Observational Study

Medicine

OPEN

Early survival after acute myocardial infarction with ST-segment elevation

What could be improved? Insights from France PCI French registry

Benjamin Duband, MD[a,*], Pascal Motreff, MD, PhD[a], Pierre Marcollet, MD[b], Alexandre Gamet, MD[c], Marie-Pascale Decomis, MD[d], Olivier Bar, MD[e], Christophe Saint Etienne, MD[f], Radwan Hakim, MD[g], Alexandre Canville, MD[h], Louis Viallard, MD[i], Farzin Beygul, MD, PhD[j], Pierre Francois Lesault, MD[k], Philippe Bonnet, MD[l], Eric Durand, MD, PhD[m], Emmanuel Boiffard, MD[n], Jean-Philippe Collet, MD, PhD[o], Hakim Benamer, MD[p], Philippe Commeau, MD[q], Guillaume Cayla, MD, PhD[r], Bruno Pereira, MD, PhD[s], Rene Koning, MD[h], Gregoire Rangé, MD[g]

Abstract

Early mortality post-ST-segment elevation myocardial infarction (STEMI) in France remains high. The multicentre France Percutaneous Coronary Intervention Registry includes every patient undergoing coronary angiography in France. We analyzed the prevalence and impact of unmodifiable and modifiable risk factors on 30-day survival in patients experiencing STEMI.

Patients admitted for STEMI between 01/2014 and 12/2016 were included in the analysis. Patients with nonobstructive coronary artery disease, with cardiogenic shock or cardiac arrest without STEMI, were excluded. Prehospital, clinical and procedural data were collected prospectively by the cardiologist in the cath lab using medical reporting software. Information on outcomes, including mortality, was obtained by a dedicated research technician by phone calls or from medical records. Marginal Cox proportional hazards regression was used to test the predictive value for survival at 30 days in a multivariable analysis.

Included were 2590 patients (74% men) aged 63 ± 14 years. During the first month, 174 patients (6.7%) died. After adjustment, unmodifiable variables significantly associated with reduced 30-day survival were: age > 80 years (prevalence 15%; hazard ratio [HR] 2.7; 95% confidence interval [CI] 1.5–4.7), chronic kidney disease (2%; HR 5.3; 95% CI 2.6–11.1), diabetes mellitus (14%; HR 1.6; 95% CI 1.0–2.5), anterior or circumferential electrical localization (39%; HR 2.0; 95% CI 1.4–2.9), and Killip class 2, 3, or 4 (7%; HR 3.4; 95% CI 1.9–5.9; 2%; HR 10.1; 95% CI 5.3–19.4; 4%; HR 18; 95% CI 10.8–29.8, respectively). Among modifiable variables, total ischemic time > 3 hours (68%; HR 1.8; 95% CI 1.1–3.0), lack of appropriate premedication (18%; HR 2.2; 95% CI 1.5–3.3), and post-PCI TIMI < 3 (6%; HR 4.9; 95% CI 3.2–7.6) were significantly associated with reduced 30-day survival.

Most predictors of 30-day survival post-STEMI are unmodifiable, but outcomes might be improved by optimizing modifiable factors, most importantly ischemic time and appropriate premedication.

Abbreviations: CKD = chronic kidney disease, FAST-MI = French registry of acute ST-elevation or non-ST-elevation myocardial infarction, FMC = first medical contact, PCI = percutaneous coronary intervention, SAMU = Service d'aide médicale d'urgence, STEMI = ST-segment elevation myocardial infarction.

Keywords: France, prognostic factors, ST-elevation myocardial infarction, survival analysis

This work was supported by the regional health agency of Centre Val de Loire, Auvergne Rhône Alpes, and the French Ministry of Health.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Trial registration: The France PCI study is registered on clinicaltrial.gov (NCT02778724).

Supplemental Digital Content is available for this article.

[a] Cardiology Department, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, France, [b] Cardiology Department, Centre Hospitalier Jacques Cœur, Bourges, France, [c] Cardiology Department, Centre Hospitalier Régional d'Orléans, Orléans, France, [d] Cardiology Department, Clinique Oréliance, Orléans, France, [e] Cardiology Department, Centre Hospitalier Universitaire de Tours, Tours, France, [f] Cardiology Department, Nouvelle Clinique Tourengelle, Saint-Cyr-sur-Loire, France, [g] Cardiology Department, Les hôpitaux de Chartres, Chartres, France, [h] Cardiology Department, Clinique Saint-Hilaire, Rouen, France, [i] Cardiology Department, Centre Hospitalier Henri Mondor, Aurillac, France, [j] Cardiology Department, Centre Hospitalier Universitaire de Caen, Caen, France, [k] Cardiology Department, Hôpital Privé de l'Estuaire, Le Havre, France, [l] Cardiology Department, Centre Hospitalier Le Havre, Le Havre, France, [m] Cardiology Department, Rouen University Hospital, FHU REMOD-VHF, 76000 Rouen, France; Normandie Université, UNIROUEN, INSERM U1096, 76000 Rouen, France, [n] Cardiology Department, Centre Hospitalier Départemental Vendée, La Roche-sur-Yon, France, [o] Cardiolgy Department, Groupe Hospitalier Pitié-Salpêtrière, Paris, France, [p] Cardiology Department, Clinique de la Roseraie, Soissons, France, [q] Cardiology Department, Polyclinique Les Fleurs, Ollioules, France, [r] Cardiology Department, Centre Hospitalier Universitaire de Nîmes, Nîmes, France, [s]Biostatistics Unit, Direction de la Recherche Clinique, Centre Hospitalier Universitaire de Clermont-Ferrand, Clermont-Ferrand, France

