Impact of patient delay in a modern real world STEMI network

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ABSTRACT

Background: The impact of patient delay on left ventricular ejection fraction (LVEF), when system delay has performance that meets the current recommended guidelines, is poorly investigated.
Methods: We evaluated a cohort of STEMI patients treated with primary percutaneous coronary intervention (pPCI) and with an ECG STEMI diagnosis to wire crossing time (ETW) ≤120 min. Independent predictors of pre-discharge decreased LVEF (≤45%) were analyzed.
Results: 490 STEMI patients with both ETW time ≤120 min and available pre-discharge LVEF were evaluated. Mean age was 64.2 ± 12 years, 76.2% were male, 19.5% were diabetics, 42.7% had and anterior myocardial infarction (MI), and 9.8% were in Killip class III–IV. Median time of patient's response to initial symptoms (patient delay) was 58,5 (IQR 30;157) minutes and median ETW time was 78 (IQR 62–95) minutes. 115 patients (23.4%) had pre-discharge LVEF ≤45%. At multivariable analysis independent predictors of decreased LVEF (≤45%) were anterior MI (OR 4,659, 95% CI 2,618-8,289, $p < 0{,}001$), Killip class (OR 1,449, 95% CI 1,090-1,928, $p = 0{,}011$) and patients delay above the median (OR 2,030, 95% CI 1,151–3.578, $p = 0{,}014$). These independent predictors were confirmed in patients with ETW time ≤90 min.
Conclusions: When system delay meets the recommended criteria for pPCI, patient delay becomes an independent predictor of pre-discharge LVEF. These findings provide further insights into the potential optimization of STEMI management and identify a target that needs to be improved, considering that still a significant proportion of patients continue to delay seeking medical care.

1. Introduction

Achievement of early myocardial reperfusion is one of the main goals in ST-elevation myocardial infarction (STEMI) patients [1]. The recommended therapy to restore coronary blood flow in STEMI is reperfusion with primary percutaneous coronary intervention (pPCI) and time is a pivotal factor in successful treatment of these patients [1].

Pre-hospital organization with implementation of field triage with recording of 12-lead electrocardiogram (ECG) in the ambulance as well as optimization of in-hospital pathways to minimise the time for STEMI diagnosis and primary PCI [i.e. the system-of-care-dependent time (system delay)] improved markedly [2]. Treatment delays are nowadays considered index of quality of care in STEMI and reducing the system delay, is a major focus for improving STEMI treatment [1]. According to the recently updated guidelines [1], in out of hospital patients the time from ECG STEMI diagnosis to pPCI is recommended not to exceed 120 min, with an optimum of ≤90 min [1]. However the impact of patient delay on left ventricular ejection fraction (LVEF) when system delay has performance that meets the current recommended guidelines is poorly investigated. Therefore we evaluated the potential impact of patient delay, on pre-discharge LVEF, in patient treated in a modern STEMI network and with the recommended time from ECG STEMI diagnose to wire crossing (WC).

2. Methods

2.1. Study population and study design

We evaluated a cohort of STEMI patients treated with pPCI at the Cardiovascular Department of the University Hospital of Trieste (Trieste, Italy) from 1/1/2011 to 31/12/2016 and with guidelines criteria of ECG STEMI diagnosis to wire crossing time (ETW time) ≤120 min. STEMI

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diagnosis was defined according to STEMI guidelines [1]. All STEMI patients were consecutively enrolled in a primary PCI-Registry where clinical history, main demographic, clinical, laboratory, electrocardiographic and procedural data were included in a central database. The definition of Killip classes is reported in Table 1.

Starting from 2011, detailed reperfusions times were available in the pPCI-Registry. Furthermore, according to the institutional protocol, a complete echocardiographic evaluation was performed prior to discharge and echocardiographic data were also included in the central database.

2.2. Echocardiography

Ventricular dimensions, systolic and diastolic function were assessed according to international guidelines [3,4]. Specifically, LV and left atrial volumes and LVEF were calculated by Simpson's biplane method. All volumes were indexed according to body surface area. All measurements were obtained from the mean of 3 beats (patients in sinus rhythm) or 5 beats (atrial fibrillation).

2.3. Times delay

“Patient's delay” was defined as the time of patient's response to initial symptoms (i.e. the time from symptom onset to the emergency system (EMS) call or to arrival to the emergency department) and “system's delay” was defined as the time from ECG to WC.

2.4. Outcomes

The principal outcome investigated in this study was the presence of decreased left ventricular ejection fraction (LVEF ≤ 45%) at hospital discharge.

