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CLINICAL RESEARCH

Early and late case fatality after hospitalization for acute coronary syndrome in France, 2010—2015

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KEYWORDS
Acute coronary syndrome;
Case fatality;
Determinants;
Trends

Summary
Background. — Case-fatality data for acute coronary syndromes (ACS) are scarce in unselected French patients.
Aims. — To analyse early and late case-fatality rates in patients with ACS in France, case fatality determinants and time trends between 2010 and 2015.
Methods. — For each year from 2010 to 2015, all patients hospitalized for ACS in France and aged > 18 years were selected. Multivariable Cox models were used to assess determinants of case fatality at 3 days, 4—30 days and 31—365 days after hospital admission.
Results. — In 2015, cumulative 3-day, 30-day and 1-year case-fatality rates were, respectively, 2.0%, 5.1% and 11.1% for all patients with ACS, and 3.9%, 8.5% and 13.8% for those with ST-segment elevation myocardial infarction (STEMI). Admission through the emergency department was associated with a higher risk of death, particularly at 3 days. Female sex was associated with higher case-fatality rates at 3 days, but with lower case-fatality rates at 31—365 days. Social deprivation was associated with higher case-fatality rates for all periods for all patients with ACS. A significant decrease was found between 2010 and 2015 in case-fatality rates at 31—365 days, particularly for patients with STEMI; this time trend was no longer significant after additional adjustment for hospital management.

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CI, confidence interval; CMUc, couverture maladie universelle complémentaire (complementary universal health insurance coverage); ED, emergency department; HR, hazard ratio; ICD-10, International Classification of Diseases, 10th revision; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

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Conclusions. — Case fatality up to 1 year after hospitalization for ACS was non-negligible, highlighting the need to ensure better follow-up after the acute stage, particularly in the most deprived patients. As hospital admission through the emergency department still occurs frequently, health policy should promote a national campaign to increase the awareness and preparedness of the general population regarding ACS. Finally, our results suggest that women need specific attention early after the index event.

MOTS CLÉS
Syndrome coronaire aigu ;
Létalité ;
Déterminants ;
Évolutions

Résumé
Contexte. — Peu de données existent sur la létalité post-syndrome coronaire aigu (SCA) parmi l'ensemble des patients atteints en France.
Objectifs. — Le but de cette étude était d'analyser la létalité précoce et tardive suivant un SCA hospitalisé en France, de décrire ses déterminants et d'étudier les évolutions entre 2010 et 2015.
Méthodes. — Pour chaque année de 2010 à 2015, tous les patients hospitalisés pour un SCA en France, âgés de plus de 18 ans ont été sélectionnés. Des modèles de Cox multivariés ont été utilisés afin de décrire les déterminants respectifs de la létalité à 3 jours, 4—30 jours et 31—365 jours (tardive) après l'admission à l'hôpital.
Résultats. — En 2015, la létalité cumulée à 3 jours, 30 jours et 1 an était respectivement de 2,0 %, 5,1 % et 11,1 % pour les SCA, et de 3,9 %, 8,5 % et 13,8 % pour les STEMI. L'admission à l'hôpital par les urgences était associée à un risque de décès plus élevé, en particulier sur la létalité à 3 jours. Le sexe féminin était associé à une létalité à 3 jours plus importante mais à une létalité tardive moindre. La défaveur sociale était liée à une plus grande létalité quel que soit la fenêtre retenue. Une diminution significative de la létalité tardive a été observée entre 2010 et 2015, notamment parmi les STEMI. Cette tendance n'était plus significative après ajustement sur la prise en charge durant l'hospitalisation.
Conclusions. — La létalité post-SCA demeure relativement élevée jusqu'à un an soulignant l'importance d'assurer un suivi optimal des patients après la phase aiguë, en particulier chez les patients les plus défavorisés socialement. La proportion de patients se présentant d'eux-mêmes aux urgences restant élevée, les campagnes publiques visant à informer et préparer la population sur la conduite à tenir en cas de symptômes d'un SCA doivent être poursuivies et intensifiées. Enfin, nos résultats suggèrent que les femmes nécessitent encore une attention particulière au moment de la phase aiguë.

Background

Acute coronary syndromes (ACS) continue to be a major public health concern in France, with an increase in ACS rates observed among people aged < 65 years, particularly women [1]. Despite this increase, survival following acute myocardial infarction and, more globally, ACS has improved greatly in recent years, as a result of better organization of ACS care pathways and the development of invasive therapeutic strategies [2—5]. These improvements focus on the acute stage of the disease and have led to a dramatic reduction in in-hospital mortality. Admission to cardiac rehabilitation units—associated with reduced case-fatality and recurrent-event rates after ACS in the short term, mid term and long term—has also occurred increasingly frequently in France in recent years [6]. Studies have also shown a decrease in out-of-hospital mortality rates, including prehospital mortality rates [7]. Nevertheless, overall case-fatality rates remain high: in-hospital mortality of patients with ST-segment elevation myocardial infarction (STEMI) in the national registries of the European Society of Cardiology (ESC) member countries varies between 4% and 12%, while the reported 1-year mortality rate in angiography registries is approximately 10% [3]. Available information about ACS case fatality mostly concerns short-term findings, and is based on specialized cardiology referral centres, such as in the French Registry of Acute Coronary Syndrome (FAST-MI) for acute myocardial infarction in France [8,9].

