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ORIGINAL RESEARCH

Critical Appraisal of Medical System Performance for STEMI Management – a Comprehensive Analysis of Time Efficiency

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ABSTRACT

Background: Time intervals related to ST-segment myocardial infarction (STEMI) revascularization are central determinants for patient outcomes. The current capability of the Romanian STEMI program to meet guideline-recommended time intervals is largely unknown. **Aims:** The present study aims to assess the ability of a regional STEMI network to obtain guideline-recommended time intervals for primary percutaneous coronary intervention (pPCI) and to measure the occurrence and the extent of time delays. **Materials and Methods:** This prospective study included 500 consecutive patients with STEMI at the "Prof. Dr. C.C. Iliescu" Emergency Institute for Cardiovascular Diseases, Bucharest, Romania during a period of 14 months. Complete ischemic timelines were created using several key timepoints. **Results:** A secondary route (transfer from another hospital) was noted in most cases. The main time intervals were the following: patient delay 209 min, emergency medical system delay 66 min, and PCI center delay at 70 min, totaling an ischemic time of 6.4 h. A provisional stop at another hospital involved the addition of 113 min (1.8 h) until STEMI diagnosis and an additional 83 min (1.3 h) from diagnosis to revascularization, totaling a supplementary ischemic time of 3.1 h. In total, 41.5% of the patients were revascularized between 2 and 6 h from symptoms onset. The objective of revascularization in less than 120 min (from first medical contact) was accomplished in 35.5% of the patients. Prehospital thrombolysis was performed in 6.4% of the cases, although its potential benefits could have been expected in 64.5% of the patients. **Conclusions:** Patients with STEMI arrive predominantly via secondary routes to the PCI center, which implies significantly increased ischemic times. The ambulance alert system and primary routes represent by far the most efficient, albeit still imperfect methods of prehospital approach. Prehospital thrombolysis did not compensate for the gaps existing in the performance of the current system.

Keywords: STEMI, time intervals, primary PCI, patient delay, emergency system delay

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INTRODUCTION

Ischemic heart disease remains the leading cause of death globally.[1] The relative contribution of STEMI to this wide-ranging statistic seems to be diminishing due to its declining incidence.[2] Nevertheless, the absolute number of patients with STEMI remains ominously high, and mortality rates may reach 10–12%.[3,4] pPCI represents the ideal method of reperfusion, with the caveat that it has to be performed in a timely manner. The morbidity and mor-

tality benefits observed with pPCI are substantially diminished by delays in treatment.[5,6] Thus, time intervals related to STEMI revascularization become central determinants for clinical outcomes, and they remain easily evaluable indicators of quality of care. Current guidelines offer clear definitions for each relevant time interval inside the ischemic window of a STEMI.[7,8]

By recognizing the importance of these time intervals and their optimization, it has become imperative to develop regional networks with the purpose of increasing accessibility to pPCI and, at the same time, to improve time-to-treatment intervals.[9–11] In Romania, the national program for interventional therapy in patients with STEMI was started in 2010. It managed to create an enhanced harmonization between emergency medical services, emergency departments, and tertiary centers with cardiac catheterization facilities. The impact on patient care was rapidly noticeable, leading to increased pPCI accessibility and a decreasing STEMI-related mortality.[12] However, whether the benefits from the national STEMI program have reached a plateau is currently unknown, and possible modifiable gaps might exist between guideline recommendations and the efficiency of the current healthcare system.

Consequently, there is currently a wider ongoing objective to assess and characterize the current status of the national STEMI program to identify possible elements that might benefit from particular refinements. The present study aims to assess the ability of the regional STEMI network to obtain guideline-recommended time intervals for pPCI and to measure the occurrence and the extent of time delays. Through its secondary objectives, this study plans to include a general characterization of the contemporary STEMI population and the procedural aspects of the pPCI, and to offer a brief overview regarding in-hospital outcomes. The following analysis reflects the management and outcomes of a single center and cannot expand the results with complete reliability to the entire STEMI network.

METHODS

REGIONAL STEMI NETWORK DESCRIPTION

The "Prof. Dr. C.C. Iliescu" Emergency Institute for Cardiovascular Diseases, Bucharest, Romania is part of a group of six hospitals that provide 24/7 services for emergency interventional cardiology procedures by a rotating schedule. Our institute provides these services two times per week, and referrals include the southeastern area of the country, covering approximately 71,000 km^2, with the longest distance of roughly 260 km.

DESIGN AND PATIENT SELECTION

The present analysis takes into consideration only patients admitted to the "Prof. Dr. C.C. Iliescu" Emergency Institute for Cardiovascular Diseases, which will be referred to as the "PCI center" throughout this manuscript. We prospectively included 500 consecutive patients admitted with a working diagnosis of STEMI, during a period of time of 14 months, from April 2022 to May 2023. STEMI was defined as persistent chest pain and/or other symptoms of myocardial ischemia associated with ST-segment elevation on at least two contiguous ECG leads, or newly diagnosed bundle branch block, accompanied by an increase in highly-sensitive cardiac troponin.[8] Patients with non-ST elevation myocardial infarction were excluded from this analysis, regardless of the risk group. Patient outcomes were evaluated during index hospitalization, until discharge.

