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ORIGINAL RESEARCH

Incidence, Characteristics, and Outcomes of Ventricular Fibrillation Complicating Acute Myocardial Infarction in Women Admitted Alive in the Hospital

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BACKGROUND: Little data are available in women presenting with ventricular fibrillation (VF) in the setting of acute myocardial infarction (AMI). We assessed frequency, predictors of VF, and outcomes, with a special focus on women compared with men.

METHODS AND RESULTS: Data were analyzed from the FAST-MI (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) program, which prospectively included 14 406 patients admitted to French cardiac intensive care units ≤48 hours from AMI onset between 1995 and 2015 (mean age, 66±14 years; 72% men; mean left ventricular ejection fraction, 52±12%; 59% with ST-segment–elevation myocardial infarction). A total of 359 patients developed VF during AMI, including 81 women (2.0% of 4091 women) and 278 men (2.7% of 10 315 men, P=0.02). ST-segment–elevation myocardial infarction (odds ratio [OR], 2.29 [95% CI, 1.75–2.99]; P<0.001) was independently associated with the onset of VF during AMI. In contrast, female sex (OR, 0.73 [95% CI, 0.56–0.95]; P=0.02), hypertension (OR, 0.75 [95% CI, 0.60–0.94]; P=0.01), and prior myocardial infarction (OR, 0.69 [95% CI, 0.50–0.96]; P=0.03) were protective factors. Women were less likely to have cardiac intervention than men (percutaneous coronary intervention during hospitalization 48.1% versus 66.9%, respectively; P=0.04) with a higher 1-year mortality in women compared with men (50.6% versus 37.4%, respectively; P=0.03), including increased in-hospital mortality (42.0% versus 32.7%, respectively; P=0.12). After adjustment, female sex was no longer associated with a worse 1-year mortality (adjusted hazard ratio, 1.10 [95% CI, 0.75–1.61]; P=0.63).

CONCLUSIONS: Women have lower risk of developing VF during AMI compared with men. However, they are less likely to receive cardiac interventions than men, possibly contributing to missed opportunities of improved outcomes.

Key Words: myocardial infarction ■ sex ■ sudden cardiac death ■ women

Life-threatening ventricular arrhythmias such as ventricular fibrillation (VF) may occur at any time in the setting of an acute myocardial infarction (AMI). Despite considerable progress in AMI management, including prompt revascularization and early introduction of recommended medical therapy, ventricular arrhythmias

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CLINICAL PERSPECTIVE

What Is New?

- This is the first study to provide information about the incidence of ventricular fibrillation after acute myocardial infarction in women.
- Ventricular fibrillation after acute myocardial infarction occurred less frequently in women than in men, with female sex being an independently protective factor against ventricular fibrillation occurrence.
- Crude 1-year death rate was 5-fold higher in women than in men, but this difference disappeared after adjustment on age, type of myocardial infarction, comorbidity, and percutaneous coronary intervention.

What Are the Clinical Implications?

- Ventricular fibrillation complicating acute myocardial infarction is less frequent in women but remains unexceptional.
- Women were less likely to receive cardiac interventions, possibly contributing to missed opportunities of improved outcomes.
- Bridging the gap between in-hospital treatment after acute myocardial infarction between men and women may enable significant improvement of women's outcomes.

Nonstandard Abbreviations and Acronyms

FAST-MI	French Registry of Acute ST-Elevation or Non–ST-Elevation–Myocardial Infarction

still occur in a nonnegligible proportion of patients.[1,2] Right from the onset of ischemia until the late post–myocardial infarction period, the risk of cardiac arrest and sudden cardiac death is increased in patients with AMI.[1,3] Furthermore, VF in AMI remains associated with poor short-term prognosis and worsened outcomes, especially in the first 90 days after AMI.[4–6]

Ventricular arrhythmias are mainly triggered by myocardial acute ischemia, which has a wider range of mechanisms in women than in men. In addition to the classic thrombotic plaque rupture, women have a higher proportion of cases caused by coronary spasm, dissection, hematoma, plaque erosion, or even normal epicardial coronaries with microvascular involvement.[7] These differences may partly account for the trend to excess mortality in women with obstructive coronary artery disease, although undertreatment may also play a role.[8–10] In nonobstructive coronary artery disease, historically described as a more benign presentation, there is still nonnegligible morbidity and mortality in both men and women.[9,11]

Although several sex differences have already been reported with regard to coronary artery disease, acute coronary syndrome incidence, and rates of out-of-hospital cardiac arrest, there are almost no data on ventricular arrhythmia incidence and its predictors in women in the context of a myocardial infarction.[12–16] Given the pathophysiological and prognostic differences discussed above, we hypothesized that women have a distinctive risk profile for ventricular arrhythmias in the setting of AMI.[12,13,17]

We therefore aimed to investigate sex discrepancies in the incidence, characteristics, and outcomes of AMI complicated with VF, through a nationwide program encompassing 2 decades.