2.5. Statistical analysis

Data on a continuous scale are reported as mean and standard deviations or median and interquartile range as appropriate; categorical parameters are reported as counts and percentages. Descriptive comparisons between groups were tabulated and tested by means of the ANOVA test on continuous variables, using the Brown-Forsythe robust tests when appropriate or the non-parametric Median test for non-Gaussian variables. The Chi-square test or Fisher exact test was calculated on categorical parameters. Uni- and multi-variable odds ratios (OR) to identify factors associated with the outcome of interest (pre-discharge LVEF ≤45%) were estimated using logistic regression and taking into account the number of events per variable (EPV) of at least 1:10, a full model approach was applied to build the multivariable model.

3. Results

From January 2011 to December 2016, 1081 patients with STEMI were treated with pPCI. The time of the diagnostic ECG was not available in 270 patients. Out of the 811 remaining patients, 663 patients had ECG to WC within 120 min and out of these patients 490 had a pre-discharge LVEF evaluation and represent the study population.

Baseline characteristics of the study population are reported in Table 2. Mean age was 64.2 ± 12 years, 76.2% were male, 19.5% were diabetics, 42.7% had and anterior myocardial infarction (MI), and 9.8% were in Killip classes III–IV.

Median time of patient's response to initial symptoms (patient delay) was 58,5 (IQR 30;157) minutes (min), median ECG to WC time was 78 (IQR 62–95) min. 115 patients (23.4%) had pre-discharge LVEF ≤45% (Table 2).

Baseline differences between patients with pre-discharge moderate-severe LVEF dysfunction (≤45%) and mildly impaired-normal LVEF (>45%) are represented in Table 2.

Uni- and multivariable logistic regression model are presented in Table 3. The independent predictors of pre-discharge LVEF ≤45% were: anterior MI (OR 4,659, 95% CI 2,618-8,289, p < 0,001), Killip class (OR 1,449, 95% CI 1,090-1,928, p = 0,011) and patient delay above the median (OR 2,030, 95% CI 1,151–3.578, p = 0,014).

These independent predictors were confirmed in patients with ECG to WC time ≤90 min (n = 337): anterior MI (OR 6.834, 95% CI 3.237–14.427, p < 0,01), Killip class (OR 1.514, 95% CI 1.077–2.130, p = 0,07) and patient delay above the median (OR 2.386, 95% CI 1.158–4.917, p = 0,018).

4. Discussion

We evaluated in a contemporary real world STEMI network, the impact of patient delay on pre-discharge LVEF. We focused on patient treated with pPCI and with recommended times from ECG STEMI diagnose to WC. In this group of patients we showed that patient delay is an independent predictor of pre-discharge LVEF ≤45%. These findings provide further insights into the potential optimization of STEMI management in the current era of STEMI reperfusion, and are particularly important because they identify patients who need particular attention. When the time from qualifying ECG to reperfusion (i.e. the system-of-care-dependent time (system delay)) is as brief as it is recommended by current guidelines [1], this time may become a smaller fraction of total ischemic time. Therefore in this situation the patient-dependent time is a fundamental factor influencing myocardial savage. Despite the efforts to reduce “door-to-balloon” time over the past decade, an analysis from the Cath-PCI registry [5] questioned the usefulness of decreasing door-to-balloon times in the contemporary era of STEMI treatment. Indeed ECG to WC is only one component of total ischemic time, and the prognostic importance of short ECG to pPCI times [6] is likely to be modulated by the duration of ischaemia until diagnostic ECG is performed [7-9]. Considering that still a significant proportion of patients continue to delay seeking medical care [10] and that the education profile of patients is an important component to reduce delay [11], considerable efforts should still be made to educate the general public about the positive effects of an early and adequate first emergency call.

4.1. Limitations

Our research is subject to limitations. The results of this study are from a single STEMI network and our findings should be interpreted in light of the common limitations of a registry-based cohort studies. For the observational nature of the study we were able to provide only correlation with the explored outcome but not causation. Finally residual confounding cannot be excluded.

Table 1
Killip classification in patients presenting with acute myocardial infarction.

Killip class I	Patients with no clinical signs of heart failure
Killip class II	Patients with rales or crackles in the lungs, an S_3 gallop, and elevated jugular venous pressure
Killip class III	Patients with frank acute pulmonary edema
Killip class IV	Patients in cardiogenic shock or hypotension (systolic blood pressure < 90 mmHg), and evidence of low cardiac output (oliguria, cyanosis, or impaired mental status).

Table 2
Baseline characteristics of the study population.