The aims of this study were to: (1) evaluate case-fatality rates after ACS (including STEMI) in France, at different time intervals from hospital admission up to 1 year; (2) investigate whether the determinants of case fatality differed; and (3) analyse associated time trends in case-fatality rates from 2010 to 2015.

Methods

Data sources

The study was conducted using the French national health data system (Système national des données de santé [SNDS]), which contains individual information on the sociodemographic and medical characteristics of almost the entire French population.

Study population

Patients hospitalized with a main discharge diagnosis of ACS from 2010 to 2015 were selected. Patients with ACS were defined by the following International Classification of Diseases, 10th revision (ICD-10) codes: I20.0 and I21—I23, with I21.0 and I21.1—I21.3 for STEMI. Patients with their first hospitalization—the index hospital admission—were selected for each year. We excluded patients hospitalized for ACS between 1 and 28 days before the index hospitalization; patients aged < 18 years; and patients who did not live in metropolitan France (97% of the overall French population, which does not include the French overseas territories of Guadeloupe, Martinique, French Guyana and La Réunion). Moreover, as date of death was exhaustive for all years of the study period for patients affiliated to the national general health insurance scheme (approximately 86% of the French population), we limited the analysis to this population. Sensitivity analyses for the entire population for the year 2015 showed similar results to those for the 86% selected.

Case fatality was assessed by vital status and the related date of death. Sociodemographic characteristics recorded at hospital admission included age, sex and social deprivation level of the area of residence. The Social Deprivation Index used was developed by Rey et al. (the first index quintile group [Q1] represented the 20% of the population with the lowest deprivation level, while the fifth index quintile group [Q5] represented the 20% with the highest deprivation level) [10]. The degree of individual social deprivation can also be estimated by the free complementary universal health insurance coverage (CMUc), available for low-income persons aged < 60 years and living in France under the poverty line. CMUc provides access to care without advance payment or extra billing, covering total medical expenditures.

The Charlson Comorbidity Index was computed using the 2011 method of Quan et al., including 12 conditions (congestive heart failure, dementia, chronic pulmonary disease, rheumatological disease, mild liver disease, diabetes with chronic complications, hemiplegia or paraplegia, renal disease, any malignancy, moderate or severe liver disease, metastatic solid tumour or AIDS/HIV), identified by diagnostic codes recorded during the hospital stay, with ponderation attributed to each condition [11]. A history of ACS was recorded if a hospitalization for ACS occurred in the 5 years preceding the index hospital admission. Heart failure incidence in the year after hospital admission was recorded using hospitalization codes (I50, I110, I130, I132 as primary diagnoses or associated diagnoses with I139, J81, K761 as primary diagnoses). Coronary artery procedures, including coronary angiography, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG), were all recorded for the 5 years before hospital admission and for the first 3 days after hospital admission among patients still alive at this point. At least one reimbursement for medication in the 6 months before the index hospital admission and up to 1 year was recorded (Anatomical Therapeutic Chemical [ATC] classification): antithrombotic agents (B01), beta-blockers (C07), other antihypertensive drugs, including diuretics, calcium-channel blockers and drugs acting on the renin—angiotensin system (C02, C03, C08, C09), and lipid-lowering agents (C10) were searched for. Finally, the proportion of patients simultaneously receiving recommended treatment (a beta-blocker, a platelet aggregation inhibitor, a statin and an angiotensin-converting enzyme inhibitor) was also calculated.

Admission to hospital through the emergency department (ED) was defined as a patient presenting themselves to the ED versus being admitted directly to a care unit or entering the hospital by ambulance. Finally, cardiogenic shock was recorded using ICD-10 code R570 at the time of hospitalization.

Analysis

Because of changes in the coding of unstable angina and myocardial infarction other than STEMI (other myocardial infarction) over the study period, analyses were conducted for all ACS cases and thereafter in the STEMI subgroup. All the results for unstable angina and other myocardial infarction are presented separately in Table A.1 and Table A.2.

Crude cumulative case-fatality rates were calculated at 3 days, 30 days and 1 year after the index hospital admission for ACS in 2015 as the ratio between the number of deceased persons and the study population for that year. Multivariable Cox regression models were used to individually examine the determinants of case fatality at 3 days, 4—30 days and 31—365 days after hospital admission. For the two latter outcomes, the analysis was restricted to the survivors of each preceding period. The following covariates were included: age (polynomial), Charlson Comorbidity Index score (polynomial), sex, deprivation index of the area of residence, previous hospitalization for ACS, admission through the ED and year of hospital admission (Model 1). For the case-fatality outcomes at 4—30 days and 31—365 days, the following binary variables related to hospital management in the first 3 days were added: coronary angiography, PCI (including other coronary procedures, such as percutaneous recanalization, atherectomy, etc.) and CABG (Model 2). Sensitivity analyses in patients still alive at the end of their hospital stay were performed by adding—as covariates—the refund for antiplatelets, beta-blockers, antihypertensive drugs and lipid-lowering drugs in the 3 months after hospital admission (Model 3). These analyses were performed to avoid any bias arising from patients still alive after the initial hours of hospitalization. Supplementary analyses were conducted in patients aged < 60 years, to examine the effect of being a CMUc beneficiary on case-fatality outcomes.

All analyses were performed with SAS® Enterprise Guide®, version 7.1 (SAS Institute, Cary, NC, USA).

