ORIGINAL ARTICLE

Temporal trends and prognostic impact of reperfusion modalities in Tunisian patients presenting with ST-elevation myocardial infarction: A 20-year analysis

Tendances temporelles et impact pronostique des modalités de reperfusion chez les patients Tunisiens se présentant pour infarctus avec sus décalage du segment ST : Analyse sur 20 ans

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Abstract

Introduction: With the advent of reperfusion therapies, management of patients presenting with ST-elevation myocardial infarction (STEMI) has witnessed significant changes during the last decades.
Aim: We sought to analyze temporal trends in reperfusion modalities and their prognostic impact over a 20-year period in patients presenting with STEMI the Monastir region (Tunisia).
Methods: Patients from Monastir region presenting for STEMI were included in a 20-year (1998-2017) single center registry. Reperfusion modalities, early and long-term outcomes were studied according to five four-year periods.
Results: Out of 1734 patients with STEMI, 1370 (79%) were male and mean age was 60.3 ± 12.7 years. From 1998 to 2017, primary percutaneous coronary intervention (PCI) use significantly increased from 12.5% to 48.3% while fibrinolysis use significantly decreased from 47.6% to 31.7% (p<0.001 for both). Reperfusion delays for either fibrinolysis or primary PCI significantly decreased during the study period. In-hospital mortality significantly decreased from 13.7% during Period 1 (1998-2001) to 5.4% during Period 5 (2014-2017), (p=0.03). Long-term mortality rate (mean follow-up 49.4 ± 30.7 months) significantly decreased from 25.3% to 13% (p<0.001). In multivariate analysis, age, female gender, anemia on-presentation, akinesia/dyskinesia of the infarcted area and use of plain old balloon angioplasty were independent predictors of death at long-term follow-up whereas primary PCI use and preinfaction angina were predictors of long-term survival.
Conclusions: In this long-term follow-up study of Tunisian patients presenting for STEMI, reperfusion delays decreased concomitantly to an increase in primary PCI use. In-hospital and long-term mortality rates significantly decreased from 1998 to 2017.

Key words: ST-elevation myocardial infarction, prognosis, myocardial reperfusion, primary percutaneous coronary intervention, Tunisia, North Africa

Résumé

Introduction: Grace aux thérapeutiques de reperfusion, la prise en charge des patients se présentant pour infarctus du myocarde avec sus-décalage du segment ST (IDMST) a vécu une métamorphose durant les dernières décennies.
Méthodes: Les tendances en termes de reperfusion et de mortalité ont été analysées dans ce registre de 20 ans de patients se présentant pour IDMST dans la région de Monastir.
Résultats: Sur 1734 patients atteints d'IDMST, 1370 (79%) étaient des hommes et l'âge moyen était de 60,3 ± 12,7 ans. De 1998 à 2017, l'utilisation de l'intervention coronarienne percutanée (ICP) primaire est passée de 12,5% à 48,3%, tandis que l'utilisation de la fibrinolyse est passée de 47,6% à 31,7% (p<0,001 pour les deux). La mortalité hospitalière est passée de 13,7% au cours de la période 1998-2001 à 5,4% au cours de la période 2014-2017 (p=0,03). La mortalité à long terme (suivi moyen de 49,4 ± 30,7 mois) a significativement diminué de 25,3% à 13% (p<0,001). En analyse multivariée, l'âge, le sexe féminin, l'anémie à la présentation, l'akinésie/dyskinésie de la région infarcie et l'utilisation de l'angioplastie par ballonnet ordinaire étaient des prédicteurs indépendants de décès à long terme, tandis que l'ICP primaire et l'angor pré-infarctus étaient des prédicteurs de survie à long terme.
Conclusions: Dans cette étude entre 1998 et 2017, les délais de reperfusion des IDMST ont diminué concomitamment à une augmentation de l'utilisation de l'ICP primaire. La mortalité hospitalière et à long terme a significativement diminué.