**Correspondence: Benjamin Duband, Cardiology Department, Centre Hospitalier Universitaire de Clermont-Ferrand, 58, Rue Montalembert, 63000 Clermont-Ferrand, France (e-mail: b.duband@gmail.com).*

Received: 2 October 2021 / Received in final form: 12 June 2022 / Accepted: 17 June 2022

http://dx.doi.org/10.1097/MD.0000000000030190

1. Introduction

Despite major improvements in treatment and increased survival in the past 30 years, mortality remains high in ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PCI). Mortality 1 month after the event is 4% to 5%.[1,2]

Certain unmodifiable factors have been identified as predictors of mortality (e.g., advanced age, higher Killip class, or diabetes mellitus).[3] However, there is scope to improve a number of modifiable factors, such as shorter prehospital delays, pretreatment strategy, and primary PCI according to international guidelines.[4] These factors depend on emergency medical system-based STEMI networks, including mobile intensive care units, emergency wards, and the availability of an interventional cardiology center. Little is known about the adherence of French emergency medical STEMI networks to international guidelines in patients experiencing STEMI.

The France PCI registry is a multicentre registry of patients admitted for coronary angiography in France.[5] We have previously shown that the registry can answer questions about the impact of prehospital care on delays in the management of STEMI patients.[6,7]

The aim of the present study was to assess the prevalence and importance of known prognostic factors on early survival in a real-life cohort of STEMI patients undergoing PCI.

2. Methods

2.1. Study aims

The first objective was to evaluate the prevalence and impact of known prognostic factors on early survival after STEMI. The primary endpoint was all-cause mortality at 1 month. The second aim was to characterize a real-life population of STEMI French patients, their clinical presentation and management.

2.2. Registry design and study population

The ongoing France PCI registry includes all patients undergoing coronary angiography, with or without PCI, after January 1, 2014. The current study used data from 6 secondary care interventional cardiology centers in 2 regions in France: Centre Val de Loire and Auvergne Rhône Alpes. The analysis included all consecutive patients admitted to cath lab for STEMI within 24 hours (time between last chest pain and first medical contact [FMC]) between January 2014 and December 2016. Patients with nonobstructive coronary artery disease were excluded, but patients with cardiac arrest or in cardiogenic shock (associated with STEMI) and/or first treated with fibrinolysis were included. Patients lost to follow-up were excluded.

2.3. Data collection

The methodology of the registry has been described previously.[5] Prehospital, clinical and procedural data are entered prospectively by the cardiologist in the cath lab, using medical reporting software (CardioReport, CVX Medical, Croissy-Beaubourg, France or Hemolia, Paris, France) in a single capture process at the end of procedure. Each cath lab has a dedicated research technician in charge of local reporting and the collection of 1-year follow-up data. Information about vital status and outcomes is obtained by telephone calls and/or direct access to medical records. After anonymization, data are automatically transferred daily to the secured central France PCI database. A France PCI clinical research associate coordinated continual data monitoring and external quality control.

2.4. Prognostic factors

Potential prognostic factors included in the analysis were classified as unmodifiable (e.g., age, comorbidities, location of infarction) or modifiable (e.g. delays, medical treatment, angiographic procedures). Patient delay was defined as time between symptom onset and FMC or call to *Service d'Aide Medicale d'Urgence* (SAMU). If a mobile intensive care unit was involved, time between the call and FMC was defined as SAMU delay. ECG delay was defined as time between FMC and the ST-elevation ECG recording. Cath lab delay was defined as time between hospital admission (including at emergency ward) and guidewire passage through the culprit lesion. System delay was defined as time between FMC (or the call to SAMU) and guidewire passage through the culprit lesion. Total ischemic time was calculated from symptom onset to guidewire passage through the culprit lesion. For all delays, the cutoff times were adapted from the European guidelines on acute STEMI management.[4] Appropriate premedication was defined as prehospital anticoagulation (bivalirudine, low-molecular-weight heparin, unfractionated heparin, or fondaparinux) plus aspirin and P2Y12 inhibitor (ticagrelor, prasugrel, or clopidogrel), according to European guidelines. The distance between cath lab and patient was determined using the post code of the location where symptoms occurred, using a web mapping service (Google Maps, Google LLC). nonworking hours were defined as 6:00 PM to 8:00 AM.

2.5. Ethical aspects

The study was conducted according to contemporary clinical practice guidelines and French regulations (Advisory Committee on Information Processing in Material Research in the Field of Health no.13.245). The French Persons Protection Committee (IRB00003888) approved the study protocol (no. 15-231). Data collection and storage were approved by the French National Commission for Data Protection and Liberties (no. 2014-073). The France PCI study is registered on clinicaltrial.gov (NCT02778724). All included patients gave their informed written consent to participate.