Results

In 2015, 84,202 patients were hospitalized for an ACS, including 29,358 with STEMI (34.9%, Table 1). The Charlson Comorbidity Index score was 0 for 63.8% of all patients with ACS (65.2% among men and 61.1% among women). In patients with ACS overall, 23.0% lived in the most deprived areas, and in those aged < 60 years, 13.8% benefited from CMUc; this percentage was higher in women (16.6%) than in men (13.0%). Finally, 46.1% of all patients with ACS were hospitalized through the ED (50.5% in women and 43.9% in men). At 3 days following hospital admission, 58.7% of patients with ACS (77.4% for STEMI) who were still alive had a PCI. Among patients still alive at the end of their hospital stay, 71.9% of those with STEMI received the four recommended medications simultaneously (64.8% of women versus 74.7% of men). Cardiogenic shock was diagnosed in 4.2% of patients with ACS and 7.2% of those with STEMI. Finally, among 1-year survivors, 11% of patients were hospitalized for heart failure.

In 2015, cumulative 3-day, 30-day and 1-year case-fatality rates were, respectively, 2.0%, 5.1% and 11.1% for all patients with ACS, and 3.9%, 8.5% and 13.8% for patients with STEMI (Table A.2). Compared to patients with STEMI, the 1-year case-fatality rate was lower in patients with unstable angina (7.2%; Table A.2) and higher in those with other myocardial infarction (14.4%; Table A.2). Three-day case fatality accounted for 16.4% of the overall 1-year ACS case-fatality rate for men and 20.7% for women, and 25.5% for men and 31.0% for women when considering only patients with STEMI (Fig. 1).

Between 2010 and 2015, crude case-fatality rates among all patients with ACS were unchanged, except for those at 31—365 days, which decreased from 5.6% to 5.4% in men and from 8.3% to 7.8% in women (Fig. 2). These trends were significant according to Cox univariate analyses (Table A.3). After adjustment, no significant time trends in case-fatality rates at 3 days and 4—30 days were found, but a significant decrease in case-fatality rates at 31—365 days remained for ACS (hazard ratio [HR] 0.88, 95% confidence interval [CI] 0.84—0.91), including STEMI (HR 0.86, 0.81—0.93) (Model 1, Table 2). After supplementary adjustment for invasive management and recommended medication delivery, trends were attenuated when considering overall ACS, and were no longer significant in patients with STEMI (Models 2 and 3, Table 2).

Age and the Charlson Comorbidity Index score were associated with an increased risk of death in all groups (data not shown). Hospitalization through an ED was associated with a higher risk of case fatality for all timeframes, with a global HR of 1.32 (95% CI 1.30—1.34) at 1 year for ACS (Model 1, Table 2). The risk was particularly high at 3 days (HR 1.56, 95% CI 1.50—1.63, for ACS). In sensitivity analyses, among 3-day survivors, with additional adjustment for early invasive management, the effect of hospital admission through the ED remained significant in patients with ACS for all outcomes (Model 2, Table 2). For patients with STEMI, the effect remained significant at 4—30 days only (HR 1.08, 95% CI 1.03—1.13) (Model 2, Table 2).

Female sex was associated with an increased 3-day case-fatality rate in patients with ACS, particularly in patients with STEMI (HR 1.27, 95% CI 1.21—1.34) (Model 1, Table 2). This association was stronger among patients aged < 65 years (data not shown). By contrast, female sex was associated with a significantly lower case-fatality rate at 31—365 days in patients with ACS (HR 0.84, 95% CI 0.82—0.86).

A higher deprivation level was significantly associated with higher case-fatality rates for all periods for all patients with ACS (HR 1.26, 95% CI 1.23—1.30 at 1 year) (Model 1, Table 2). Patients aged < 60 years receiving CMUc had a higher risk of death at 31—365 days, but not at 3 days or 4—30 days (Table A.4).

Discussion

In 2015, in metropolitan France, 11.1% of patients admitted to hospital for an ACS and, specifically, 13.8% of those with STEMI, died in the following year. Among deceased patients with STEMI, 63% of women and 59% of men died in the first 30 days after hospital admission. Patients hospitalized through an ED were at higher risk of death, and represented 46% of those with an ACS. Female sex was associated with much higher case-fatality rates at 3 days, but with lower case-fatality rates at 31—365 days. The level of social deprivation of the area of residence was associated with higher case-fatality rates for all periods investigated after hospital admission. A significant decrease in case-fatality rates at 31—365 days was observed between 2010 and 2015.

Although the French FAST-MI programme reported lower 30-day mortality rates in patients who had STEMI in 2015 (3%), the population considered came from cardiac intensive care units, and therefore under-represented patients admitted to general intensive care units and very elderly patients admitted to geriatric units or general wards [8]. In international studies based on hospital databases similar to those that we used, higher 30-day and 1-year mortality rates were found in Sweden, Italy and New Zealand [12—14].

The lower likelihood of survival in women than in men in the early days after an ACS that we observed might be explained by their higher risk profile and the prolonged delay between onset of pain and first medical contact [15]. The most recent publication from the FAST-MI programme highlighted important sex differences in terms of delays in seeking medical attention, with women taking much longer before consulting [16,17]. Interestingly, the e-MUST registry showed that women faced higher in-hospital mortality after STEMI, even after adjusting for delay before consulting (i.e. hospital admission) and other confounding factors [18].