METHODS

Patient Population

Five nationwide French prospective registries were conducted 5 years apart between 1995 and 2015, using a similar methodology detailed in Data S1. These included USIK 1995, USIC (Unité de Soins Intensifs Coronaires) 2000, FAST-MI (French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction) 2005 (NCT00673036), FAST-MI 2010 (NCT01237418), and FIAST-MI 2015 (NCT02566200).[18–20] In brief, the primary objectives of these registries were to evaluate the characteristics, management, and outcomes of patients with AMI. The methods used for these studies have been detailed previously, with definition of myocardial infarction (MI) periodically updated according to latest guidelines.[21,22] Each study was conducted in accordance with the guidelines on good clinical practice and French law. The study protocols for all surveys were reviewed by the relevant Committees for the Protection of Human Subjects. All of the subjects gave informed consent to participate in the registry. The data that support the findings of this study are available according to French data protection regulations, from the last author (N.D.) upon reasonable request.

All 5 registries included consecutive patients with AMI admitted to cardiac intensive care units within 48 hours of symptom onset, during a specified 3-month period (1995, 2000, 2005, 2010, and 2015). Patients ≥18 years of age admitted within 48 hours of symptom onset were included if they had: (1) elevated serum markers of myocardial necrosis more than twice the upper limit of normal and (2) either symptoms compatible with AMI and/or suggestive electrocardiographic changes on at least 2 contiguous leads, namely pathologic Q waves (at least 0.04-s duration) and/or ST-elevation or depression >0.1 mV. Exclusion criteria were (1) refusal to participate, (2) iatrogenic

MI (in particular, types 4 and 5 AMI), and (3) AMI diagnosis invalidated in favor of another diagnosis. ST-segment–elevation myocardial infarction (STEMI) was diagnosed when ST-segment elevation ≥1 mm was seen in at least 2 contiguous leads corresponding to any coronary territory on the index or qualifying ECG, or when presumed new left bundle-branch block or documented new Q waves were observed. In the absence of ST-segment elevation, patients satisfying the inclusion criteria were considered to have non–ST-segment–elevation myocardial infarction (NSTEMI).

In the present study, we analyzed patients with AMI according to whether they developed VF (or hemodynamically poorly tolerated ventricular tachycardia) during the acute phase (defined by occurrence of VF within the hospital stay after AMI diagnosis) and stratified by sex. Patients with regular ventricular tachycardia, such as accelerated idioventricular rhythm, were not included in the VF group.

Participation in the study was offered to all French institutions, including university teaching hospitals, general and regional hospitals, as well as private hospitals managing patients with AMI. Physicians were instructed that the study should not affect usual clinical care or management. The study was conducted in accordance with guidelines on good clinical practice and French law. The study protocols for all surveys were reviewed by the relevant Committees for the Protection of Human Subjects. Data file collection and storage were approved by the Commission Nationale Informatique et Liberté. All patients were informed of the nature and the aims of the surveys and could request to be excluded; in addition, written consent was obtained for the 2005, 2010, and 2015 studies.

Among all centers managing patients with AMI in France, 62% (312 centers, 2152 patients) participated in 1995, 83% in 2000 (369 centers, 2317 patients), 60% in 2005 (223 centers, 3059 patients), 76% in 2010 (213 centers, 3079 patients), and 78% in 2015 (204 centers, 3813 patients).

Data Collection

Data on baseline characteristics, including demographics (age, sex, and body mass index), risk factors (hypertension, diabetes, current smoking, hypercholesterolemia, and family history of coronary artery disease), and medical history (MI, stroke, heart failure, and peripheral artery disease) were collected prospectively. Information on left ventricular ejection fraction, cardiac intervention including percutaneous coronary intervention (PCI), use of medications (anticoagulants, antiplatelet agents, β-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and statins) and whether they were started within the first 48 hours (within the first 5 days for the 1995 survey) was collected as well. Complete medical therapy was defined as concomitant use of antiplatelet agents and statins for all patients, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and β-blockers when appropriate. In the USIK 1995 survey, in-hospital mortality was not specifically recorded; for analyzing survival in patients leaving the hospital alive, we used 10-day mortality as a surrogate of hospital mortality for the 1995 survey.