Mots clés: Infarctus du myocarde avec sus-décalage du ST, pronostic, reperfusion myocardique, intervention coronaire percutanée primaire, Tunisie, Afrique du Nord

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Introduction

In the last four decades, management of ST-elevation myocardial infarction (STEMI) has witnessed a significant transformation worldwide [1-3]. In Western countries, fibrinolytic therapy, antithrombotic treatments, and the implementation of primary percutaneous coronary intervention (PCI) networks led to a substantial decline in early and long-term mortality and complications [4-7]. Main modifications consisted in the rapid shift to primary PCI for over than 90% of patients with STEMI, the introduction of clopidogrel then of more potent anti P2Y12 antiplatelet agents, and the implementation of new lipid lowering drugs aiming at reducing atherosclerosis related events [2, 4, 8]. In countries of the Middle East and North Africa (MENA) region, STEMI management is still affected in one hand by a somewhat random access to reperfusion therapies and territorial discrepancies in coronary care units (CCU) distribution, and in the other, by insufficient patient follow-up and secondary prevention. In the last few years, available publications from national registries and surveys addressed the high cardiovascular risk profile that characterizes these patients and the dire short-term prognosis in this setting [9-11]. Reports concerning the progressive implementation of reperfusion therapeutics in STEMI over time and their potential long-term prognostic impact are clearly lacking.

In this study, we sought to delineate temporal trends in reperfusion therapy utilization, short and long-term mortality in patients presenting for STEMI in the Monastir region (Tunisia) over a 20-year study period.

Methods

The current study was carried-out on data extracted from a single center retrospective registry. All consecutive patients aged 18 and older presenting to a major tertiary care facility in the Monastir region (Tunisia) for STEMI between January 1998 and December 2017 were enrolled. The registry was updated in a regular fashion (every 1 to 2 years) by two senior academic staff for data integrity, patient follow-up and outcomes. Patients presenting with STEMI were admitted via the emergency department (ED) or via the regional emergency medical service (EMS). STEMI diagnosis was retained in the presence of a significant ST-segment elevation (2 mm in precordial leads or 1 mm in frontal leads) in two contiguous leads on electrocardiogram (ECG) or in the presence of a presumably new left bundle branch block concomitantly to a prolonged (>20 minutes) chest pain or discomfort. For STEMI early management, medical staff in our department, our regional EMS as well as ED were basically implementing the European guidelines for the diagnosis and management of patients presenting with STEMI [12]. That is patients presenting to the ED or to a nearby healthcare facility (in the Monastir Governorate area) were whenever possible swiftly transferred for primary PCI. When long transfer delays (>90 to 120 minutes) were expected, and in the absence of contra-indications, fibrinolytic therapy is administered then patients are referred as soon as possible to our department for reassessment and potential rescue PCI or diagnostic invasive coronary angiography (ICA). Notwithstanding, the registry included patients with STEMI managed with no reperfusion therapy (conservative treatment) at the early phase. Reasons for that include late presentation, spontaneous reperfusion, very old age. At the exception of a negligible number, all patients received clopidogrel (loading dose of 300 or 600 mg and 75 mg/day thereafter), aspirin and intravenous unfractionated heparin or enoxaparin as recommended. In patients receiving fibrinolytic therapy, thrombolytic agents used included streptokinase, alteplase and tenecteplase. In case of primary or rescue PCI, dilatation balloons, bare metal/drug-eluting stents, thrombus aspiration and GP IIb-IIIa inhibitors were used at the operator's discretion, depending on availability and in accordance with European guidelines. Symptoms, transfer and reperfusion delays were estimated using ED and EMS records and during thrombolysis and PCI procedures. We opted to report the symptom-to-reperfusion delay, i.e symptom-to-fibrinolysis or symptom-to-balloon delay rather than door-to-needle or door-to-balloon time, due to a better availability of these data in patient files and to the good predictive value of total ischemic time for early outcomes in previous studies [13-15]. Risk profile, baseline demographic and clinical characteristics were specified in all patients upon admission. Routine biology tests were withdrawn in all patients according to local protocols. Creatinine clearance was calculated using the Modification of Diet in Renal Disease (MDRD) formula. For the purpose of the current study, chronic kidney disease was considered in patients presenting with a creatinine clearance ≤60 mL/min. In accordance with the World Health Organization criteria, anemia was defined as a hemoglobin rate <13 g/dL in men and <12 g/dL in women [16]. Transthoracic echocardiography was performed in the first 48 hours and anytime a complication was suspected. Parameters reported were left ventricle (LV) systolic and diastolic diameters, LV ejection fraction by the Simpson method, regional kinetic abnormalities, LV filling pressures and pulmonary pressures. Patients were observed in the coronary care unit (CCU) for at least 48 hours and put on adjunctive medications (beta blockers, statins, angiotensin converting enzyme inhibitors/angiotensin receptor blockers) as guideline recommended. Major bleeding was defined as any fatal, cerebral bleeding or overt bleeding mandating urgent transfusion. After discharge, patients were followed in outpatient clinics at one to two months, at 6 months, then biyearly. Patients lost to clinical follow-up were contacted by phone. Time between index STEMI and last follow-up or death was documented.