PROCEDURE

Interventional procedures were performed in accordance with conventional and local practices. All patients underwent emergency coronary angiography. PCI with stent implantation was performed in all cases where technical feasibility allowed it. All stents used in this population were second-generation drug-eluting stents (DESs). Angioplasty with drug-eluting balloons (DEBs) or plain-balloon-angioplasty (POBA) were used at the operator's discretion. Adjuvant equipment (such as aspiration thrombectomy) and the intraprocedural usage of GP IIb/IIIa antagonists are noted accordingly. If PCI was performed, the antiplatelet regimen included association of aspirin with a thienopyridine at the physician's preference (75 mg of clopidogrel or 180 mg of ticagrelor).

ARRIVAL METHOD AND TIMING – DEFINITIONS

The methods of arrival at the PCI center assumed four possible scenarios: *Arrival by ambulance from home* (defined also as *Primary route*) was defined as transport from the scene of symptoms onset directly to the PCI center with an ambulance, without a provisional stop at another hospital. *Transport from another hospital* (defined also as *Secondary route*) implied a provisional stop at a different hospital before arrival at the PCI center (because of imperfect data, for this category of patients the *First medical contact* (FMC)

timepoint was omitted, and only the *First ECG* timepoint was used, as it will be described). *Self-presenter* was defined as presentation to the emergency department of the PCI center using personal means of transportation. *Already in-hospital* was reserved for patients with a STEMI diagnosis established while already admitted to the PCI center.

The complete ischemic timelines were created using several key timepoints. *Symptoms onset* was used as the start point for the total ischemic time (if the patient presented with intermittent symptoms, the time recorded was the one of the symptoms that required ambulance notification or self-presentation to the hospital). *First contact with ambulance* (or FMC) was defined as the time when the ambulance arrived to the patient. *First ECG* was the time when the first recorded ECG was interpreted as ST-segment elevation or equivalent. *Hospital arrival* was defined as the time when the patient arrived in the emergency department of the PCI center. *Arrival to cath lab* was used interchangeably with *Arterial access time*, defined as the moment when the arterial sheath was in place. *Wire passage* was used as the timepoint when the coronary wire was placed distal to the culprit lesion regardless of the coronary flow. *Revascularization time* was defined as the moment when coronary flow was secured (mainly when the stent was placed, but the same timepoint was used if POBA or DEB were used as final angioplasty method). *Total ischemic time* (TIT) was defined as the period from symptoms onset to revascularization. *Emergency system delay* (EMS) was defined as the period from *First contact with ambulance* or *First ECG* (for transfers) until arrival at the PCI center. *Hospital delay* (delay within the PCI center) was defined as the period from arrival to the PCI center to revascularization.

OTHER RELEVANT DEFINITIONS

PCI attempted was considered when an attempt was made to place a coronary wire in the culprit vessel, regardless of the outcome of angioplasty. *Successful PCI* was defined as <20% residual stenosis by visual inspection associated with TIMI 3 flow. For *In-hospital myocardial reinfarction* the fourth universal definition was used.[13] Current recommendations were used to define *In-hospital bleeding* events.[14]

STATISTICAL ANALYSIS

Categorical data is shown as absolute and relative values. Continuous variables are shown as mean ± standard deviation for values with normal distribution, or as median and interquartile range (IQR) for non-normally distributed values. Histograms and the Shapiro–Wilk test were used to assess for normality. Intergroup comparison for categorical variables was performed using the chi-squared test or Fisher's exact test, if appropriate. For continuous data, Student's *t* test or the Kolmogorov–Smirnov test were used. All reported p values are two-sided, and significance was established for values of <0.05. Data analysis was performed using IBM SPSS Statistics for Windows, version 20 (IBM Corp).

RESULTS

BASELINE POPULATION CHARACTERISTICS

The final analysis includes a total number of 500 patients. Baseline characteristics and admission data for the study population are presented in Table 1. The large majority of the patients were male (74.6%), and the overall median age was 61.7 ± 12.08 years. There is also a clear preponderance of active or former smokers (63.4%). Arterial hypertension was the most frequently encountered comorbidity (75.2%), followed by type 2 diabetes (23.4%).

The vast majority of patients (93%) presented with chest pain as the main symptom. Cardiac arrest was found as the sole clinical manifestation in 4.2% of the cases, and as an accompanying manifestation prior to hospital arrival in 7.6% of the cases. Prehospital thrombolysis was performed in 32 patients (6.4%). On the ECG from admission, ST-segment elevation was localized most often in inferior leads in 45% of cases, followed closely by anterior location in 43% of the cases. At the moment of arrival, a clinical picture equivalent of Killip classes II–IV was observed in 81 cases (16.2%), and overt cardiogenic shock was noted in 27 cases (5.4%). Transthoracic echocardiography was performed in all cases at the emergency department, before emergency angiography. Left ventricular ejection fraction was normal in 24.2% of the patients and below 30% in 10.2% of the patients (Table 1).