With regard to case-fatality rates at 31—365 days, female sex was associated with a significantly lower risk, even before adjusting for early hospital management. Our results are in line with those from the Swedish registries and a meta-analysis of 35 studies on patients with STEMI who all had a primary PCI [12,19]. These results could be explained by the higher life expectancy in general in women. Several studies have shown that, despite similar adjusted all-cause mortality rates, women had much higher acute myocardial infarction-related excess mortality rates than men [20,21].

One interesting finding of our study was the substantial increased risk of case fatality among patients admitted to

Table 1 Characteristics of patients hospitalized for acute coronary syndrome and included in the study in 2015.

	All ACS			STEMI		
	Total (*n* = 84,202)	Men (*n* = 56,465)	Women (*n* = 27,737)	Total (*n* = 29,358)	Men (*n* = 20,437)	Women (*n* = 8921)
Mean age (years)	67.3	64.7	72.4	65.2	62.2	71.3
18–65 years	42.6	49.2	29.1	50.1	57.9	32.1
65–85 years	44.7	43.2	47.8	37.6	35.7	42.1
≥ 85 years	12.7	7.6	23.1	12.3	6.4	25.8
Charlson Comorbidity Index score						
0	63.8	65.2	61.1	64.1	67. 1	57.2
1	7.8	7.6	8.1	6.2	5.9	7.0
2–3	24.7	23.7	26.6	26.0	23.9	30.7
4–5	2.9	2.6	3.5	2.9	2.3	4.2
≥ 6	0.8	0.8	0.7	0.9	0.9	0.9
Cardiogenic shock at admission	4.2	4.1	4.4	7.2	6.7	8.2
Previous hospitalization for ACS[a]	10.8	11.3	9.8	5.3	5.5	5.0
Hospitalization for heart failure at 1 year[b]	11.3	10.1	13.8	10.9	9.3	15.3
Social Deprivation Index score[c]						
1 (the least deprived)	16.6	17.0	15.7	16.4	16.6	15.8
2	18.5	18.8	17.9	19.2	19.4	18.6
3	20.1	20.3	19.6	19.7	20.0	19.0
4	21.8	21.4	22.5	21.8	21.5	22.6
5 (the most deprived)	23.0	22.4	24.3	22.9	22.5	23.9
CMUc[d]	13.8	13.0	16.6	13.2	12.6	16.0
Management						
Admission to resuscitation unit or ICU stay	66.2	68.8	60.9	85.3	87.8	79.6
ICCU stay	64.0	66.4	59.1	82.7	85.2	77.1
Admission through ED	46.1	43.9	50.5	46.2	43.9	50.5
Coronary artery procedure during the first 3 days in those who died early						
Coronary angiography only	15.8	17.7	13.7	14.8	17.7	11.7
PCI	39.7	46.0	32.1	48.1	56.5	38.7
CABG	1.6	1.7	1.4	0.6	0.4	0.9
Coronary artery procedure during the first 3 days after hospital admission[e]						
Coronary angiography only	34.3	33.1	36.9	21.6	21.0	23.0
PCI	58.7	64.2	47.4	77.4	82.1	66.2
CABG	2.1	2.5	1.3	1.3	1.5	1.0
Medication delivered in the 3 months following hospital admission[f]						
Antithrombotics	88.9	90.9	84.5	92.8	93.9	90.3
Beta-blockers	76.8	78.6	72.9	85.7	87.3	82.0
Other antihypertensive drugs	76.0	76.7	74.5	82.5	83.2	80.9
Lipid-lowering drugs	83.1	86.7	75.7	88.7	91.4	82.1
Combination of the four categories above	57.6	60.9	50.5	71.9	74.7	64.8

Data are expressed as mean (age only) or %. ACS: acute coronary syndrome; CABG: coronary artery bypass graft; CMUc: couverture maladie universelle complémentaire (complementary universal health insurance coverage); ED: emergency department; ICCU: intensive cardiac care unit; ICU: intensive care unit; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

[a] In the 5 years before the index hospital admission.

[b] In 1-year survivors.

[c] Of the area of residence.

[d] In patients aged < 60 years (*n* = 26,172 patients with ACS).

[e] Among patients still alive 3 days after hospital admission (*n* = 82,448 patients with ACS).

[f] Among patients leaving the hospital alive and with a length of stay < 30 days (*n* = 80,157 patients with ACS).

Table 2 Hazard ratios for determinants of case-fatality rates at 3 days, 4—30 days, 31—365 days and 1 year (multivariable analyses[a]).

