter in the patients with more comorbidities, only the latter difference reached statistical significance in a report by Balzi et al.[21] In our study, the patients with comorbidities had a shorter OTDT but a longer time from admission to PCI-mediated reperfusion. As stated earlier, the reduced OTDT might result from greater patient awareness of typical symptoms of MI.

As previously investigated, a higher CK-MB level on admission to a hospital strictly correlates with increased mortality, more extensive area of MI, and worse prognosis—a peak CK-MB of 300 IU/l or higher was reported to predict with moderate accuracy both large infarct size and a left ventricular ejection fraction lower than or equal to 40%.[22,23] However, it is not clear how this parameter influences treatment delays. In our study, a lower CK-MB plasma level was related to longer OTDT and longer time from admission to wire crossing, which has not been reported so far.

The assessment of both OTDT and time from admission to wire crossing is critical because their prolongation may affect in-hospital mortality. According to the ESC guidelines, the mortality rate alone is not recommended for appraising in the context of quality-of-care evaluation because of its high dependence on the specific features of the studied population (eg, mean age, baseline clinical status) and methodology of data collection (eg, including or not including patients with cardiogenic shock).[2,24] Kristensen et al[24] assessed the in-hospital mortality among patients with STEMI in 12 European countries (including Poland). Based on data from the Polish patients, the estimated in-hospital mortality ranged from 4.4% in the individuals treated with pPCI to 11.5% in the group without reperfusion therapy. Park et al[14] showed that any reduction in OTDT and time from admission to wire crossing was related to a survival benefit. In our study, the overall in-hospital mortality rate was 7.85% (ranging from 5.6% in the patients without any delay to 9.6% in those with a delay; $P = 0.21$). Terkelsen et al[17] reported a mortality rate ranging from 15.4% (delay of 0–60 minutes) to 30.8% (delay of 181–360 minutes). The influence of time prolongation on mortality in our study may be underestimated as a result of a restricted follow-up.

Study limitations Most of the study participants were residents of a large city, which makes the study outcomes not fully applicable to all areas. Because of limited data on the time from diagnosis to wire crossing in patients transported by EMS from non-PCI centers, this group was not included in the study. Moreover, the study was retrospective, with a short follow-up after the intervention, which was limited by the length of hospitalization. This restricts our knowledge of the possible future adverse events associated with treatment delays.

Conclusions In summary, for most individuals with STEMI treated in Tricity, OTDT was within the range recommended by the European guidelines; however, about half of the patients did not meet the recommended time from admission to PCI-mediated reperfusion. There was no significant impact of prolonged times on in-hospital mortality. We also identified groups of patients with the highest risk of treatment delays. Female sex, older age, renal failure, shorter height, and absence of dyslipidemia were the predictors of OTDT prolongation. Regarding the time from admission to wire crossing, the factors associated with a delay were female sex, older age, lower weight, height, and hemoglobin level, as well as higher frequency of β-blocker administration, higher score on the GRACE 2.0 scale, and prevalence of comorbidities, such as hypertension, renal failure, and chronic lung disease. Moreover, lower CK-MB level on admission was related to prolongation of both OTDT and time from admission to wire crossing. The aforementioned groups of patients may require additional caution in terms of transportation and diagnostic procedures. Periodic measurement of OTDT and time from admission to PCI-mediated reperfusion is a simple and effective way of assessing the efficiency of the health care system, and allows for maintaining treatment delays within time frames outlined in recent ESC recommendations. This procedure should be an indispensable part of the care quality evaluation.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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