PROCEDURAL DETAILS

Data related to the diagnostic coronary angiography and to the PCI procedures are detailed in Table 2. The most frequent finding was single coronary vessel involvement (52.2%), followed by two-vessel disease (26.6%). Significant left main disease was identified in 5.8% of cases, most frequently associated with three-vessel involvement. Right coronary artery was considered the culprit vessel in 41.7% of cases, followed by left anterior descend-

TABLE 1. General patient characteristics and admission details

Parameter	*n* (%)	Parameter	*n* (%)
Male sex	373 (74.6%)	Killip class	
Age (years)	61.7 ± 12.08	I	419 (83.8%)
≥80	51 (10.2%)	II	33 (6.6%)
<40	10 (2%)	III	21 (4.2%)
Body mass index (kg/m^2)	28 ± 5.1	IV	27 (5.4%)
>30	153 (30.6%)	Hemoglobin (g/dl)	14.4 ± 1.9
Smoking (at any time)	317 (63.4%)	Creatinine (mg/dl)	0.98 ± 0.5
Current smoker	251 (50.2%)	LDL cholesterol (mg/dl)	160 ± 51.6
Former smoker	66 (13.2%)	TTE assessment at ED	500 (100%)
Never	183 (36.6%)	Left ventricular ejection fraction	
Hypertension	376 (75.2%)	>50%	121 (24.2%)
Diabetes mellitus	117 (23.4%)	40–50%	142 (28.4%)
Chronic obstructive pulmonary disease	8 (1.6%)	30–40%	186 (37.2%)
Moderate or severe chronic kidney disease	37 (7.4%)	<30%	51 (10.2%)
Previous stroke	9 (1.8%)	ST-segment elevation on ECG	
Previous myocardial infarction	33 (6.6%)	Inferior	225 (45%)
Heart failure	24 (4.8%)	Anterior	215 (43%)
Atrial fibrillation or atrial flutter	14 (2.8%)	Other	60 (12%)
Previous percutaneous coronary intervention	33 (6.6%)	ECG – QRS morphology	
Previous coronary artery bypass grafting	1 (0.2%)	Normal	389 (77.8%)
Presenting symptoms		Q waves	85 (17%)
Chest pain	465 (93%)	LBBB	9 (1.8%)
Dyspnea	10 (2.0%)	RBBB	15 (3%)
Cardiac arrest	21 (4.2%)	Pacing	2 (0.4%)
Other	4 (0.8%)	Other	
Cardiac arrest prior to hospital arrival	38 (7.6%)	ECG – rhythm	
Prehospital thrombolysis	32 (6.4%)	Sinus rhythm	459 (91.8%)
Heart rate	84.8 ± 19.8	Atrial fibrillation	30 (6%)
Systolic blood pressure	137.9 ± 27.5	Other	11 (2.2%)

ECG, electrocardiogram; ED, emergency department; TTE, transthoracic echocardiography; LBBB, left bundle branch block; RBBB, right bundle branch block

ing artery (38.8%). The detailed distribution of culprit lesions by coronary segment is shown in Table 2. The culprit artery showed total flow obstruction (TIMI 0) in the majority of cases (62.6%) and normal coronary flow (TIMI 3) regardless of the underlying stenosis in 9.8% of cases. In patients with prehospital thrombolysis, a TIMI 0 flow was less frequently encountered (43.3% vs. 63.7%, p = 0.107), with the difference being distributed towards TIMI flows 1 and 2 (Table 3).

During the index procedure, PCI was attempted in 477 patients (95.4%) (Table 2). Radial access was the preferred vascular approach in 61.2% of the cases. The main predictors for femoral access were cardiac arrest prior to hospital admission, Killip classes III and IV, and body mass index <21 kg/m^2. There were no significant differences in procedural time variables between the two vascular approaches (Supplementary Table 2). With respect to possible vascular complications capable of prolonging hospitalization time, there appeared to be a significant difference in favor of the radial approach compared to the femoral approach (mean number of days until discharge 5.6 vs. 8.39, p = 0.03). However, the difference became non-significant when correction for confounding factors was made (5 vs. 5.93, p = 0.18) (Supplementary Table 2).