2.6. Statistical analyses

Demographic data, comorbidities, management, and procedural aspects are presented as numbers and percentages for categorical variables, and as mean and standard deviation or median with interquartile range for continuous variables, according to the distribution. Normal distribution was assessed using the Shapiro–Wilk test. For censored data, estimates were constructed using the Kaplan–Meier method. The log-rank test was used in the univariate analysis to test the predictive value for death since time of coronary angiography of patient characteristics. Marginal Cox proportional hazards regression was used to test the predictive value for survival at 30 days in a multivariable analysis taking into account patient effect (due to several procedures for a patient). A stepwise approach (backward and forward) was carried out on the clinical relevance of covariates identified in the univariate analysis with particular attention paid to multicollinearity and interactions between covariates: relationship between covariables, impact on the addition or deletion of variables in the multivariable model, and rules of thumb of satisfactory number of variables in multivariable analysis.[8–10] The center effect was evaluated as random effect. The proportional-hazard hypothesis was verified using Schoenfeld test and plotting residuals. Results were expressed as hazard ratio (HR) and 95% confidence intervals (CIs). A sensitivity analysis was performed to assess the robustness of results and the possible impact of missing data. A sensitivity analysis was also conducted with cardiovascular death at 30 days as censored endpoint. All analyses were performed

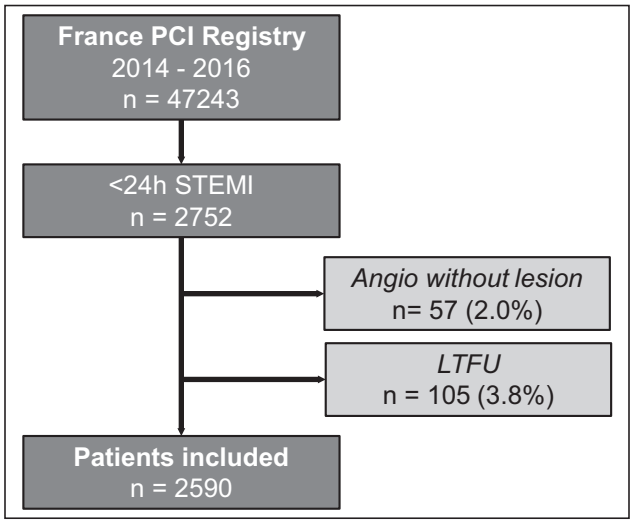

Figure 1. Study flow chart. The France PCI Registry enrolled every patient undergoing angiography and/or percutaneous coronary intervention in a participating cath lab. This study analyses data from January 2014 to December 2016. Angio = angiography, LTFU = lost to follow-up, PCI = percutaneous coronary intervention.

using Stata software (Version 15, StataCorp, College Station, TX) using a 2-sided type I error of 5%.

3. Results

Among 47,243 patients who underwent coronary angiography between January 1, 2014, and December 31, 2016, 2752 (5.8%) patients were admitted to cath lab within 24 hours of a STEMI. After exclusion of patients with nonobstructive coronary artery disease (n = 57) and those lost to follow-up (n = 105), 2590 patients aged 63 ± 14 (1922 or 74% men) were analyzed. The flow chart is shown in Figure 1.

3.1. Baseline characteristics

Medical history and clinical presentation are summarized in Table 1. Of the infarcts, 998 (38.9%) were of anterior or circumferential electrical location and 147 (5.9%) were classified as Killip ≥ 3. Most (n = 1690; 72.4%) had TIMI flow < 3. Multivessel or left main disease was found in 1407 patients (54.3%).

Management data are shown in Table 2. The median delay was 69 (30–172) minutes. Symptoms occurred at a median distance of 42 (12–64) km from the cath lab. In 1464 (56.6%) cases, SAMU was phoned by patients or nonmedical bystanders. Median system delay was 135 (103–193) minutes and median total ischemic time 235 (160–390) minutes. A lack of appropriate premedication was recorded for 461 (17.8%) patients. Few (9.5%) patients were initially treated with fibrinolysis. For the primary PCI, femoral access was used in 237 (9.2%) patients and thromboaspiration in 1030 (44.2%). Stents were implanted in 2170 (93.1%) cases. TIMI 3 post-PCI flow was not obtained in 150 (6.4%) cases.

3.2. Factors predictive of 30-day survival

During the first month, 174 patients died; a 1-month mortality rate was 6.7%. The univariate analysis is summarized in Tables 3 and 4. Among unmodifiable variables with significant impact on survival were higher age, female sex, medical history of diabetes mellitus, hypertension, cardiovascular past, higher Killip class (Killip 4; HR 27.7; 95% CI 18.9–40.7), cardiac arrest (HR 7.74; 95% CI 5.17–11.61), chronic kidney disease (CKD) (HR 4.88; 95% CI 2.77–8.60), and anterior or circumferential electrical location. Low left ventricular ejection fraction <40% was associated with lower survival (HR 6.59; 95% CI 3.02–14.34; $P < .001$). Some variables were associated with improved survival (e.g., BMI > 30 kg/m^2, current/past smoking, and familial history). These factors were associated with lower age. Kaplan–Meier survival curves are available in supplementary data (see Figures S1–S4, Supplemental Digital Content, http://links.lww.com/MD/H87).