	Total population $N = 490$	Pre-discharge LVEF > 45% $N = 375$	Pre-discharge LVEF ≤ 45% $N = 115$	*p*-value
Age	**64 ± 12**	**63 ± 12**	**67 ± 12**	**0,003**
Male sex	370 (75,5%)	280 (74,7%)	90 (78,3%)	0,433
Prior MI	41 (8,4%)	29 (7,7%)	12 (10,4%)	0,36
Hypertension	294 (60%)	228 (60,8%)	66 (57,4%)	0,514
Family history	157 (32%)	120 (32%)	37 (32,2%)	0,986
Smoking	281 (57,3%)	220 (58,7%)	61 (53,0%)	0,286
Diabetes mellitus	97 (19,8%)	68 (18,1%)	29 (25,2%)	0,095
Peripheral-artery disease	18 (3,7%)	12 (3,2%)	6 (5,2%)	0,317
Dyslipidaemia	280 (57,1%)	212 (56,5%)	68 (59,1%)	0,622
Cardiac arrest	43 (8,8%)	32 (8,5%)	11 (9,6%)	0,732
Anterior MI	**232 (47,3%)**	**144 (38,4%)**	**88 (76,5%)**	**0,001**
Killip class III–IV	**48 (9,8%)**	**28 (7,5%)**	**20 (17,4%)**	**0,002**
Chronic renal disease	**67 (13,7%)**	**46 (12,3%)**	**21 (18,2%)**	**0,039**
Basal TIMI flow II–III	**107 (21,8%)**	**90 (24%)**	**17 (14,7%)**	**0,033**
Anemia	150 (30,6%)	114 (30,4%)	36 (31,3%)	0,66
Systolic blood pressure	133,6 ± 29,6	134,5 ± 29,7	130,8 ± 28,6	0,243
Diastolic blood pressure	75,6 ± 15,6	75,5 ± 15,3	75,9 ± 16,6	0,815
Patient delay (min) (IQR[a])	58,5 (30;157)	52 (30;128)	90 (30;203)	0,068
Patient delay above the median	**50%**	**46,6%**	**60,7%**	**0,011**
Call to Wire crossing (min) (IQR)	97 (79; 115)	97 (79; 115)	100 (81;120)	0,405
ECG to Wire crossing (min) (IQR)	77 (61; 95)	75 (61;93)	83 (61;94)	0,167
Door to Wire crossing (min) (IQR)	57 (33; 93)	58 (33;96)	59,5 (34; 94)	0,985

[a] IQR = interquartile.

5. Conclusions

When system delay meets the recommended time for pPCI, patient delay becomes an independent predictor of pre-discharge LVEF. These findings provide further insights into the potential optimization of STEMI management in the current era of STEMI reperfusion, and are particularly important because they identify a target that needs to be improved, considering that still a significant proportion of patients continue to delay seeking medical care.

Author statement

Enrico Fabris: study concept and design, drafting of the manuscript, analysis and interpretation of data.

Table 3
Uni- and multivariable analyses.

Unadjusted ORs				Adjusted ORs		
	OR	CI	*p*-value	OR	CI	*p*-value
Age	1,027	1,009–1,046	0,004	1.012	0,988-1,037	0,311
Male sex	1,221	0,74–2,015	0,433			
Prior MI	1,39	0,685–2,821	0,362			
Hypertension	0,868	0,568–1,327	0,514			
Family history	1,004	0,642–1,571	0,986			
Diabetes Mellitus	1,522	0,927–2,5	0,097	0,970	0,500–1,881	0,928
Smoking	0,796	0,523–1,211	0,287			
Dyslipidaemia	1,112	0,728–1,7	0,623			
Peripheral-artery disease	1,661	0,609–4,528	0,322			
Cardiac arrest	1,134	0,552–0,328	0,732			
Anterior MI	**5,406**	**3,33–8,776**	**<0,001**	**4,659**	**2,618–8,289**	**<0,01**
Killip class	**1,579**	**1,270–1.963**	**<0,001**	**1,449**	**1,090–1,928**	**0,011**
Systolic blood pressure	0,996	0,988–1,003	0,243			
Diastolic blood pressure	1,002	0,988–1,015	0,815			
Chronic renal disease	1,826	1,024–3,255	0,041	1,363	0,656–2,831	0,406
Anemia	1,11	0,696–1,77	0,66			
Basal TIMI flow II-III	0,543	0,307–0,958	0,035	0,501	0,236–1,062	0,071
Patient delay above the median[a]	**1,774**	**1,139–2,764**	**0,018**	**2,030**	**1,151–3.578**	**0,014**

[a] Median time 58,5 (30;157) min.

Paola Arrigoni: acquisition, analysis, interpretation of data and critical revision of the manuscript for important intellectual content.

Giulia Barbati: analysis, interpretation of data and critical revision of the manuscript for important intellectual content.

Luca Falco, Davide Stolfo, Alberto Peratoner, Giancarlo Vitrella, Serena Rakar, Andrea Perkan: *interpretation of data and critical revision of the manuscript for important intellectual content.*

Gianfranco Sinagra: Study concept and design. Critical revision of the manuscript for important intellectual content.

Declaration of competing interest

The authors report no relationships that could be construed as a conflict of interest.

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