Successful PCI was achieved in 96.6% of the *PCI attempted* cases. Angioplasty with at least one stent was performed in 428 patients (85.6% of the entire population), with a total number of 540 stents implanted (DESs exclusively) (Table 2). The median stent length was 23 mm, and the median diameter was 3 mm. DEB was used in three cases (0.5%) in secondary culprit vessels: a diagonal artery and two marginal branches of the left circumflex. The median diameter of the DEB was 2.5 mm. POBA was used in 33 lesions (5.7%). Complete revascularization dur-

TABLE 2. Emergency coronary angiography findings and PCI procedural findings

Parameter	*n* (%)
Overall coronary findings	373 (74.6%)
Normal	14 (2.8%)
1-vessel disease	261 (52.2%)
2-vessel disease	133 (26.6%)
3-vessel disease	63 (12.6%)
LM + 1-vessel disease	5 (1%)
LM + 2-vessel disease	10 (2%)
LM + 3-vessel disease	14 (2.8%)
Spontaneous coronary artery dissection	0
Culprit vessel	183 (36.6%)
RCA	243 (41.7%)
LAD	226 (38.8%)
Cx	96 (16.5%)
LM	14 (2.4%)
RI	4 (0.7%)
TIMI flow	
TIMI 0	62.60%
TIMI 1	9.30%
TIMI 2	18.40%
TIMI 3	9.80%
In-stent restenosis	10 (2%)
In-stent thrombosis	6 (1.2%)
Percutaneous coronary intervention	10 (2.0%)
During index procedure	477 (95.4%)
Planned after discharge	6 (1.2%)
Not performed/planned	17 (3.4%)
PCI attempted	477 (95.4%)
Primary PCI	447 (93.7%)
Rescue PCI	27 (5.6%)
Pharmacoinvasive strategy	3 (0.62%)
Arterial access	
Radial artery	306 (61.2%)
Femoral artery	194 (38.8%)

Parameter	*n* (%)
Adjuvant therapies/equipment	84 (16.8%)
Thrombectomy	84 (16.8%)
Angioplasty with at least one stent (no. of patients)	428
One stent	333
Two stents	82
Three stents	9
Four stents	4
Median stent length (mm)	23.18-28]
Median stent diameter (mm)	3.3-3.5]
Lesions treated with DEB	3 (0.5%)
Median DEB diameter	2.5.2.5-2.5]
POBA	33 (5.7%)
Successful PCI	461 (96.6%)
Any periprocedural events	37 (7.4%)
Type of periprocedural events	60 (12%)
Bradyarrhythmia requiring pacing	5 (1%)
Arrhythmia requiring cardioversion	5 (1%)
Coronary perforation	1 (0.2%)
Coronary dissection persisting	1 (0.2%)
Access site-related complication	3 (0.6%)
Stroke/TIA	1 (0.2%)
Cardiogenic shock	11 (2.2%)
Death	3 (0.6%)
Other	7 (1.4%)
Complete revascularization	269 (53.8%)
Glycoprotein IIb/IIIa inhibitors	0
Pharmacological vascular support	27 (5.4%)
Any mechanical circulatory support	13 (2.6%)
Mechanical circulatory support type	
IABP	10 (2%)
ECMO	3 (0.6%)

Cx, circumflex artery; DEB, drug-eluting balloon; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; LAD, left anterior descending; LM, left main coronary; PCI, percutaneous coronary intervention; POBA, plain-old balloon angioplasty; RCA, right coronary artery; RI, intermediate ramus; TIA, transient ischemic attack

ing the index procedure was achieved in 53.8% of the patients. The rate of periprocedural events was 7.4%; details are shown in Table 2. Pharmacological and mechanical vascular support were required in 5.4% and 2.6% of the cases, respectively.

In-hospital events are described in Supplementary Table 3. The median duration of hospitalization was 5 days, and the rate of in-hospital death was 5.6%. Treatment at discharge included aspirin in 97.6% of the cases, and a P2Y12 inhibitor was included in 93.8% of cases, predominantly ticagrelor (59.6%). Discharge treatment details are available in Supplementary Table 4.

ARRIVAL TO THE PCI CENTER

Overall, the patients arrived to the PCI center predominantly via the secondary route (transfer from another hospital) in 59% of the cases, followed, in approximately a third of the instances, by the primary route (ambulance transport directly from the scene of symptoms onset) (Supplementary Table 5). However, when patients arrived from outside of Bucharest, primary route decreased to 14.5%, and the large majority of cases (75.3%) involved a provisional stop at another hospital, as illustrated in Figure 1. Regarding patients arriving from Bucharest, 55.3%

TABLE 3. Comparison of time intervals between the two methods of arrival at the PCI center. Values are expressed in min (medians).