Among modifiable variables, total ischemic time > 3 hours (due to ECG delay > 10 minutes and system delay > 2 hours) were significantly associated with lower 30-day survival (HR 1.5; 95% CI 1.0–2.2). Further, >1 intervention before angiography (HR 1.4; 95% CI 1.0–1.9), lack of appropriate premedication (HR 5.0; 95% CI 3.7–6.7), and coronary angiography outside working hours (HR 1.4; 95% CI 1.0–1.8) were significant predictors. Among variables related to the angiographic procedure, femoral access (HR 6.2; 95% CI 4.6–8.5), absence

Table 1

Demographic characteristics, comorbidities, clinical presentation, and angiographic findings in the overall population and in patients alive and deceased at 30 d, respectively.

	Overall	Alive	Deceased
	N = 2590, n/N (%)	N = 2416, n (%)	N = 174, n (%)
Demographic data			
Age (yr)	62.8 ± 14	62.4 ± 14	71.3 ± 14
Age <60	1110/2590 (42.9)	1076 (44.5)	34 (19.5)
Age 60–80	1097/2590 (42.4)	1016 (42.1)	81 (46.6)
Age >80	383/2590 (14.8)	324 (13.4)	59 (33.9)
Female	668/2590 (25.8)	600 (24.8)	68 (39.1)
BMI 20–25	873/2587 (33.8)	801 (33.2)	72 (42.1)
BMI <20	103/2587 (4.0)	96 (4.0)	7 (4.1)
BMI 25–30	1102/2587 (42.6)	1033 (42.8)	69 (40.4)
BMI >30	509/2587 (19.7)	486 (20.1)	23 (13.5)
CV risk factors			
Diabetes mellitus	353/2590 (13.6)	313 (13.0)	40 (23.0)
Current/past smoking	1364/2590 (52.7)	1306 (54.1)	58 (33.3)
Hypertension	1047/2590 (40.4)	958 (39.7)	89 (51.2)
Hypercholesterolemia	985/2590 (38.0)	924 (38.3)	61 (35.1)
Familial history	555/2589 (21.4)	545 (22.6)	10 (5.8)
Medical history			
PCI	313/2589 (12.1)	286 (11.8)	27 (15.5)
CABG	37/2590 (1.4)	31 (1.3)	6 (3.5)
Myocardial infarction	209/2590 (8.1)	190 (7.9)	19 (10.9)
Stroke*	64/2590 (2.5)	54 (2.2)	10 (5.8)
PAD	89/2590 (3.4)	74 (3.1)	15 (8.6)
Chronic kidney disease	47/2587 (1.8)	34 (1.4)	13 (7.5)
Clinical presentation			
Anterior ischemia	998/2563 (38.9)	905 (37.8)	93 (55.0)
Cardiac arrest	74/2588 (2.9)	46 (1.9)	28 (16.1)
Killip 1	2178/2508 (86.8)	2126 (89.9)	52 (36.4)
Killip 2	183/2508 (7.3)	160 (6.8)	23 (16.1)
Killip 3	39/2508 (1.6)	25 (1.1)	14 (9.8)
Killip 4	108/2508 (4.3)	54 (2.3)	54 (37.8)
Angiographic result			
Multivessel/left main disease	1407/2590 (54.3)	1303 (53.9)	104 (59.8)
Occlusion (90%–100% stenosis)	1934/2337 (82.8)	1801 (82.4)	133 (87.5)
Pre-PCI TIMI <3	1690/2336 (72.4)	1570 (71.9)	120 (79.0)
Long lesion ≥20 mm	654/2323 (28.2)	593 (27.3)	61 (40.4)
LVEF <40%	291/1671 (17.4)	276 (16.8)	15 (57.7)

Data are expressed as absolute number/available data (%) and mean ± SD.
BMI = body mass index, CABG = coronary artery bypass graft, LVE = left ventricular ejection fraction, PAD = peripheral artery disease, PCI = percutaneous coronary intervention, SD = standard deviation, TIMI = thrombolysis in myocardial infarction flow.
*Transient ischemic attack or stroke.

Table 2

Patients management in the overall population and in patients alive and deceased at 30 days, respectively.