Statistical analysis

For the current analysis, the overall study period was divided into five periods of four years each: Period 1, from 1998 to 2001, Period 2, from 2002 to 2005, Period 3, from 2006 to 2009, Period 4, from 2010 to 2013, and Period 5, from 2014 to 2017. Trends in risk profile,

reperfusion therapy, early and long-term mortality were determined. Categorical variables are expressed in absolute values and percentages. Continuous variables are expressed in means ± SD or by median value and interquartile range in case of non-normal distribution. The chi-square test was applied to compare categorical variables. The one-way ANOVA or the Kruskal Wallis tests were applied to compare continuous variable means or medians between periods as appropriate. Kaplan Meier curves for long-term survival were represented according to the reperfusion strategy adopted (i.e., thrombolysis, primary PCI or no reperfusion). Log rank test was applied for comparison between different reperfusion modalities outcome. Independent long-term predictors of death or survival were determined using multivariable binary logistic regression applied on a variable set. Categorical variables chosen to be included in the multivariate model were determined using chi-square univariate analysis on long-term mortality (cut-off p for selection <0.2) in addition to other forced variables judged as relevant for the model. Odds and accompanying 95% confidence intervals were reported and a p value <0.05 was set for statistical significance. Data collection and statistical analysis were performed using Statistical Package for Social Sciences (SPSS) V. 21 for Windows.

Results

A total of 1734 patients presenting for STEMI were enrolled in the present study. Mean age was 60.3 ± 12.7 and 1370 (79%) were male. Prevalence of tobacco smoking, hypertension and diabetes mellitus in the overall study population was 66.8%, 30.1% and 35.9%, respectively. Baseline characteristics of study population according to study period are presented in table I. Prevalence of female gender in STEMI patients increased from 16.9% during Period 1 to 34.2% during Period 5 (p<0.001). Prevalence of classical cardiovascular risk factors remained relatively stable throughout the study periods at the exception of dyslipidemia that moderately decreased throughout the study period (table III).

Table 1. Baseline characteristics according to study period.

	Period 1 [1998-2001] (n=473)	Period 2 [2002-2005] (n=495)	Period 3 [2006-2009] (n=263)	Period 4 [2010-2013] (n=188)	Period 5 [2014-2017] (n=315)	P
Mean age, ± SD	60.8 ± 12.8	61 ± 12.9	59.9 ± 12.2	58.5 ±12.7	59.8 ± 12.4	0.15
Age ≥75 years	68 (14.4%)	79 (16%)	29 (11%)	23 (12.2%)	49 (15.6%)	0.34
Female Gender	80 (16.9%)	91 (18.4%)	47 (17.9%)	40 (21.3%)	106 (34.2%)	<0.001
Hypertension	131 (27.7%)	146 (29.5%)	99 (37.6%)	49 (26.1%)	97 (30.8%)	0.04
Diabetes Mellitus	168 (35.5%)	173 (34.9%)	96 (36.5%)	63 (33.5%)	123 (39%)	0.7
Hypercholesterolemia	52 (11%)	53 (10.7%)	32 (12.2%)	27 (14.4%)	56 (17.8%)	0.028
Current Smoker	309 (65.3%)	347 (70.1%)	167 (63.5%)	125 (66.5%)	211 (67%)	0.37
Prior STEMI	24 (5.1%)	29 (5.9%)	10 (3.8%)	6 (3.2%)	8 (2.5%)	0.002
Prior PCI	7 (1.7%)	21 (4.2%)	15 (5.7%)	15 (8%)	77 (24.4%)	<0.001
History of Heart Failure	11 (2.3%)	15 (3%)	3 (1.1%)	4 (2.1%)	5 (1.6%)	0.46
Peripheral Artery Disease	19 (4%)	17 (3.4%)	6 (2.3%)	6 (3.2%)	10 (3.2%)	0.80
Chronic Kidney Disease	41 (8.7%)	45 (9.1%)	15 (5.7%)	16 (8.5%)	16 (5.2%)	0.047

PCI, Percutaneous Coronary Intervention, STEMI, ST-elevation Myocardial Infarction.