	Ambulance from home	Transportation from another hospital	p value
Symptoms to ambulance (time to FMC)	126 (53–257)	N/A	N/A
Symptoms to first ECG	132 (78–327)	245 (120–465)	0.003
Ambulance to hospital	60 (40–95)	N/A	N/A
Symptoms to hospital arrival	203 (126–371)	372 (260–614)	<0.0001
First ECG to hospital arrival (EMS delay)	40 (5–76)	119 (53–204)	<0.0001
Hospital arrival to arterial access (ED delay)	39 (27–60)	46 (33–71)	0.08
Hospital arrival to wire passage	57 (45–78)	66 (50–92)	0.04
Arterial access to wire passage	17 (13–24)	18 (14–24)	0.07
Arterial access to revascularization	24 (18–32)	25 (20–33)	0.33
Wire passage to revascularization	5 (3–10)	5 (3–10)	0.99
Ambulance to revascularization (FMC to revascularization)	134 (109–197)	N/A	N/A
First ECG to wire crossing	112 (71–160)	190 (114–268)	<0.0001
First ECG to revascularization	117 (73–167)	200 (117–290)	<0.0001
Hospital arrival to revascularization (door-to-balloon time)	63 (49–88)	72 (55–99)	0.06
Symptoms onset to revascularization(TIT)	260 (199–441)	453 (333–635)	<0.0001

arrived via a primary route and 35.2% were transferred from other hospitals.

TIMING RESULTS

General

For data reliability and consistency, the following analyses include time intervals that were calculated for patients *without thrombolysis*. For the relevant differences created by thrombolysis, a separate analysis was performed, and it is presented accordingly.

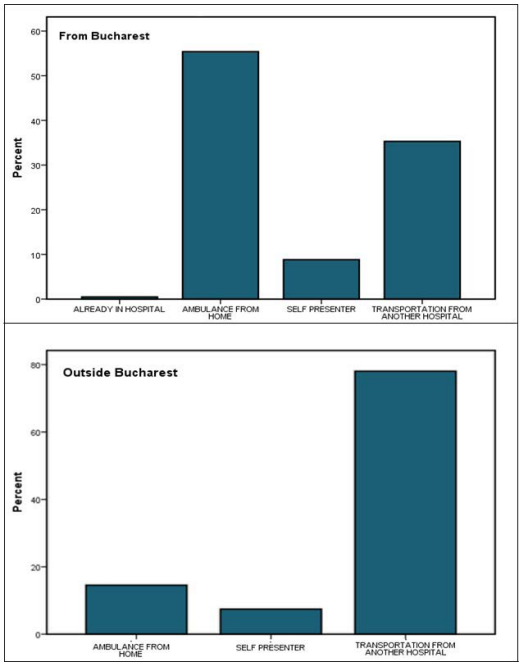


FIGURE 1. Arrival method to the PCI center according to scene of symptoms onset

The analysis of the main components of TIT is detailed in Supplementary Table 6. The main time intervals were the following: *Patient delay* 209 min, *EMS delay* 66 min, and *PCI center delay* 70 min, totaling an ischemic time of approximately 389 min (6.4 h). The categorical analysis of the TIT reveals that 41.5% of the patients were revascularized between 2 and 6 h from symptoms onset, while a largely equal number of patients were revascularized between 6 and 12 h.

As expected, for the subgroup of patients with prehospital thrombolysis the TIT was significantly longer compared to patients with primary PCI (an additional 154 min, p = 0.01), with the difference originating from pre-PCI center time intervals (Supplementary Table 7).

Bucharest vs. outside of Bucharest

Concerning the patients arriving from outside of Bucharest, regardless of the method of transport, all EMS times were significantly longer, leading to a total ischemic time of 454 min (7.5 h) compared to 303 min (5.05 h) for patients arriving from Bucharest, creating a difference of 151 min (2.5 h), p < 0.0001 (Supplementary Table 8). Given that the majority of patients (n = 295) arrived by transfer from another hospital, we performed a subanalysis regarding the difference between arriving from Bucharest vs. from outside of Bucharest (Supplementary Table 9). Although there were longer time intervals for the secondary route outside