	All ACS				STEMI			
	3 days	4—30 days	31—365 days	1 year	3 days	4—30 days	31—365 days	1 year
Model 1								
Period 2015 versus 2010	1.01 (0.95—1.09)	0.98 (0.93—1.03)	0.88 (0.84—0.91)	0.93 (0.90—0.96)	1.03 (0.95—1.12)	0.97 (0.90—1.05)	0.86 (0.81—0.93)	0.94 (0.90—0.98)
Female versus male	1.19 (1.14—1.24)	0.98 (0.94—1.01)	0.84 (0.82—0.86)	0.93 (0.91—0.95)	1.27 (1.21—1.34)	1.01 (0.97—1.06)	0.92 (0.88—0.96)	1.04 (1.01—1.07)
Previous ACS	0.55 (0.50—0.60)	0.67 (0.63—0.72)	1.17 (1.13—1.21)	0.94 (0.91—0.97)	0.92 (0.82—1.04)	0.93 (0.84—1.03)	1.45 (1.34—1.57)	1.22 (1.15—1.29)
Social deprivation level (most versus least)	1.26 (1.18—1.34)	1.29 (1.23—1.36)	1.28 (1.23—1.32)	1.26 (1.23—1.30)	1.28 (1.18—1.39)	1.30 (1.21—1.40)	1.32 (1.24—1.41)	1.28 (1.23—1.34)
Admission through ED	1.56 (1.50—1.63)	1.29 (1.24—1.33)	1.19 (1.16—1.22)	1.32 (1.30—1.34)	1.28 (1.22—1.35)	1.18 (1.13—1.24)	1.15 (1.10—1.20)	1.24 (1.20—1.27)
Model 2[b]								
2015 versus 2010	—	1.05 (0.99—1.11)	0.94 (0.90—0.97)	0.99 (0.96—1.02)	—	1.06 (0.98—1.15)	0.95 (0.89—1.02)	1.00 (0.95—1.05)
Female versus male	—	0.95 (0.92—0.99)	0.79 (0.77—0.81)	0.86 (0.85—0.88)	—	0.99 (0.94—1.03)	0.87 (0.83—0.91)	0.92 (0.89—0.95)
Previous ACS	—	0.65 (0.61—0.69)	1.12 (1.08—1.16)	0.92 (0.89—0.94)	—	0.89 (0.80—0.99)	1.39 (1.28—1.50)	1.13 (1.07—1.21)
Social deprivation level (most versus least)	—	1.20 (1.14—1.26)	1.20 (1.16—1.25)	1.18 (1.14—1.21)	—	1.18 (1.10—1.27)	1.21 (1.13—1.29)	1.19 (1.13—1.25)
Admission to ED	—	1.17 (1.14—1.21)	1.07 (1.05—1.10)	1.12 (1.10—1.14)	—	1.08 (1.03—1.13)	1.04 (0.99—1.08)	1.06 (1.03—1.09)
Coronary angiography only	—	0.51 (0.49—0.53)	0.75 (0.73—0.77)	0.64 (0.62—0.65)	—	0.59 (0.56—0.63)	0.80 (0.76—0.84)	0.70 (0.67—0.73)
PCI[c]	—	0.59 (0.57—0.61)	0.53 (0.52—0.55)	0.54 (0.52—0.55)	—	0.46 (0.44—0.49)	0.44 (0.42—0.46)	0.45 (0.44—0.47)
CABG	—	1.09 (0.97—1.22)	0.57 (0.51—0.63)	0.66 (0.61—0.71)	—	1.04 (0.85—1.28)	0.58 (0.46—0.73)	0.74 (0.64—0.87)

Table 2 (*Continued*)

	All ACS				STEMI			
	3 days	4–30 days	31–365 days	1 year	3 days	4–30 days	31–365 days	1 year
Model 3[d]								
2015 versus 2010	–	1.05 (0.96–1.15)	0.92 (0.89–0.96)	0.96 (0.92–0.99)	–	1.04 (0.91–1.19)	0.94 (0.87–1.00)	0.96 (0.90–1.02)
Female versus male	–	0.70 (0.66–0.74)	0.74 (0.72–0.76)	0.73 (0.72–0.75)	–	0.76 (0.70–0.82)	0.80 (0.76–0.83)	0.79 (0.75–0.82)
Previous ACS	–	0.93 (0.85–1.02)	1.23 (1.19–1.27)	1.16 (1.12–1.19)	–	1.00 (0.84–1.19)	1.43 (1.32–1.54)	1.30 (1.21–1.40)
Social deprivation level (most versus least)	–	1.40 (1.29–1.52)	1.21 (1.17–1.26)	1.24 (1.20–1.28)	–	1.34 (1.18–1.52)	1.23 (1.15–1.31)	1.24 (1.17–1.32)
Admission through ED	–	1.27 (1.20–1.34)	1.10 (1.08–1.13)	1.13 (1.10–1.15)	–	1.07 (0.99–1.15)	1.03 (0.99–1.07)	1.05 (1.01–1.09)
Coronary angiography only	–	0.80 (0.75–0.85)	0.76 (0.74–0.78)	0.76 (0.74–0.78)	–	0.94 (0.85–1.03)	0.92 (0.87–0.97)	0.91 (0.87–0.95)
PCI[c]	–	1.21 (1.15–1.29)	0.65 (0.63–0.67)	0.70 (0.68–0.72)	–	0.91 (0.83–0.99)	0.59 (0.56–0.62)	0.63 (0.60–0.66)
CABG	–	1.50 (1.25–1.80)	0.63 (0.57–0.70)	0.60 (0.54–0.67)	–	1.22 (0.89–1.67)	0.60 (0.47–0.75)	0.66 (0.53–0.81)
Antithrombotics	–	0.34 (0.32–0.37)	0.70 (0.68–0.73)	0.61 (0.59–0.63)	–	0.36 (0.31–0.42)	0.65 (0.60–0.69)	0.57 (0.54–0.61)
Beta-blockers	–	0.52 (0.49–0.57)	0.81 (0.79–0.83)	0.76 (0.74–0.79)	–	0.50 (0.44–0.58)	0.71 (0.67–0.75)	0.68 (0.64–0.71)
Other antihypertensive drugs	–	0.42 (0.39–0.45)	0.91 (0.88–0.94)	0.77 (0.75–0.79)	–	0.46 (0.41–0.53)	0.84 (0.79–0.89)	0.73 (0.69–0.77)
Lipid-lowering drugs	–	0.29 (0.26–0.31)	0.54 (0.53–0.56)	0.49 (0.48–0.51)	–	0.26 (0.23–0.31)	0.51 (0.48–0.54)	0.46 (0.43–0.48)

Data are expressed as hazard ratio (95% confidence interval). ACS: acute coronary syndrome; CABG: coronary artery bypass graft; ED: emergency department; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

[a] Adjusted for age, Charlson Comorbidity Index score and all other covariates.