Follow-up information was organized at the French Society of Cardiology and performed by dedicated research technicians of the Unite de Recherche Clinique de l'Est Parisien. Hospital discharge reports were sought for each reported event leading to hospitalization or death and analyzed by at least 1 physician from the research team. A systematic review of all death notifications was performed, with central adjudication of all events by 2 independent cardiologists blinded to VF status. In cases of divergent opinions on the mode of death, a third expert was asked to arbitrate.

Statistical Analysis

Continuous variables are reported as means and SDs or medians and interquartile ranges, when appropriate. Discrete variables are described as counts and percentages. Groups were compared by analysis of variance, Mann-Whitney or Kruskall-Wallis tests for continuous variables, and χ^2 or Fisher exact tests for discrete variables. Temporal trends were tested using linear-by-linear association tests for binary and Jonckheere-Terpstra tests for continuous variables. Odds ratios (ORs) and hazard ratios (HRs) are presented with their 95% CIs.

To determine independent predictors of VF occurrence in men and women, binary logistic regression analysis was used, considering survey period, age, sex, risk factors, previous cardiovascular history, type of MI (STEMI versus NSTEMI), left ventricular ejection fraction, and use of PCI.

Multivariable analyses of correlates of 1-year mortality were performed using Cox backward stepwise multiple modeling, using a threshold of 0.10 for variable elimination. Beside time period, variables included in the final models were selected ad hoc, based on their physiological relevance and potential to be associated with outcomes; they comprised age, sex, risk factors, comorbidity, type of MI, year of survey, use of PCI, use of antiplatelet agents, β-blockers, statins, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers during the first 2 days (5 days for the 1995 survey), and repeated in 3-day survivors to avoid healthy survivor bias. In patients with VF discharged alive, only age, sex, and type of MI were used as covariables because of the low number of events at 1 year.

Statistical analyses were performed by using IBM SPSS 25.0 (IBM). For all analyses, 2-sided *P* values <0.05 were considered significant.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the article as written.

RESULTS

VF Incidence According to Sex

Among 14 406 patients admitted with AMI, 359 patients (2.5%) developed VF, of whom, 15.0% were women (N=81) (Figure 1). VF incidence was 2.0% in women (81/4091) and 2.7% in men (278/10315) (*P*=0.02). The incidence of VF decreased over time from 1995 until 2015 in both men and women (*P*<0.001, respectively). Among patients with STEMI (N=8566), 26.7% (N=2276) were women and 66 (2.9%) developed VF during the acute phase, mostly with anterior STEMI (40/66 VF during STEMI, 60.6%). In men, 3.5% of patients with STEMI (219/6289) had VF, with about half being attributable to anterior STEMI (105/219, 47.9%). Conversely, of 5840 patients with NSTEMI, 59 men (1.5%) and 15 women (0.8%), presented with VF. Thus, most VF cases occurred in the STEMI setting (78.8% of cases in men and 81.5% in women) rather than in NSTEMI.

Factors Associated With VF Occurrence

Patients with VF had fewer cardiovascular comorbidities and risk factors compared with those without VF (Table 1). In women, those with VF were younger (70.2±15.1 versus 72.9±13.4 years of age, *P*=0.07), with less hypertension (51.9% versus 66.6%, *P*=0.005) and hypercholesterolemia prevalence (29.6% versus 41.7%, *P*=0.03). Current smoking was, however, more frequent in women with VF (25.9% versus 17.2%, *P*=0.04). Results were similar among men, with less prevalent cardiovascular risk factors overall. History of prior MI or PCI was also less frequent in men with VF (11.9% versus 19.0%, *P*=0.001 and 8.3% versus 16.7%, *P*=0.001, respectively). Chronic medication use before the index episode was recorded since 2000; the percentage of patients with VF was not significantly different in those with or without β-blocker treatment before the AMI, both in women (25.4% versus 26.5%, *P*=0.85) and men (19.0% versus 22.9%, *P*=0.17).