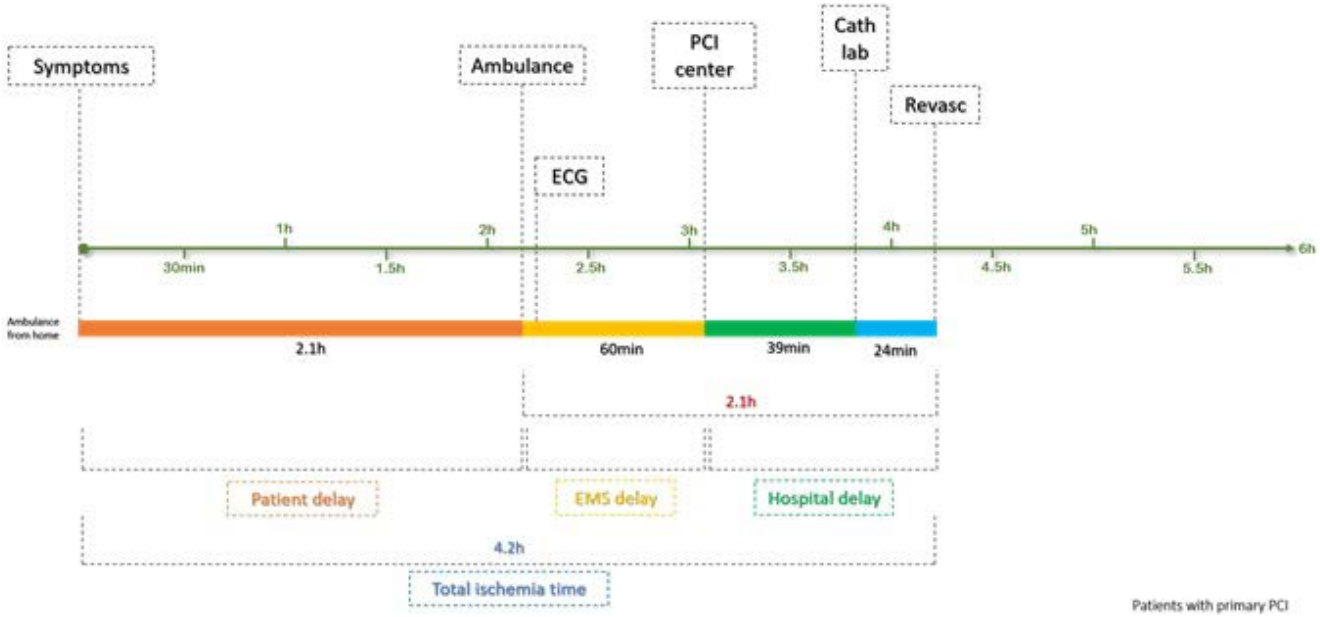


FIGURE 2. Visual representation of time intervals for patients arriving to the PCI center via primary route (6-hour time scale)

of Bucharest, the difference in TIT was 62 min, without statistical significance (p = 0.46). The categorical analysis for these subgroups revealed that patients arriving from Bucharest were largely revascularized within the first 6 h from symptoms onset, whereas 66.2% of the patients from outside of Bucharest were revascularized after 6 h, with 17.6% having a TIT above 12 h (Supplementary Table 10).

Primary route vs. secondary route

Arriving by ambulance directly from home showed the best ischemic times (Figure 2 and Table 3). The median time from *First contact with ambulance* to PCI center arrival was 60 min, while the time from the diagnosis (*First ECG*) to *Wire passage* was 112 min, contributing to an *FMC*

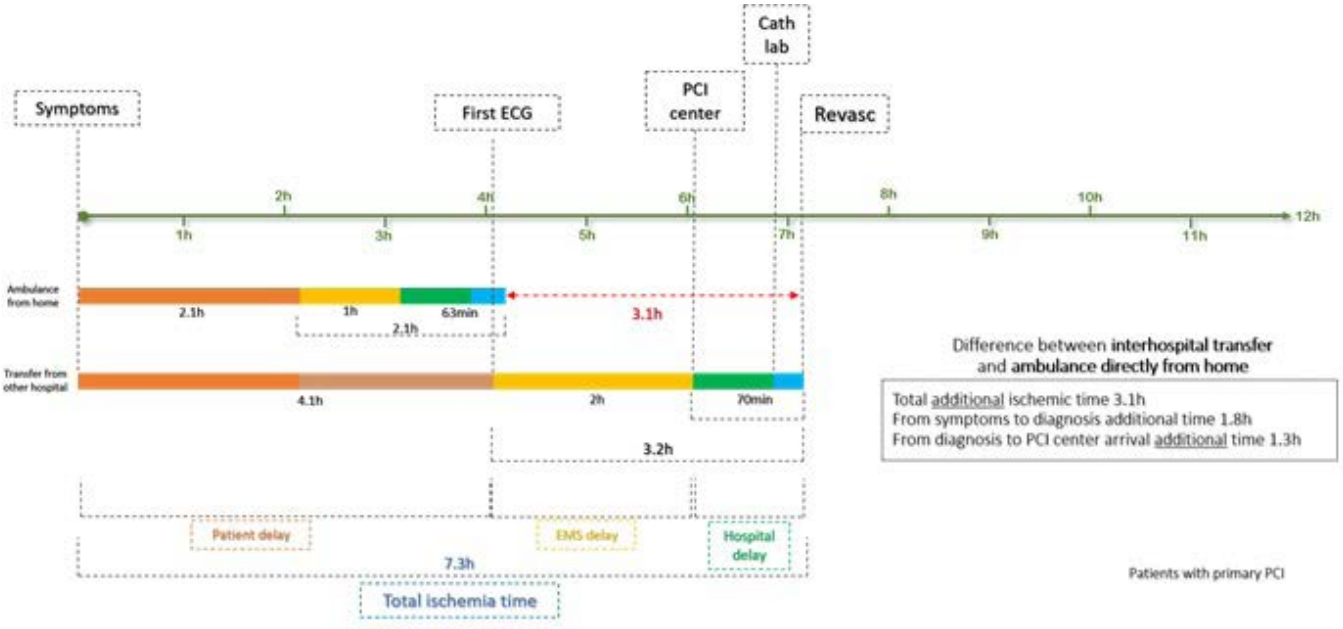


FIGURE 3. Visual representation of time intervals for patients arriving to the PCI center via secondary route and comparison with primary route (12-hour time scale)