	Overall	Alive	Deceased
	N = 2590	N = 2416	N = 174
Delays			
Patient delay (min)	69 (30–172)	70 (30–170)	53.5 (15–210)
Patient delay >1 hr	1323/2575 (51.4%)	1247 (51.9%)	76 (44.7%)
SAMU delay (min)*	24 (15–36)	24 (15–36)	24.5 (15–33)
SAMU delay >30 min*	455/1459 (31.2%)	428 (31.4%)	27 (28.1%)
ECG delay (min)	5 (1–10)	5 (1–9)	6.5 (1–20)
ECG delay >10 min	371/1744 (21.3%)	329 (20.3%)	42 (35.0%)
Cath lab delay (min)	30 (21–58)	30 (21–57)	35 (21–61)
Cath lab delay >1 hr 30 min	375/2376 (15.8%)	349 (15.7%)	26 (16.4%)
System delay (min)	135 (103–193)	135 (101–190)	170 (125–225)
System delay >2 hr	1453/2372 (61.3%)	1328 (60.0%)	125 (78.6%)
Total ischemic time (min)	235 (160–390)	233 (160–388)	277 (180–473)
Total ischemic time >3 hr	1606/2374 (67.7%)	1487 (67.1%)	119 (75.8%)
Emergency care			
No SAMU	1124/2588 (43.4%)	1047 (43.4%)	77 (44.3%)
Nonoptimal way (SAMU-Angio)	1713/2590 (66.1%)	1587 (65.7%)	126 (72.4%)
Interventions before angio >1	1508/2590 (58.2%)	1393 (57.7%)	115 (66.1%)
Distance to cath lab (km)	42 (12–64)	42 (12–64]	45.5 (10–70]
Distance to cath lab ≥50 km	1030/2582 (39.9%)	949 (39.4%)	81 (46.6%)
Nonworking hours	1098/2587 (42.4%)	1011 (41.9%)	87 (50.0%)
Pretreatment			
No aspirin	132/2589 (5.1%)	101 (4.2%)	31 (17.8%)
No P2Y12	230/2588 (8.9%)	168 (7.0%)	62 (35.6%)
No ATC	286/2588 (11.1%)	236 (9.8%)	50 (28.7%)
No appropriate premedication	461/2587 (17.8%)	374 (15.5%)	87 (50.0%)
Fibrinolysis	245/2590 (9.5%)	232 (9.6%)	13 (7.5%)
Angiographic procedure			
Sheath size >6F	25/2587 (1.0%)	20 (0.8%)	5 (2.9%)
Femoral access	237/2590 (9.2%)	175 (7.2%)	62 (35.6%)
Thromboaspiration	1030/2331 (44.2%)	961 (44.1%)	69 (45.4%)
No stent implantation	161/2331 (6.9%)	141 (6.5%)	20 (13.2%)
Anti-gp2b3a administration	882/2590 (34.1%)	815 (33.7%)	67 (38.5%)
Contrast (mL)	141 ± 61	140 ± 60	147 ± 75
Radiation time (min)	8.5 ± 7	8.3 ± 7	10.6 ± 8
Post-PCI TIMI <3	150/2331 (6.4%)	106 (4.9%)	44 (29.0%)
Intra-aortic balloon pump	75/2562 (2.9%)	39 (1.6%)	36 (21.3%)

Data are expressed as absolute number/available data (%) and median (IQR) or mean ± SD.
ATC = anticoagulation therapy, ECG = electrocardiogram, IQR = interquartile range, PCI = percutaneous coronary intervention, SAMU = service d'aide medicale urgente, TIMI = thrombolysis in myocardial infarction flow.
*In cases of patients or nonmedical witness called SAMU.

Table 3

Univariate analysis of predictive value of unmodifiable factors on 30-d survival.

	HR (95% CI), *P* value
Demographic data	
Age <60	Ref
Age 60–80	2.46 (1.64–3.67), *P* < .001
Age >80	5.37 (3.52–8.18), *P* < .001
Female	1.90 (1.40–2.57), *P* < .001
BMI 20–25	Ref
BMI < 20	0.82 (0.37–1.77), *P* = .605
BMI 25–30	0.75 (0.54–1.04), *P* = .087
BMI >30	0.54 (0.34–0.86), *P* = .009
CV risk factors	
Diabetes mellitus	1.93 (1.36–2.75), *P* < .001
Current/past smoking	0.44 (0.32–0.60), *P* < .001
Hypertension	1.56 (1.16–2.10), *P* = .003
Hypercholesterolemia	0.87 (0.64–1.19), *P* = .396
Familial history	0.22 (0.11–0.41), *P* < .001
Medical history	
PCI	1.35 (0.89–2.03), *P* = .152
CABG	2.58 (1.14–5.82), *P* = .023
Myocardial infarction	1.41 (0.88–2.27), *P* = .157
Stroke*	2.53 (1.33–4.78), *P* = .004
PAD	2.80 (1.65–4.76), *P* < .001
Chronic kidney disease	4.88 (2.77–8.60), *P* < .001
Clinical presentation	
Anterior ischemia	1.96 (1.45–2.65)}, *P* < .001
Cardiac arrest	7.74 (5.17–11.61), *P* < .001
Killip 1	Ref
Killip 2	5.55 (3.40–9.07), *P* < .001
Killip 3	18.46 (10.22–33.31), *P* < .001
Killip 4	27.74 (18.93–40.66), *P* < .001
Angiographic result	
Multivessel/left main disease	1.26 (0.93–1.70), *P* = .141
Occlusion (90%–100% stenosis)	1.47 (0.91–2.38), *P* = .115
Pre-PCI TIMI <3	1.45 (0.98–2.13), *P* = .064
Long lesion ≥20 mm	1.76 (1.27–2.44), *P* = .001
LVEF <40%	6.59 (3.02–14.34), *P* < .001

BMI = body mass index, CABG = coronary artery bypass graft, LVEF = left ventricular ejection fraction, PAD = peripheral artery disease, PCI = percutaneous coronary intervention, TIMI = thrombolysis in myocardial infarction flow.
*Transient ischemic attack or stroke.

of stent implantation, post-PCI TIMI < 3 (HR 6.9; 95% CI 4.9–9.9), and intra-aortic balloon pump (HR 11.5; 95% CI 7.9–16.6) were significantly associated with lower 30-day survival.