When comparing men and women who presented with VF during AMI, women were older than men (70.2±15.1 versus 64.2±14.1 years old, *P*=0.001). The cardiovascular risk profile also differed with more hypertension among women (51.8% versus 38.8%, *P*=0.04), whereas smoking was more prevalent among men with VF (42.1% versus 25.9%, *P*=0.009).

Multivariate analysis (Table 2) showed that, in the total population, older age (OR, 1.01 [95% CI, 1.00–1.02]; *P*=0.05) and STEMI (OR, 2.29 [95% CI, 1.75–2.99]; *P*<0.001) were independently associated with the onset of VF during AMI. In contrast, female sex (OR, 0.73 [95% CI, 0.56–0.95]; *P*=0.02), hypertension (OR, 0.75 [95% CI, 0.60–0.96]; *P*=0.03), and prior MI (OR, 0.69 [95% CI, 0.50–0.96]; *P*=0.03) were associated with lower risk for VF. In addition, the more recent years of the registry were inversely associated with VF occurrence (OR, 0.53 [95% CI, 0.37–0.74]; *P*<0.001 in 2010 and OR, 0.55 [95% CI, 0.40–0.77]; *P*<0.001 in 2015 versus 1995), and this was true in both men and women (data not shown).

Among women, after considering potential confounding factors, STEMI (OR, 2.79 [95% CI, 1.56–4.99]; *P*<0.001) and current smoking (OR, 1.84 [95% CI, 1.10–3.10]; *P*=0.02) were significantly associated with VF occurrence.

In-Hospital Management According to VF and Sex Status

In-hospital care, complications, and treatments by VF and sex are detailed in Table 3. Women who presented with VF during AMI underwent coronary angiography and PCI as

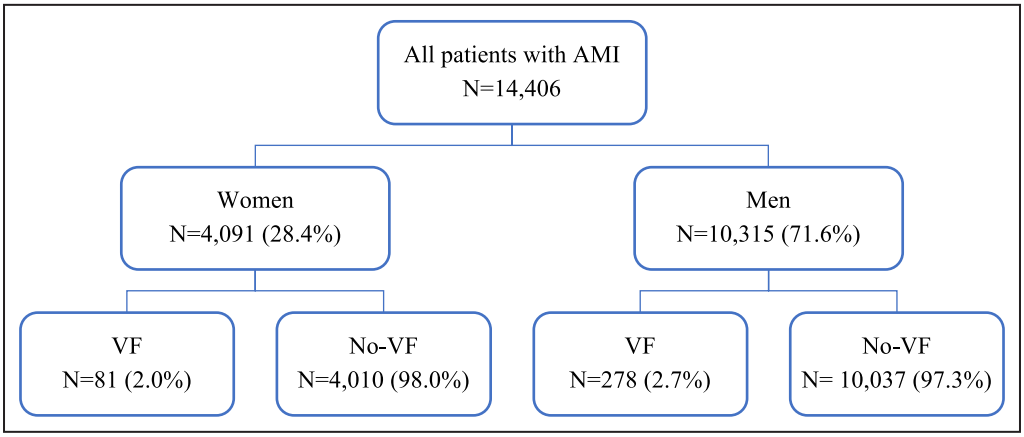

Figure 1. Flowchart of the study population.
AMI indicates acute myocardial infarction; and VF, ventricular fibrillation.

Table 1. Main Characteristics and Admission Parameters According to Sex and VF Status