[b] Model 1 in 3-day survivors, adjusted for coronary treatment in the first 3 days.

[c] Including coronary procedures other than CABG.

[d] Model 2 in inpatient survivors, adjusted for medication delivery in the first 30 days.

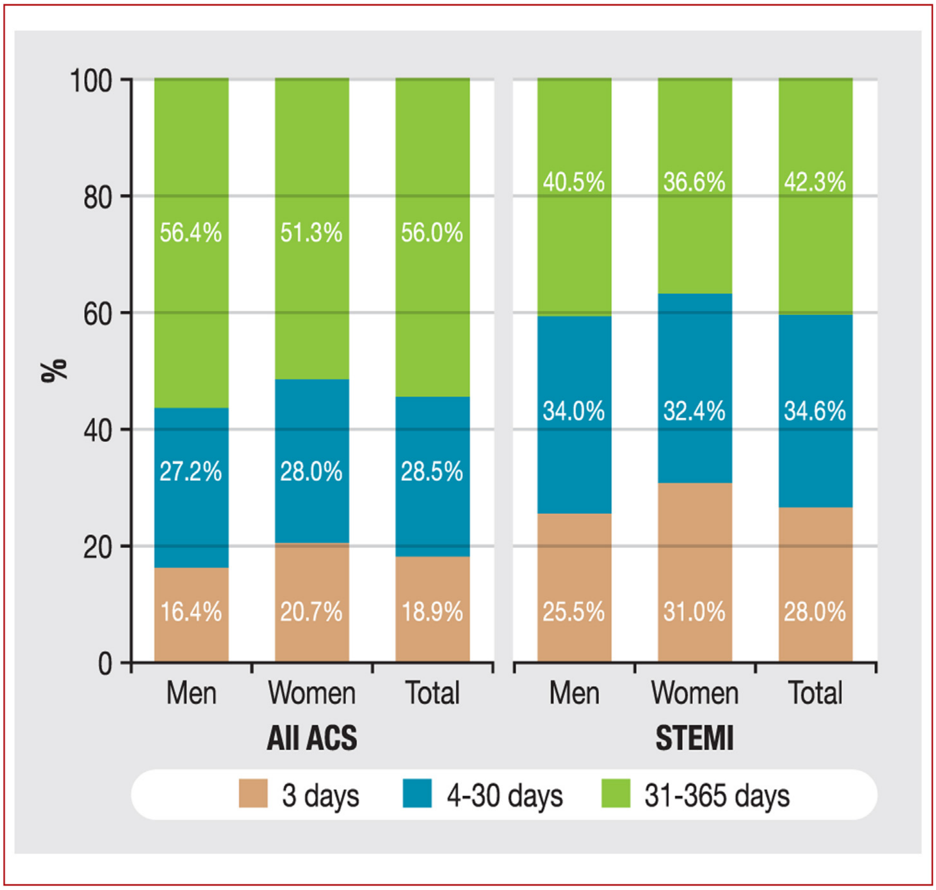

Figure 1. Distribution of deceased patients according to time between hospitalization and death in 2015. ACS: acute coronary syndrome; STEMI: ST-segment elevation myocardial infarction.

hospital through an ED, especially during the initial phase. The French USIC 2000 survey demonstrated that bypassing the ED, and entering a cardiac care unit directly, was associated with lower mortality among patients with STEMI [22]. Furthermore, among patients admitted through an ED, no higher proportion of cardiogenic shock was found (data not shown).

The effect of social deprivation we described reflects results from previous studies [23,24]. A higher proportion of CMUc beneficiaries was reported in patients with ACS compared with that in the general French population (8.8%), and the higher risk of death among CMUc beneficiaries has been demonstrated previously [25,26]. A recent study showed that patients from more deprived neighbourhoods experienced substantial delays from symptom onset to hospital care, leading to higher early case-fatality rates, until 30 days after hospital admission [27]. Lower rates of referral to cardiac rehabilitation at discharge were also observed in the same study, and may have affected 1-year case-fatality rates [27]. Residing in a rural area might affect ACS outcomes, as distance plays a particularly important role in prehospital and posthospital case-fatality rates [28]. Furthermore, patients living in disadvantaged neighbourhoods might have a higher risk profile [29]. When looking at drug deliveries at 1 year (Table A.5), patients living in the most deprived area had higher rates for all drugs compared with those living in the least deprived area. This is probably the result of a higher proportion of cardiovascular risk factors in the most deprived patients.

A decrease in the case-fatality rate at 31—365 days was observed over our study period, even after adjusting for sociodemographic factors. According to the FAST-MI programme, 6-month mortality continued to decline between 2010 and 2015, whereas patients' characteristics did not change [8]. Therefore, increased adherence to ACS management guidelines mainly explained the decrease in late case-fatality rates. The FAST-MI programme clearly showed an increased use of primary PCI and in-hospital PCI or CABG. In a previous study we observed an increase in admissions to cardiac rehabilitation units after acute myocardial infarction in France, which might certainly play a role in reducing late case-fatality rates after ACS, including STEMI [6]. The non-significant trend in our present study period in 30-day case-fatality rates could be related to longer delays before calling emergency services—something reported in the most recent FAST-MI study [8].