Patients presented to ED or to EMS with chest pain in a large majority of cases (table II). Recourse to EMS for transport increased throughout study periods reaching 57.8% during Period 5. Although prevalence of cardiogenic shock on-presentation remained stable over time, heart failure on-presentation decreased significantly from 25.4% during Period 1 to 18.7% during Period 5 (p=0.008). Prevalence of patients undergoing ICA during hospitalization increased over time to reach 98.4% during Period 5. Prevalence of three vessel disease on ICA declined significantly from 28.4% in Period 1 to 14.5% in Period 5 (p<0.001).

Regarding reperfusion therapies (table III, Figure 1), thrombolysis was the most adopted strategy in Period 1 with 47.6%, significantly decreasing to 31.7% in Period 5 (p<0.001). Conversely, recourse to primary PCI increased over time from 12.5% in Period 1 to attain 48.3% in Period 5 (p<0.001).

As for reperfusion delays (i.e., symptom-to-fibrinolysis delay and symptom-to-primary PCI delay), and irrespective to reperfusion therapy, they steadily

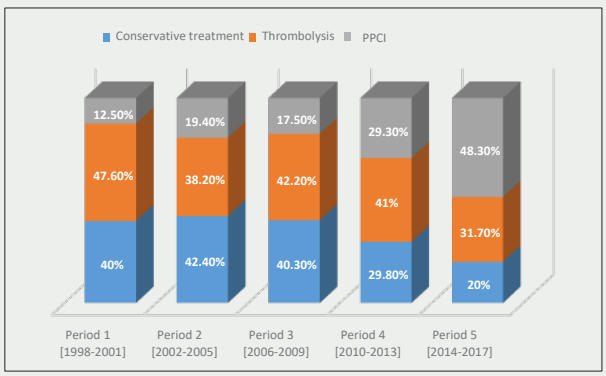

Figure 1. Trends in reperfusion strategies according to study period.
PPCI, primary percutaneous coronary intervention.

Table 2. Clinical characteristics on-presentation according to study period.

	Period 1 [1998-2001] (n=473)	Period 2 [2002-2005] (n=495)	Period 3 [2006-2009] (n=263)	Period 4 [2010-2013] (n=188)	Period 5 [2014-2017] (n=315)	P
Chest Pain on Presentation	435 (92%)	433 (87.5%)	245 (93.2%)	177 (94.1%)	306 (97.1%)	<0.001
Transport by EMS	229 (48.4%)	263 (53.1%)	107 (55.5%)	107 (56.9%)	182 (57.8%)	<0.001
Systolic Blood Pressure (mmHg), [IQR]	120 [110-140]	120 [110-140]	127 [115-150]	130 [120-145]	122 [110-140]	0.28
Heart Failure	120 (25.4%)	120 (24.2%)	49 (18.6%)	28 (14.9%)	59 (18.7%)	0.008
Cardiogenic Shock	17 (3.6%)	15 (3%)	9 (3.4%)	8 (4.3%)	10 (3.2%)	0.94
Q Wave on Presentation	231 (48.8%)	234 (47.3%)	80 (30.4%)	53 (28.2%)	85 (27%)	<0.001
LBBB	20 (4.2%)	21 (4.2%)	8 (3%)	5 (2.7%)	6 (1.9%)	0.034
Median Tn I Peak (µg/L), [IQR]	31.3 [3.5-352.1]	29.3 [3.9-236]	25 [4.3-123.1]	20.5 [1.9-109]	19.5 [2.3-89.6]	0.020
Median Plasma Creatinin (µmol/L), [IQR]	104 [90-122]	92 [78-114]	89 [76-106]	85 [74-103]	79 [68-98]	<0.001
Median Hemoglobin (g/dL), [IQR]	13.2 [12.1-14.5]	13.2 [12-14.5]	13.4 [12-14.8]	13.4 [12-14.8]	13.4 [12.1-14.4]	0.29
Anemia	90/473 (19%)	82/495 (16.5%)	39/263 (14.8%)	27/188 (14.3%)	42/310 (13.5%)	0.032
ICA	333 (70.4%)	406 (82%)	221 (84%)	179 (95.2%)	310 (98.4%)	<0.001
Normal Coronary Artery Angiogram	18 (5.4%)	6 (1.5%)	9 (4.1%)	2 (1.1%)	8 (2.6%)	0.074
Single Vessel Disease	160 (48%)	218 (53.7%)	120 (54.1%)	109 (60.9%)	196 (63.2%)	<0.001
3-Vessel Disease	134 (28.4%)	123 (24.9%)	47 (18%)	32 (17.3%)	46 (14.5%)	<0.001
LVEF <50%	97/229 (42.3%)	114/276 (41.3%)	39/101 (38.6%)	45/141 (31%)	82/295 (27.7%)	0.021
Akinesia/Dyskinesia of the infarcted area	73/229 (31.8%)	72/276 (26.1%)	24/101 (23.7%)	19/141 (13.4%)	21/295 (7.1%)	<0.001