Variables	Men		*P* value	Women		*P* value
	No VF, N=10 037	VF, N=278		No VF, N=4010	VF, N=81	
Main characteristics						
Age, y, mean±SD	63.4±13.6	64.2±14.1	0.30	72.9±13.4	70.2±15.1	0.07
BMI, mean±SD	26.9±4.2, N=9427	26.6±4.1, N=230	0.23	26.2±5.3, N=3610	25.7±4.8, N=69	0.48
Diabetes	1962 (19.5)	53 (19.1)	0.84	1019 (25.4)	21 (25.9)	0.92
Hypertension	4688 (46.7)	108 (38.8)	0.01	2679 (66.6)	42 (51.9)	0.005
Current smoking	3881 (38.7)	117 (42.1)	0.25	690 (17.2)	21 (25.9)	0.04
Hypercholesterolemia	4342 (43.3)	88 (31.7)	<0.001	1672 (41.7)	24 (29.6)	0.03
History of MI	1909 (19.0)	33 (11.9)	0.001	574 (14.3)	9 (11.1)	0.41
Prior PCI	1439 (16.7)	18 (8.3)	0.001	359 (10.3)	4 (6.8)	0.38
History of stroke	554 (5.5)	16 (5.8)	0.86	272 (6.8)	8 (9.9)	0.27
Chronic kidney disease	391 (4.6)	9 (4.2)	0.78	191 (5.6)	4 (6.8)	0.70
Previous β-blocker use	1962 (22.9), N=8566	41 (19.0), N=216	0.17	905 (26.5), N=3413	15 (25.4), N=59	0.85
Admission parameters						
LVEF, mean±SD	51.8±12.2, N=8090	45.3±15.4, N=203	<0.001	51.7±12.5, N=3018	46.2±13.1, N=54	0.001
Heart rate, mean±SD	78±19, N=8355	82±24, N=206	<0.001	81±20, N=3322	81±24, N=58	0.87
Systolic BP, mean±SD	139±27, N=8366	128±32, N=207	<0.001	141±30, N=3332	119±36, N=59	<0.001
STEMI	6071 (60.5)	219 (78.8)	<0.001	2210 (55.1)	66 (81.5)	<0.001
Admission Killip class ≥2	1281 (15.1)	62 (29.2)	<0.001	843 (25.0)	22 (37.3)	0.03

Variables are N (%) unless otherwise specified.

BMI indicates body mass index; BP, blood pressure; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; and VF, ventricular fibrillation.

frequently as those without VF (74.6% versus 82.6%, *P*=0.11 and 48.1% versus 52.8%, *P*=0.54, respectively). These results were similar among men. Secondary prevention treatments were prescribed similarly in women irrespective of VF status. Statins, β-blockers, and renin-angiotensin-aldosterone system inhibitors were prescribed equally as frequently, as was full guideline-recommended treatment (48.5% of women with VF versus 48.1% with no VF, *P*=0.96).

In the population with VF, compared with men, women underwent less coronary angiography (74.6% versus 89.4% in men, *P*=0.004), less PCI (48.1% versus 66.9% in men, *P*=0.004), and less primary PCI for STEMI (39.4% versus 53.9% in men, *P*=0.039). The OR adjusted on age, type of MI, and period for use of PCI during the hospital stay was 0.60 (95% CI, 0.33–1.08) for women versus men. Women with VF were less frequently prescribed

Table 2. Factors Associated With Ventricular Fibrillation in Multivariate Analysis

	Global population		Women		Men	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Women	0.73 (0.56–0.95)	0.02	…	…	…	…
Age	1.01 (1.00–1.02)	0.05	…	…	1.01 (1.004–1.02)	0.005
Year						
1995	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
2000	0.86 (0.63–1.17)	0.34	0.88 (0.48–1.62)	0.69	0.95 (0.59–1.22)	0.37
2005	0.65 (0.47–0.91)	0.01	0.53 (0.27–1.02)	0.06	0.69 (0.47–1.002)	0.05
2010	0.53 (0.37–0.74)	<0.001	0.28 (0.12–0.64)	0.003	0.60 (0.61–0.88)	0.009
2015	0.55 (0.40–0.77)	<0.001	0.37 (0.18–0.75)	0.006	0.60 (0.41–0.87)	0.006
Current smoking	…	…	1.84 (1.10–3.10)	0.02		
Hypertension	0.75 (0.60–0.94)	0.01	…	…	0.75 (0.59–0.995)	0.045
STEMI	2.29 (1.75–2.99)	<0.001	2.79 (1.56–4.99)	0.001	2.18 (1.61–2.95)	<0.001
Prior MI	0.69 (0.50–0.96)	0.03	…	…	0.63 (0.43–0.92)	0.02

MI indicates myocardial infarction; OR, odds ratio; Ref., reference; and STEMI, ST-segment–elevation myocardial infarction.