After adjustment in the multivariate model (Fig. 2), unmodifiable variables significantly associated with lower 30-day survival were age >80 years (HR 2.7; 95% CI 1.5–4.7), CKD (HR 5.3; 95% CI 2.6–11.1), diabetes mellitus (HR 1.6; 95% CI 1.0–2.5), anterior or circumferential electrical location (HR 2.0; 95% CI 1.4–2.9), and Killip class 2, 3, and 4 (HR 3.4; 95% CI 1.9–5.9; HR 10.1; 95% CI 5.3–19.4; HR 18; 95% CI 10.8–29.8, respectively). Among modifiable variables, total ischemic time > 3 hours (HR 1.8; 95% CI 1.1–3.0), no appropriate premedication (HR 2.2; 95% CI 1.5–3.3), and post-PCI TIMI < 3 (HR 4.9; 95% CI 3.2–7.6) remained significantly associated with reduced 1 month survival. Repeating the modeling for the endpoint of cardiovascular death at 30 days yielded similar results, except for diabetes mellitus (HR 1.36; 95% CI 0.8–2.3; *P* = .24) and for total ischemic time > 3 hours (HR 1.51; 95% CI 0.83–2.74; *P* = 0,17; see Table S1, Supplemental Digital Content, http://links.lww.com/MD/H88).

4. Discussion

This study from an all-comers registry of patients admitted for coronary angiography at 6 regional French centers identified modifiable as well as nonmodifiable factors affecting 30-day survival post-STEMI in conditions representative of everyday care. To our knowledge, this is the largest cohort of consecutive STEMI patients managed at French PCI centers with a real-life description of patients' profiles, management, and outcomes during this period.

Age, sex, risk factors, and comorbidities in the population were comparable to those in the French registry of acute ST-elevation or non-ST-elevation myocardial infarction (FAST-MI), which is considered the gold standard French registry of patients with acute coronary syndrome.[11] The main difference in our registry is that the France PCI cohort included every consecutive patient undergoing angiography, whereas FAST-MI included

Table 4

Univariate analysis of predictive value of modifiable factors on 30-day survival.

	HR (95% CI) *P* value
Delays	
Patient delay >1 hr	0.76 (0.56–1.02), *P* = .072
SAMU delay >30 min*	0.86 (0.55–1.34), *P* = .504
ECG delay >10 min	2.04 (1.40–2.97), *P* < .001
Cath lab delay >1 hr 30 min	1.04 (0.68–1.58), *P* = .861
System delay >2 hr	2.38 (1.63–3.48), *P* < .001
Total ischemic time >3 hr	1.52 (1.05–2.18), *P* = .025
Emergency care	
No SAMU call	1.03 (0.76–1.39), *P* = .840
nonoptimal way (SAMU-Angio)	1.35 (0.97–1.88), *P* = .076
Interventions before angio >1	1.41 (1.03–1.93), *P* = .032
Distance to cath lab ≥50 km	1.33 (0.98–1.78), *P* = .064
Nonworking hours	1.37 (1.01–1.84), *P* = .039
Pretreatment	
No aspirin	4.38 (2.97–6.46), *P* < .001
No P2Y12	6.42 (4.70–8.75), *P* < .001
No ATC	3.47 (2.50–4.81), *P* < .001
No appropriate premedication	4.98 (3.70–6.71), *P* < .001
Fibrinolysis	0.77 (0.44–1.36), *P* = .366
Angiographic procedure	
Sheath size >6F	3.34 (1.37–8.13), *P* = .008
Femoral access	6.21 (4.56–8.48), *P* < .001
Thromboaspiration	1.06 (0.77–1.45), *P* = .737
No stent implantation	2.12 (1.32–3.39), *P* = .002
Anti-gp2b3a administration	1.22 (0.90–1.65), *P* = .204
Contrast (mL)	1.00 (0.99–1.00), *P* = .145
Radiation time (min)	1.03 (1.01–1.04), *P* < .001
Post-PCI TIMI <3	6.95 (4.89–9.87), *P* < .001
Intra-aortic balloon pump	11.46 (7.92–16.56), *P* < .001

ATC = anticoagulation therapy, ECG = electrocardiogram, PCI = percutaneous coronary intervention, SAMU = service d'aide medicale urgente; TIMI = thrombolysis in myocardial infarction flow.

*In cases of patients or nonmedical bystanders called SAMU.

only investigator-selected patients admitted to cardiology care units, during 1 month of the year every 5 years. It possibly excluded severe conditions such as cardiogenic shock (4.3% in our study vs 3.3% in FAST-MI 2015) or cardiac arrest (2.9% vs 1.0%) that are managed in general intensive care unit and associated with high mortality. This difference in inclusion criteria can explain that 30-day mortality was 6.7% in our cohort, more than double the 3.1% reported in the FAST-MI registry in 2015.[11] The other difference is that FAST-MI included 204 French centers in 2015,[12] while 6 centers from FRANCE PCI were included in the present analysis. The representativeness of the 2 populations may hence differ.

Regarding the modifiable factors identified, reducing delays would seem highly important, as total ischemic time > 3 hours was common and independently associated with poorer survival. Oddly, shorter delay was associated with poorer outcomes: a complementary analysis showed that patient delay < 60 minutes was associated with Killip ≥ 1. A greater sense of urgency among healthcare workers confronted with patients with more serious clinical presentations may have increased delays in lower-risk patients.