EMS, Emergency Medical Service, ICA, Invasive Coronary Angiography, LBBB, Left Bundle Branch Block, LVEF, Left Ventricle Ejection Fraction, Tn I, Troponin I

Table 3. Trends in reperfusion modalities and delays over 20 years.

	Period 1 [1998-2001] (n=473)	Period 2 [2002-2005] (n=495)	Period 3 [2006-2009] (n=263)	Period 4 [2010-2013] (n=188)	Period 5 [2014-2017] (n=315)	P
Symptoms-to-FMC delay * (h), [IQR]	5 [4-8.25]	5 [3-6.25]	4 [3-6]	4 [3-6]	2 [1.5-5]	0.028
Thrombolysis	225 (47.6%)	189 (38.2%)	111 (42.2%)	77 (41%)	100 (31.7%)	<0.001
Symptom-to-thrombolysis delay (h), [IQR]	4 [3-6]	4 [3-7]	3 [2-4]	3 [2-4]	3 [2-4.75]	0.040
Primary PCI	59 (12.5%)	96 (19.4%)	46 (17.5%)	55 (29.3%)	152 (48.3%)	<0.001
Symptom-to-balloon delay (h), [IQR]	6 [3-16]	4 [2-7.75]	5 [3-8]	3,5 [1-6.25]	3 [1-4]	<0.001
Stent use	52 (85.2%)	89 (91.8%)	41 (89.1%)	52 (94.5%)	147 (96.7%)	0.042
Thrombus aspiration	0 (0%)	1 (1%)	1 (2.2%)	4 (7.3%)	7 (4.6%)	0.013
POBA only	112/309 (36.2%)	103/395 (26%)	52/233 (22.3%)	29/168 (17.2%)	12/226 (5.3%)	<0.001

* Symptoms-to-FMC delay was calculated for the overall study population. FMC, First Medical Contact, PCI, Percutaneous Coronary Intervention, POBA, Plain Old Balloon Angioplasty

In-hospital complications and mortality are presented in table IV. In summary, ventricular arrhythmia, new-onset atrial fibrillation and major bleeding significantly decreased from Period 1 to Period 5. In-hospital mortality significantly decreased from 13.7% during Period 1 to 5.4% during Period 5 (p=0.03). Mean long-term follow-up was 49.4 ± 30.7 months in the overall population, with an overall long-term mortality rate of 19.4%. Long-term mortality rate decreased significantly from 25.3% (mean follow-up 40.3 ± 25.7 months) during Period 1 to 13% (mean follow-up 47 ± 23.9 months) during Period 5 (p<0.001). Figure 2 illustrates Kaplan Meier curves for long-term survival according to reperfusion strategy used with better long-term survival for patients treated with primary PCI compared to those treated with fibrinolysis or with no reperfusion therapy (log-rank p<0.001).

Table 4. In-hospital complications and mortality according to study period.