Study strengths and limitations: The major strength of our study was that it recorded nationally and exhaustively hospital admissions for ACS from both private and public hospitals, and complete follow-up. One limitation was that we had no access to data on prehospital death. Therefore, the case-fatality rates after an ACS may have been

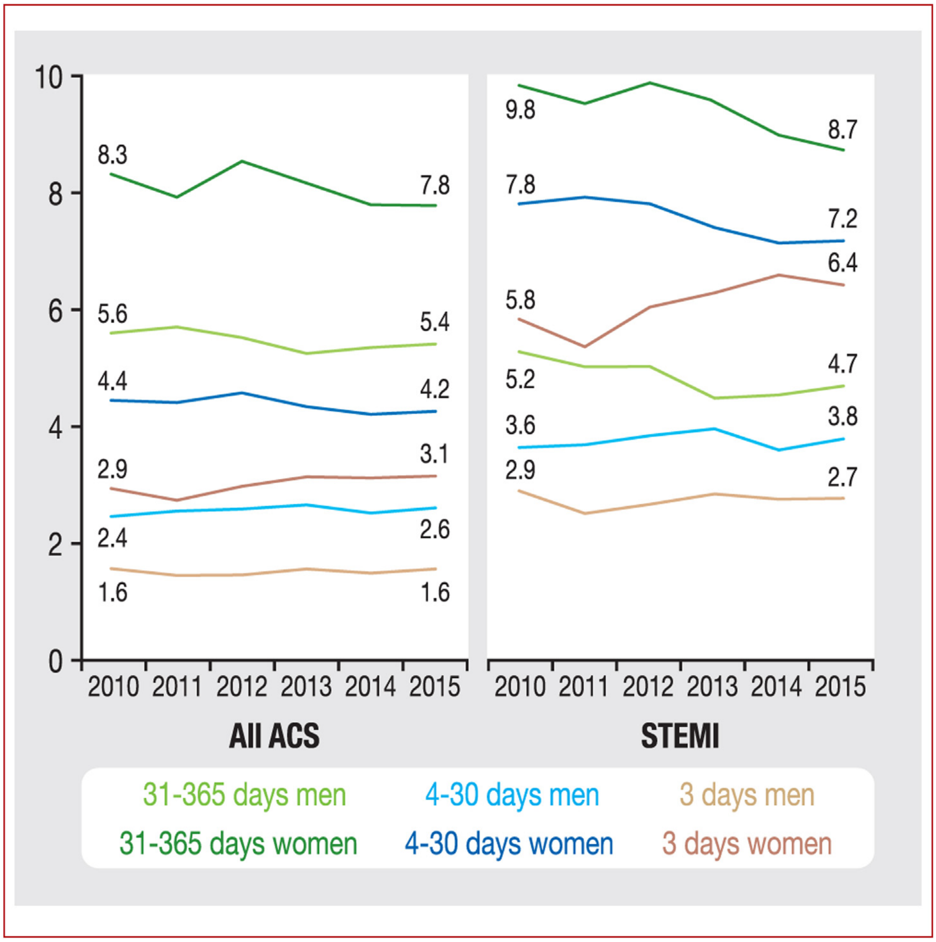

Figure 2. Time trends of crude case-fatality rates between 2010 and 2015, at 3 days, 4—30 days[a] and 31—365 days[a]. STEMI: ST-segment elevation myocardial infarction. [a] Among survivors of the preceding period.

underestimated. The lack of information about the severity of hospitalized cases limited the interpretation of the results. As we did not have access to the exact hour of hospital admission or coronary procedure, we were unable to adjust correctly for early invasive management without introducing a bias. Finally, the coding of unstable angina and other myocardial infarction changed over the study period, leading to difficulties in case identification. We observed low 1-year mortality in patients with unstable angina, which could reflect miscoding of stable angina as unstable angina. Validation of unstable angina codes should be addressed.

Conclusions

Our study showed high case-fatality rates after hospitalization for ACS, including STEMI, in France. There is still a great need for improved general population awareness and preparedness regarding ACS—particularly acute myocardial infarction—as well as follow-up of patients after the acute stage. Forty-six per cent of the patients analysed were admitted to hospital through an ED; these patients were associated with higher case-fatality rates. This highlights the importance of supporting national campaigns encouraging people to call the emergency services in case of ACS symptoms, instead of going directly to a hospital ED. After adjustment for sociodemographic factors, women had a particularly high risk of death in the early stage of hospitalization. The level of social deprivation of the patient's area of residence impacted case-fatality outcomes from 3 days to 1 year, meaning that optimal ACS management does not erase socioeconomic discrepancies. While no change in 30-day case-fatality rates was observed between 2010 and 2015, a favourable and encouraging trend was found for case-fatality rates at 31—365 days.

Ethics approval

In line with French governmental regulations and the National Ethics Committee, no patient consent was required.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2019.09.004.

Disclosure of interest

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The other authors declare that they have no competing interest.

References

[1] Gabet A, Danchin N, Juilliere Y, Olie V. Acute coronary syndrome in women: rising hospitalizations in middle-aged French women, 2004—2014. Eur Heart J 2017;38:1060—5.

[2] Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J 2016;37:267—315.

[3] 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. The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2018;39:119—77.