TABLE 4. Total ischemic time by categories of time intervals as a function of method of arrival

Arrival method (p < 0.0001)	Revascularization timing categories			
	<2 h	2–6 h	6–12 h	>12 h
By ambulance	4.6%	58%	29%	8.4%
Transfer from another hospital	0.5%	31%	50.2%	18%

to *Revascularization* of 134 min and a total ischemic time of 260 min (4.3 h). By comparison, a provisional stop at another hospital implied the addition of 113 min (1.8 h) until diagnosis and 83 min (1.3 h) from diagnosis to revascularization, totaling a supplementary ischemic time of 3.1 h (Figure 3 and Table 3). Categorical analysis revealed that 62.6% of patients were revascularized before the sixth ischemic hour if they arrived directly by ambulance, compared to less than a third if a provisional stop was made at another hospital (Table 4).

PCI center

There were no significant differences between the time intervals registered for different categories of patients at the PCI center. The median door-to-balloon time was 70 min, with the largest contribution being attributed to the period between arrival and vascular access, i.e., time spent at the emergency department (median value of 44 min). The median time consumed with the procedure (time from *Arterial access* to *Revascularization*) was 24 min.

The overall achievement of guideline-recommended time intervals is shown in Table 5.

DISCUSSION

Several key points should be extrapolated from this analysis. 1) Arrival to the PCI center was achieved mainly through secondary routes (transfers from other hospitals) in 59% of the patients, with the large majority (75%) arriving from outside of Bucharest. 2) The median total ischemic time was 389 min (6.4 h), with the longest delays observed in the case of patients arriving via secondary routes from outside of Bucharest (472 min, 7.8 h), whereas the most favorable ischemic times were observed in patients arriving by primary route (TIT 260 min, 4.3 h). 3) For patients arriving by secondary routes, there was a median delay in STEMI diagnosis of 1.8 h and an additional time of 1.3 h from diagnosis to arrival at the PCI center, adding up to more than 3 h of supplementary ischemic time when compared to the primary route. 4) The revascularization target of <120 min from STEMI diagnosis was met in 35.5% of the patients, with the largest contribution from those arriving by ambulance, directly from home (46.7%), whereas the target was met in just 18.9% of transferred patients. 5) Prehospital thrombolysis was performed in 6.4% of the cases, while potential benefits from pharmacoinvasive reperfusion could have been expected in 64.5% of the patients.

TIT

The TIT represents the interval from symptoms onset to culprit vessel revascularization. Given that it embodies all the other time intervals used in STEMI studies, it has lost some of its robustness and significance as a target indicator. Therefore, current guidelines focus more on the components of the TIT.[7,8] Nevertheless, each second of myocardial ischemia leads to increases in infarct size and area of microvascular obstruction area.[15–17] Thus, TIT ap-

TABLE 5. Achievement of target time intervals in patients who underwent pPCI

Interval	Target	Percentage achieved
FMC to ECG	≤10 min	63 (40.3%)
Diagnostic to wire passage (overall)	≤120 min	159 (35.5%)
Diagnosis to wire passage (for self-presenters)	≤60 min	14 (29.1%)
	≤120 min	29 (60.4%)
Diagnosis to wire passage (for ambulance arrival)	≤120 min	73 (46.7%)
Diagnosis to wire passage (for transfers)	≤120 min	56 (18.9%)
Door-to-balloon	≤90 min	300 (67.1%)

pears to be able to independently predict short- and long term mortality,[18] even with greater accuracy compared to door-to-balloon time.[19] There is no clear prognostic cut-off for TIT, with several studies reporting statistically relevant prognostic values from 180 min to 240 min.[20,21] A recent analysis revealed a linear relationship between TIT and mortality, with a cutoff of 300 min that determines an exponential increase in mortality.[22] In our analysis, the median TIT was 389 min, with only 43.4% of the patients having a TIT shorter than 360 min. The most favorable category, by time efficacy, was represented by patients arriving directly by ambulance, of which 62.6% had a TIT of less than 360 min. This is concerning particularly when considering that a reduction in other relevant intervals, such as door-to-balloon time, seems to offer mortality advantages only in case of lower TIT.[15,20] Some authors consider that patient negligence and lack of awareness are main contributors to increased TIT,[23] suggesting that *Patient delay* is a core reason for increased ischemic time.

PATIENT DELAY

In our analysis, overall patient delay was 200 min. Considering that TIT was 389 min, it becomes clear that more than half of the ischemic time is determined by the patient's lack of reaction. Even if we analyze only the patients who presented by ambulance (considering that EMS data for these patients is more accurate and there are no statistical interferences with emergency department delays), the patient delay remains at 48.4% of the TIT (Table 3). This can be attributed to various factors, most of which are related to patient education. However, correction of this behavior has proved harder than initially anticipated,[24-26] and more productive measures to increase patient awareness should be sought.