ECG and transfer time are 2 probable key factors behind delays. Delayed ECG may be particularly harmful for patients with atypical symptoms or initial NSTEMI presentation. We recently found that helicopter transport was not associated with shorter delay than other modes of transport.[6] Furthermore, SAMU involvement was not associated with better survival, but additional analyses have shown a strong association between SAMU involvement and shorter total ischemic time. Other factors associated with longer delay have been described.[7] Puymirat et al[13] demonstrated the prognostic impact of noncompliance with guidelines-recommended times for reperfusion therapy. We could not analyze fibrinolysis delay as the time of fibrinolysis was not captured in the registry. However, fibrinolysis was provided in only 10% of the population, and any analysis would have low statistical power. Distance to the cath lab had no impact on survival, probably because the French cath

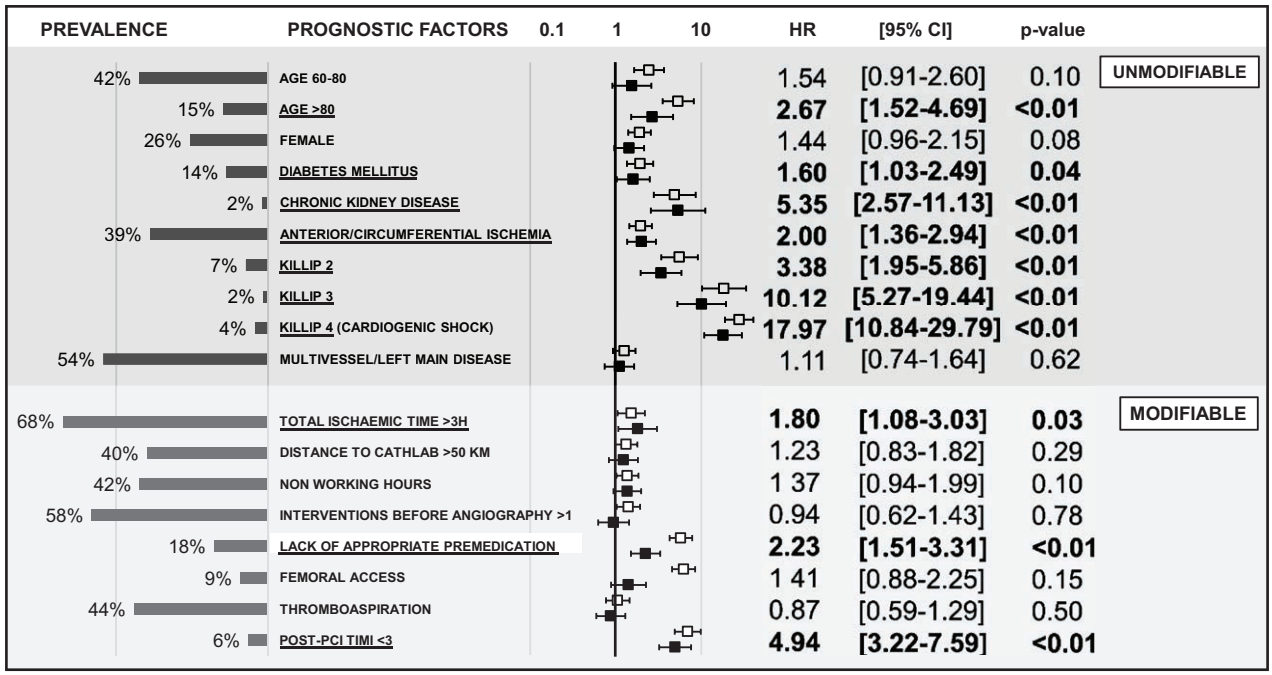

Figure 2. Prevalence and impact of prognostic factors (unmodifiable and modifiable) on STEMI patients 30 days survival according to univariate and multivariate analysis. Impact on 30-d survival is shown on the right of the list of prognostic factors. The forest plot shows the results of univariate analysis (white boxes) and multivariate analysis (black boxes), using a logarithmic scale. To the right of the forest plot, hazard ratio, 95% confidence interval, and *P* value from the multivariate analyses are summarized. Prevalence is shown to the left of the list of prognostic factors. STEMI = ST-segment elevation myocardial infarction.

lab network is dense, and <5% of STEMI patients were located >100 km from a cath lab.

Despite guideline-based local protocols synchronized with prehospital emergency ward/SAMU, lack of appropriate premedication was reported in 1 patient out of 5 and had significant impact on survival. This likely reflects the real-life situation in this all-comers registry. Femoral access was not a significant factor after adjustment, which is in agreement with results of a recent randomized clinical trial[14] but contrasted with the 2017 ESC STEMI Guidelines, which give a class IA recommendation to radial over femoral access.[4] Our findings concerning thromboaspiration are similar to those from recent trials.[15] Post-PCI TIMI < 3 was independently associated with increased mortality. The association between mortality and no reflow is well documented.[16] This is in large part the consequence of previous management. Indeed, no reflow is associated with greater age, heart failure, and high thrombus burden.[17]

Many unmodifiable factors were found to be independently associated with lower survival. Interestingly, female sex was associated with poorer prognosis only in the univariate analysis. Previous studies have shown female patients to be older with more comorbidities than male patients, and also with longer prehospital delays.[18,19] This was also the case in our cohort. Interestingly, multivariate models including only unmodifiable factors showed no sex difference in 30-day survival, and other models with only modifiable factors have shown lower survival in female patients. This suggests that worse outcomes in female STEMI patients might be attributable to the risk profile rather than medical management.