[4] Vaccarino V, Krumholz HM, Berkman LF, Horwitz RI. Sex differences in mortality after myocardial infarction. Is there evidence for an increased risk for women? Circulation 1995;91:1861—71.

[5] Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation 2018;137:e67—492.

[6] Gabet A, De Peretti C, Iliou MC, Nicolau J, Olie V. National trends in admission for cardiac rehabilitation after a myocardial infarction in France from 2010 to 2014. Arch Cardiovasc Dis 2018;111:625—33.

[7] Degano IR, Salomaa V, Veronesi G, et al. Twenty-five-year trends in myocardial infarction attack and mortality rates, and case-fatality, in six European populations. Heart 2015;101:1413—21.

[8] Puymirat E, Simon T, Cayla G, et al. Acute myocardial infarction: changes in patient characteristics, management, and 6-month outcomes over a period of 20 years in the FAST-MI program (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) 1995 to 2015. Circulation 2017;136:1908—19.

[9] 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.

[10] Rey G, Jougla E, Fouillet A, Hemon D. Ecological association between a deprivation index and mortality in France over the period 1997—2001: variations with spatial scale, degree of urbanicity, age, gender and cause of death. BMC Public Health 2009;9:33.

[11] Quan H, Li B, Couris CM, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. Am J Epidemiol 2011;173:676—82.

[12] Berg J, Bjorck L, Nielsen S, Lappas G, Rosengren A. Sex differences in survival after myocardial infarction in Sweden, 1987—2010. Heart 2017;103:1625—30.

[13] Greco C, Rosato S, D'Errigo P, Mureddu GF, Lacorte E, Seccareccia F. Trends in mortality and heart failure after acute myocardial infarction in Italy from 2001 to 2011. Int J Cardiol 2015;184:115—21.

[14] Grey C, Jackson R, Wells S, Marshall R, Riddell T, Kerr AJ. Twenty-eight day and one-year case fatality after hospitalisation with an acute coronary syndrome: a nationwide data linkage study. Aust N Z J Public Health 2014;38:216—20.

[15] Piackova E, Jager B, Farhan S, et al. Gender differences in short- and long-term mortality in the Vienna STEMI registry. Int J Cardiol 2017;244:303—8.

[16] Manzo-Silberman S, Couturaud F, Charpentier S, et al. Influence of gender on delays and early mortality in ST-segment elevation myocardial infarction: insight from the first French Metaregistry, 2005—2012 patient-level pooled analysis. Int J Cardiol 2018;262:1—8.

[17] Langabeer 2nd JR, Henry TD, Fowler R, Champagne-Langabeer T, Kim J, et al. Sex-based differences in discharge disposition and outcomes for ST-segment elevation myocardial infarction patients within a regional network. J Womens Health (Larchmt) 2018;27:1001—6.

[18] Benamer H, Bataille S, Tafflet M, et al. Longer pre-hospital delays and higher mortality in women with STEMI: the e-MUST Registry. EuroIntervention 2016;12:e542—9.

[19] Pancholy SB, Shantha GP, Patel T, Cheskin LJ. Sex differences in short-term and long-term all-cause mortality among patients with ST-segment elevation myocardial infarction treated by primary percutaneous intervention: a meta-analysis. JAMA Intern Med 2014;174:1822—30.

[20] Alabas OA, Gale CP, Hall M, et al. Sex differences in treatments, relative survival, and excess mortality following acute myocardial infarction: National Cohort Study using the SWEDEHEART registry. J Am Heart Assoc 2017;6.

[21] Ndrepepa G, Kufner S, Mayer K, et al. Sex differences in the outcome after percutaneous coronary intervention — - A propensity matching analysis. Cardiovasc Revasc Med 2019;20:101—7.

[22] Steg PG, Cambou JP, Goldstein P, et al. Bypassing the emergency room reduces delays and mortality in ST elevation myocardial infarction: the USIC 2000 registry. Heart 2006;92:1378—83.

[23] Thorne K, Williams JG, Akbari A, Roberts SE. The impact of social deprivation on mortality following acute myocardial infarction, stroke or subarachnoid haemorrhage: a record linkage study. BMC Cardiovasc Disord 2015;15:71.

[24] Tonne C, Schwartz J, Mittleman M, Melly S, Suh H, Goldberg R. Long-term survival after acute myocardial infarction is lower in more deprived neighborhoods. Circulation 2005;111:3063—70.

[25] Tuppin P, Ricci-Renaud P, de Peretti C, et al. Frequency of cardiovascular diseases and risk factors treated in France according to social deprivation and residence in an overseas territory. Int J Cardiol 2014;173:430—5.

[26] Danchin N, Neumann A, Tuppin P, et al. Impact of free universal medical coverage on medical care and outcomes in low-income patients hospitalized for acute myocardial infarction: an analysis from the French National Health

Insurance system. Circ Cardiovasc Qual Outcomes 2011;4:619—25.
[27] Udell JA, Desai NR, Li S, et al. Neighborhood socioeconomic disadvantage and care after myocardial infarction in the National Cardiovascular Data Registry. Circ Cardiovasc Qual Outcomes 2018;11:e004054.
[28] Wei L, Lang CC, Sullivan FM, et al. Impact on mortality following first acute myocardial infarction of distance between home and hospital: cohort study. Heart 2008;94:1141—6.
[29] Canto JG, Kiefe CI, Rogers WJ, et al. Number of coronary heart disease risk factors and mortality in patients with first myocardial infarction. JAMA 2011;306:2120—7.