	Period 1 [1998-2001] (n=473)	Period 2 [2002-2005] (n=495)	Period 3 [2006-2009] (n=263)	Period 4 [2010-2013] (n=188)	Period 5 [2014-2017] (n=315)	P
RV Infarction	19 (4%)	21 (4.2%)	6 (2.3%)	7 (3.7%)	15 (4.8%)	0.62
Ventricular arrhythmia	22 (4.7%)	17 (3.4%)	9 (3.4%)	6 (3.2%)	7 (2.2%)	0.01
Atrioventricular Block	49 (10.4%)	50 (10.1%)	43 (16.3%)	38 (20.2%)	57 (18.1%)	0.72
New Onset Atrial Fibrillation	39 (8.2%)	34 (6.9%)	11 (4.2%)	7 (3.7%)	11 (3.5%)	0.019
Major Bleeding	21 (4.4%)	13 (2.6%)	6 (2.3%)	4 (2.1%)	6 (1.9%)	0.019
In-hospital mortality	64 (13.7%)	53 (10.7%)	22 (8.4%)	16 (8.5%)	17 (5.4%)	0.03
Mean follow-up (months), ± SD	40.3 ± 25.7	50.2 ± 33	61.1 ± 35.4	53.6 ± 32	47 ± 23.9	<0.001
Long-term mortality	120 (25.3%)	98 (19.8%)	48 (18.3%)	29 (15.4%)	41 (13%)	<0.001

RV, Right Ventricle

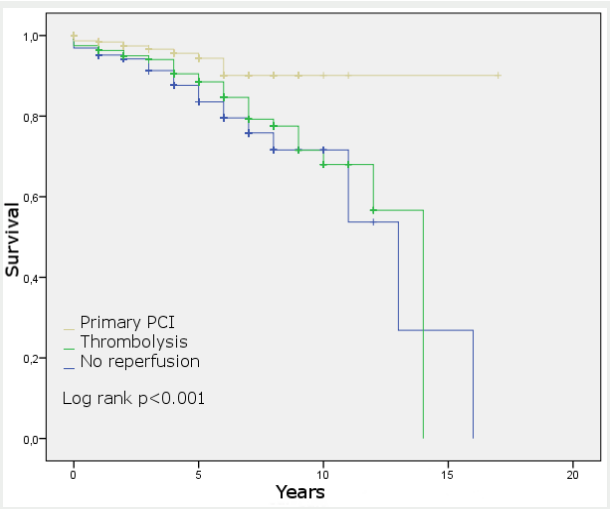

Figure 2. Kaplan Meier curves for long-term survival according to reperfusion strategy.
PCI, Percutaneous coronary intervention

In multivariate analysis, factors independently associated to long-term mortality (table V) include age (OR=1.08 by year of age, 95% CI: 1.05-1.11, p<0.001), female gender (OR=3.02, 95% CI: 1.54-5.89, p=0.001), anemia on-presentation (OR=2.54, 95% CI: 1.24-5.21, p=0.011), akinesia or dyskinesia of the infarcted area on rest echocardiography (OR=3.01, 95% CI: 1.55-5.84, p=0.001) and plain old balloon angioplasty in patients receiving PCI (OR=2.81, 95% CI: 1.47-5.39, p=0.002). Conversely, factors independently associated to long-term survival were primary PCI (OR=0.31, 95% CI: 0.17-0.58, p<0.001), and preinfarction angina (OR=0.35, 95% CI: 0.17-0.74, p=0.006).

Table 5. Factors independently associated to long-term death in multivariate analysis.

Variable	P	OR	95% Confidence Interval
Age (by year)	<0.001	1.08	1.05 - 1.11
Female Gender	0.001	3.02	1.54 - 5.89
Anemia on-presentation	0.011	2.54	1.24 - 5.21
Akinesia/Dyskinesia of the infarcted area	0.001	3.01	1.55 - 5.84
Primary PCI	<0.001	0.31	0.17 - 0.58
POBA only	0.002	2.81	1.47 - 5.39
Preinfarction angina	0.006	0.35	0.17 - 0.74

PCI, Percutaneous Coronary Intervention, POBA, Plain Old Balloon Angioplasty

Discussion

The current study presents a unique depiction of major changes in epidemiological characteristics, clinical presentation, management, early and long-term mortality in Tunisian patients presenting for STEMI in a main tertiary care facility over a 20-year period. To the best of our knowledge, this is the first large study from a North African country that focuses on trends in reperfusion modalities in STEMI with such a long inclusion period and clinical follow-up.

The first observation we depict herein is the heavy burden of cardiovascular risk factors in Tunisian patients with STEMI that was overall stable along the study duration. These findings remain in line with those from Gulf registries [17-19] and at a lesser extent with major western STEMI registries where prevalence of classical coronary risk factors, diabetes mellitus and tobacco smoking in particular, are lower than reported in the present study [6, 8, 20, 21]. Another important fact is the tangible increase in female gender prevalence along the 20-year study period. This may have a substantial impact on informing management strategies to be implemented given the higher prevalence of comorbidities and the risk of complications and mortality in women compared to men documented in several reports [22-24].