These data presented here indicate where efforts to improve post-STEMI mortality may be focused: education efforts to increase awareness of the need to call SAMU rapidly (especially in diabetic, CKD, and elderly patients), improved supervision of patients with suspected acute coronary syndromes, and systematic medication delivery prehospitalization. The findings also highlight that unmodifiable factors are at least as prevalent as modifiable factors, which may contribute to the recent stagnation in the trend towards lower post-STEMI mortality.[11]

Some limitations should be underlined. Multivariate analyses including several factors can present multicollinearity and should be interpreted with caution. Selection bias, for example, choice of access route, may have influenced the results. Although we tried to include most known risk factors, unspecific confounding factors may have distorted these results. Further, STEMI patients who were recused or died before angiography were not included.

In summary, this study from a real-life all-comers multicentre registry describes a profile of contemporary patients admitted to the cath lab for STEMI. Although several unmodifiable factors were prevalent, there seems to be room for improvement in total ischemic time, systematic pretreatment, and optimization of primary PCI. The findings would be of help to healthcare providers and public health decision makers to improve management of STEMI patients.

Acknowledgments

The authors thank all interventional cardiologists and research assistants, especially Christophe Laure, Sandra Gautier, Aurélie Formentin, Carole Bellanger, and Justine Prouteau. All of them gave permission to be named.

References

[1] Puymirat E, Simon T, Steg PG, et al. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. JAMA. 2012;308:998–1006.
[2] Massoullié G, Wintzer-Wehekind J, Chenaf C, et al. Prognosis and management of myocardial infarction: comparisons between the French FAST-MI 2010 registry and the French public health database. Arch Cardiovasc Dis. 2016;109:303–10.
[3] Pedersen F, Butrymovich V, Kelbæk H, et al. Short- and long-term cause of death in patients treated with primary PCI for STEMI. J Am Coll Cardiol. 2014;64:2101–8.
[4] Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2018;39:119–77.
[5] Rangé G, Chassaing S, Marcollet P, et al. The CRAC cohort model: a computerized low cost registry of interventional cardiology with daily update and long-term follow-up. Rev epidémiol Santé Publique. 2018;66:209–16.
[6] Hakim R, Revue E, Saint Etienne C, et al. Does helicopter transport delay prehospital transfer for STEMI patients in rural areas? Findings from the CRAC France PCI registry. Eur Heart J Acute Cardiovasc Care 2019;204887261984897.
[7] Rangé G, Saint Etienne C, Marcollet P, et al. Factors associated with delay in transfer of patients with ST-segment elevation myocardial infarction from first medical contact to catheterization laboratory: lessons from CRAC, a French prospective multicentre registry. Arch Cardiovasc Dis. 2019;112:3–11.
[8] Harrell FE, Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15:361–87.
[9] Green SB. How Many subjects does it take to do a regression analysis. Multivar Behav Res. 1991;26:499–510.
[10] Hsieh FY, Bloch DA, Larsen MD. A simple method of sample size calculation for linear and logistic regression. Stat Med. 1998;17:1623–34.
[11] Puymirat E, Cayla G, Cottin Y, et al. Twenty-year trends in profile, management and outcomes of patients with ST-segment elevation myocardial infarction according to use of reperfusion therapy: data from the FAST-MI program 1995-2015. Am Heart J. 2019;214:97–106.
[12] Belle L, Cayla G, Cottin Y, et al. French registry on acute ST-elevation and non–ST-elevation myocardial infarction 2015 (FAST-MI 2015). Design and baseline data. Arch Cardiovasc Dis. 2017;110:366–78.
[13] Puymirat E, Caudron J, Steg PG, et al. Prognostic impact of non-compliance with guidelines-recommended times to reperfusion therapy in ST-elevation myocardial infarction. The FAST-MI 2010 registry. Eur Heart J Acute Cardiovasc Care. 2017;6:26–33.
[14] Le May M, Wells G, So D, et al. Safety and efficacy of femoral access vs radial access in ST-segment elevation myocardial infarction: the SAFARI-STEMI randomized clinical trial. JAMA Cardiol. 2020;5:126.
[15] Jolly SS, James S, Džavík V, et al. Thrombus aspiration in ST-segment–elevation myocardial infarction: an individual patient meta-analysis: thrombectomy trialists collaboration. Circulation. 2017;135:143–52.
[16] de Waha S, Patel MR, Granger CB, et al. Relationship between microvascular obstruction and adverse events following primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: an individual patient data pooled analysis from seven randomized trials. Eur Heart J. 2017;38:3502–10.
[17] Al Azzoni AM, Lamelas P, Marsden T, et al. Incidence and predictors of no reflow phenomenon: insights from the total trial. J Am Coll Cardiol. 2017;69:1179.
[18] Kang S-H, Suh J-W, Yoon C-H, et al. Sex Differences in management and mortality of patients with ST-elevation myocardial infarction (from the Korean acute myocardial infarction national registry). Am J Cardiol. 2012;109:787–93.
[19] Wei J, Mehta PK, Grey E, et al. Sex-based differences in quality of care and outcomes in a health system using a standardized STEMI protocol. Am Heart J. 2017;191:30–6.