MEDICAL SYSTEM DELAY

The recommended medical system delay is <120 min from the FMC to revascularization of the incriminated artery.[8] In our analysis, this objective was accomplished in only 35.5% of the patients. The main source of system delay in accomplishing this target is identified as *EMS delay* for patients arriving by a secondary route, with a median time of 119 min from the STEMI diagnosis to arrival at the PCI center, whereas for the group of patients arriving by ambulance, the same interval had a median value of 40 min. This creates a delay of 1.8 h in STEMI diagnosis (Figure 3), which can be explained by several factors: delayed patient presentation to an emergency department (compared to those who call for an ambulance) or increased waiting time in the emergency department. Furthermore, the same group of patients showed an additional 1.3 h from the initial diagnosis to arrival at the PCI center, which can be explained by the time needed for transfer permission and ambulance arrival, by the delay created by other medical investigations (in case of atypical presentations), and transport time. Several other studies reveal similar issues when patients with STEMI arrive at the PCI center using secondary routes.[27-29] Accordingly, these delays may be considered inherent to a medical circuit in which multiple decision-making entities are involved, and their correction might be that much more problematic.

DOOR-TO-BALLOON TIME (PCI CENTER DELAY)

It is regarded as the most important indicator of quality of care and benefits from a wide array of research due to its association with mortality in pPCI and for its value as a hospital performance metric in patients with STEMI.[19] The current recommended target for door-to-balloon interval is <90 min.[8] Door-to-balloon time and mortality at 1 year seem to be independently associated, and for each 1-hour increase there is a 55% surge in 1-year mortality.[5] In our analysis, the median time for door-to-balloon interval was 69 min, and the target of <90 min was met in 67.1% of the patients. The guidelines of the American College of Cardiology and of the American Heart Association recommend reaching this target for >85% of patients with STEMI.7 However, there is a substantial number of patients outside this recommended target globally, suggesting the difficulties in reaching this goal.[30] The time consumed at the emergency department of the tertiary center represents a significant contributor to this interval. In our analysis, all patients had transthoracic echocardiography evaluation before departure to the catheterization laboratory. While an echocardiographic evaluation provides an important amount of information and perhaps is able to reveal unexpected findings that could otherwise hinder a proper STEMI management, we should emphasize that currently there seems to be no amount of supplementary information that compensates for the overall time delay before revascularization. Current evidence suggests that bypassing the emergency department could shorten the door-to-balloon time by at least 20 min.[8,31]

PREHOSPITAL THROMBOLYSIS

For pPCI to exert its clear advantage over fibrinolysis, it has to be performed inside a limited window of isch-

emia.[32,33] Although pPCI remains the preferred method of reperfusion, in this analysis the majority of patients did not meet the 120-min recommended threshold for revascularization. Nonetheless, the efficacy and safety of pharmacoinvasive reperfusion have been proven, and fibrinolytic therapy seems to compensate well for the additional ischemic time in patients who cannot reach pPCI as recommended.[34,35] Herein, prehospital thrombolysis was performed in 6.4% of the cases, while potential benefits from pharmacoinvasive reperfusion could have been expected in 64.5% of the patients. In favor of the regional reluctancy to administer fibrinolytics, an argument could be made that *PCI center delay* contributed to the underestimation of the FMC-to-revascularization interval. However, our data reveal that out of the 500 patients, 120 (24%) arrived at the PCI center more than 120 min after STEMI diagnosis, an interval which could have been more difficult to underestimate. This represents a category of patients who would have clearly benefited from fibrinolysis. The rate of prehospital thrombolysis seems unexpectedly low, but there are reports showing a steadily decreasing rate in Romania, from 45% in 2003 to 10.27% in 2011.[12]

The results of the present analysis should be interpreted in light of several limitations. First, they reveal the current situation regionally and cannot be extrapolated to a more generalized (national) level. Second, no data was collected to estimate door-in-door-out time, method of arrival at another hospital (self-presentation or ambulance transport), or reason for transport delay. Furthermore, for patients with prehospital thrombolysis, there are no data regarding the moment of fibrinolytics administration or clinical and ECG resolution.

CONCLUSIONS

The current outlook of the STEMI program suggests that further improvements are needed to obtain guideline-recommended timing targets. Patients with STEMI seem to arrive via secondary routes to the PCI center, which implies significantly increased ischemic times. The ambulance alert system and primary routes to the PCI center represent by far the most efficient, albeit still imperfect method of prehospital approach. Pharmacoinvasive therapy might be able to momentarily compensate for some of the gaps existing in the performance of the current system.

CONFLICT OF INTEREST

The authors report no conflicts of interest regarding the content herein.

ETHICAL APPROVAL

The study was conducted in accordance with the Declaration of Helsinki, and approved by the local Ethics Committee.

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