Table 3. In-Hospital Care, Complications, and Treatments According to Sex and VF Status

Variables	Men		*P* value	Women		*P* value
	No VF, N=10 037	VF, N=278		No VF, N=4010	VF, N=81	
In-hospital care						
Coronary angiography	7925 (92.5), N=8566	193 (89.4), N=216	0.08	2820 (82.6), N=3413	44 (74.6), N=59	0.11
Reperfusion therapy <24 h (STEMI)			0.001			0.72
None	1804 (29.7)	40 (18.3)		936 (42.4)	26 (39.4)	
Lysis	1472 (24.2)	61 (26.9)		385 (17.4)	14 (21.2)	
Primary PCI	2795 (46.0)	118 (53.9)		889 (40.2)	26 (39.4)	
PCI during hospitalization	6680 (66.6)	186 (66.9)	0.91	2119 (52.8)	39 (48.1)	0.54
Any revascularization (PCI or CABG)	6947 (69.2)	192 (69.1)	0.96	2197 (54.8)	40 (49.4)	0.33
In-hospital complications						
Cardiogenic shock	361 (3.6)	80 (28.8)	<0.001	257 (6.4)	21 (25.9)	<0.001
Recurrent MI	101 (1.2)	8 (53.7)	0.001	49 (1.4)	4 (6.8)	0.001
Stroke	49 (0.6)	4 (1.9)	0.02	33 (1.0)	1 (1.7)	0.57
New LBBB	76 (0.9)	0 (0.0)	0.17	37 (1.1)	1 (1.7)	0.64
New AV block	279 (2.8)	36 (12.9)	<0.001	156 (3.9)	10 (12.3)	<0.001
Secondary prevention treatments						
Antiplatelet agents	9446 (94.6), N=9700	208 (78.8), N=187	0.37	3575 (94.2), N=3726	51 (98.1), N=52	0.23
P2Y12 inhibitors	5958 (88.2), N=6752	107 (88.4), N=121	0.95	2124 (80.0), N=2655	24 (82.8), N=29	0.71
Statins	7310 (75.4), N=9689	136 (72.7), N=187	0.39	2564 (68.7), N=3724	33 (63.5), N=52	0.42
β-Blockers	7863 (81.2), N=9689	152 (81.3), N=187	0.96	2770 (74.4), N=3724	38 (73.1), N=52	0.83
RAAS inhibitors	6485 (66.9), N=9689	138 (73.8), N=187	0.048	2422 (65.0), N=3724	33 (63.5), N=52	0.81
Diuretics	1793 (21.6), N=8282	35 (22.9), N=153	0.71	1002 (31.3), N=3201	13 (30.0), N=40	0.86
Full guidelines-recommended treatment	5634 (58.5), N=9637	111 (60.0), N=165	0.67	1795 (48.5), N=3704	25 (48.1), N=52	0.96

Variables are N (%) unless otherwise specified.

AV indicates atrioventricular; CABG, coronary artery bypass graft; LBBB, left bundle-branch block; MI, myocardial infarction; PCI, percutaneous coronary intervention; P2Y12, P2Y12 adenoside diphosphate receptor; RAAS, renin-angiotensin-aldosterone system; STEMI, ST-segment–elevation myocardial infarction; and VF, ventricular fibrillation.

optimal medical therapy after AMI (statins in 63.5% versus 72.7% in men, *P*=0.04; β-blockers in 73.1% versus 81.3% in men, *P*=0.04; and full guideline recommended treatment in 48.1% versus 60.0% in men, *P*=0.07; adjusted OR, 0.87 [95% CI, 0.40–1.89]; *P*=0.73).

In-Hospital and 1-Year Mortality

In patients with VF, approximately one-third of men and women died before hospital discharge (or 10 days for the 1995 survey) (32.7% in men [91/278], 42.0% in women [34/81]; *P*=0.12). In contrast, in-hospital death occurred in only 3.7% of men (371/10037) and 7.7% of women (308/4010) who did not have VF (*P*<0.001).

One-year survival in the overall population according to VF status and sex is shown in Figure 2. In the population with VF, 1-year mortality was 50.6% in women and 37.4% in men. After adjustment, female sex was no longer associated with higher 1-year mortality (adjusted HR compared with men, 1.10 [95% CI, 0.75–1.61]; *P*=0.63).

Considering only patients with VF who were discharged alive from the hospital (or 10-day survivors for the 1995 survey), 1-year death rates were numerically higher, but not statistically different, in women (7/40, 14.9%) compared with men (13/187, 7.0%) (crude HR, 2.21 [95% CI, 0.88–5.53]; *P*=0.09; adjusted HR, 1.60 [95% CI, 0.62–4.13]; *P*=0.33).