It is remarkable that from 1998 to 2017, recourse to fibrinolysis decreased progressively along with a gradual increase in primary PCI use. This is actually related to several factors including the progressive adoption of the European guidelines by the different protagonists involved in STEMI patient care, better logistics, and better availability of catheterization platform and personnel. Primary PCI for STEMI is nowadays the gold standard for STEMI management when performed timely by experienced operators. Its superiority over fibrinolysis regarding survival, reinfarction, revascularization, and heart failure occurrence has been largely demonstrated [25]. In concurrence with that, survival analysis in the current study suggests similar findings demonstrating better long-term outcomes with primary PCI in comparison to fibrinolysis or no immediate reperfusion. Likewise, primary PCI use was found to be an independent predictor of better long-term survival in multivariable analysis. Nevertheless, fibrinolysis as a reperfusion therapy in acute STEMI remains a viable option in developing countries especially when utilized as part of the pharmacoinvasive strategy and when new fibrinospecific agents are administered by EMS [26, 27].

In parallel with the shift in reperfusion modalities, we witnessed a decrease in symptom-to-reperfusion delays in the overall study population and for each reperfusion modality, which has been proven to impact early and late outcomes in STEMI. Although symptom-to-reperfusion delay does not strictly equal total ischemic time, it seems to be a good surrogate to the latter in clinical practice [28, 29]. Furthermore, total ischemic time also depends on the time to first medical contact, a parameter that is highly dependent on the patient himself. Higher recourse to transport by EMS and better awareness of the Tunisian population about cardiovascular disease are possible explanations to the decreasing trend we observed in all these delays.

It is also interesting to notice that concomitantly to the decreasing trend in reperfusion delays, in-hospital complications and mortality declined. Indeed, between 1998 and 2017, in-hospital mortality has been more than halved with more than 8% absolute reduction. Although a causative relationship between the two phenomena may be evoked, such a conclusion should not be systematically drawn due to the multitude of other factors impacting early and long-term survival in patients with STEMI. Reduction in reperfusion delays as well as the adoption of evidence-based secondary prevention therapeutics were broadly investigated in European registries with obvious

impact on early and late outcomes in patients presenting with STEMI [3, 21, 30].

Among long-term predictors of death in the current study, most of them were already reported in previous studies, although mitigated in some instances like female gender and plain old balloon angioplasty [31, 32]. One unique factor reported herein is the occurrence of preinfarction angina that was associated with better long-term survival in patients presenting for STEMI. Preinfarction angina is frequently regarded as synonymous with ischemic preconditioning, a phenomenon found to be associated to lesser infarct size in animal as well as human studies [33, 34]. Further investigation as for actual clinical significance and factors associated with ischemic preconditioning in our context is warranted.

Study limitations

Although highly informative about STEMI risk profile, management and prognosis in the Tunisian context, our study entails several limitations that have to be acknowledged. First, the retrospective character of the study made it difficult to draw any firm conclusion regarding a cause-effect relationship between patients' characteristics and management on one hand and early and late outcomes on the other. Some variables such as vascular access route and type of stent implanted were not reported herein due to the lack of accuracy in reporting them in some patients' files. Although we insist that a great majority of patients received pharmacological therapeutics for secondary prevention according to contemporary guidelines, prevalence of their use and doses were not studied. Such therapeutics have plausibly a substantial effect on the improvement observed in the prognosis of patients presenting with STEMI in most of international studies. Finally, long-term outcomes other than mortality (such as ischemia driven revascularization or heart failure) were not studied.

Conclusions

By observing actual trends over 20 years in reperfusion strategies in STEMI patients in a Tunisian region, the current study demonstrated an upward evolution in primary PCI use concomitant to a significant reduction in reperfusion delays. These facts were associated to a decrease in early and long-term mortality in STEMI patients.

List of abbreviations
CCU: Coronary care units
ED: Emergency department
EMS: Emergency medical service
ICA: Invasive coronary angiography
MDRD: Modification of Diet in Renal Disease
MENA: Middle East and North Africa
PCI: Percutaneous coronary intervention
SPSS: Statistical Package for Social Sciences
STEMI: ST-elevation myocardial infarction

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