DISCUSSION

This is the largest study providing detailed data on the incidence, characteristics, and outcomes of women presenting with VF in the context of AMI. Our findings show that VF incidence is lower in women experiencing AMI compared with men. Though statistically significant, with a difference confirmed by multivariate analysis, the 0.7% absolute difference is unlikely to be clinically meaningful. Women with VF received coronary angiography less often, and revascularization procedures were used less than in men. Recommended medications were also less frequently prescribed in women. Although 1-year mortality was considerably higher in women after VF compared with men, this was no longer significant after adjustment for confounding factors and coronary intervention.

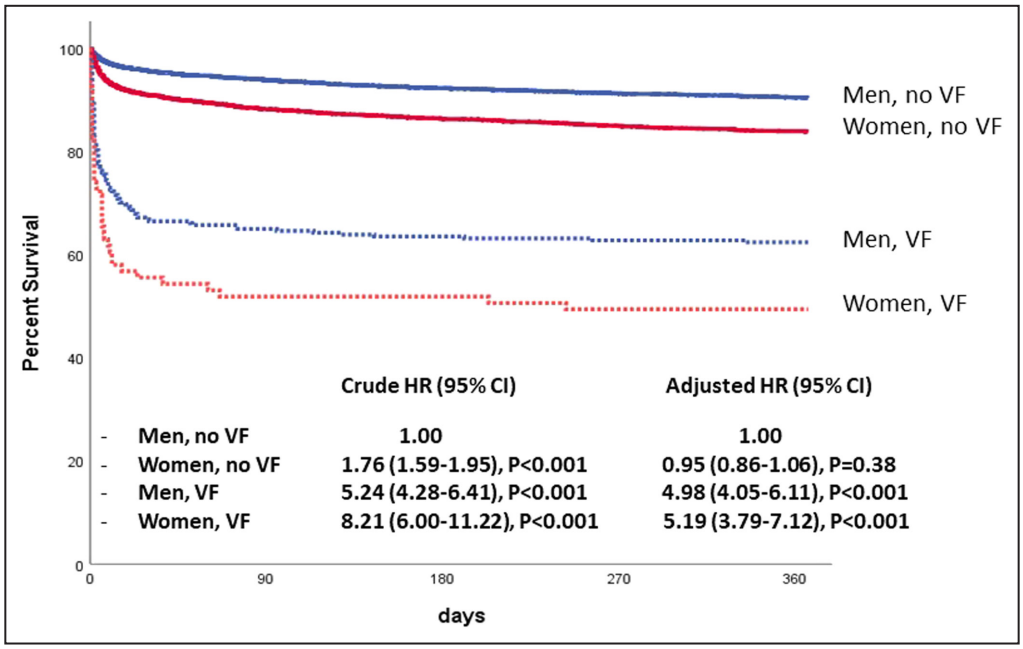

Figure 2. Kaplan-Meir curves of survival according to ventricular fibrillation (VF) status and sex.
HR indicates hazard ratio.

VF occurred in 2.0% of women and 2.7% of men. To our knowledge, no data describing VF incidence according to sex and type of AMI are available. We found a much higher proportion of VF during STEMI in both sexes (2.9% in women, 3.5% in men) compared with NSTEMI (0.8% in women, 1.5% in men), and STEMI was independently associated with the occurrence of VF in our study. These results are in line with previous studies that showed up to a 5-fold increased risk of VF in STEMI.[6,23] This increased likelihood of VF in STEMI concerns both the pre- and postreperfusion period.[1] Physiologically, acute ischemia caused by total and abrupt interruption of coronary blood flow in STEMI has deleterious effects on cardiomyocyte function, leading to anaerobic metabolism and later electrical instability, facilitating ventricular arrhythmias.[24]

VF incidence was assessed among women and men who were admitted alive in hospital, because of the design of the FAST-MI registries mentioned previously. This implies that patients who presented with VF before hospital admission, and thus presented as an out-of-hospital cardiac arrest attributable to an acute coronary syndrome, were not included. However, previous studies of out-of-hospital cardiac arrest among patients with STEMI in France, Denmark, and the United States have shown an estimated proportion of women at approximately 20% to 30% (mean age of ≈60 years).[25–27] In the FAST-MI registries, we observed a similar sex ratio (<30%) which is in line with those studies. Thus, as described in our multivariate analysis and by Jabbari et al, the small proportion of women in the subgroup of patients with VF during infarction puts female sex as a protective factor for the occurrence of this severe arrhythmia.[26]

Apart from the mode of presentation of the infarction, other factors were found to be associated with the development of VF. In previous studies, younger age, less hypertension, and hyperlipidemia seemed to protect against VF during AMI.[28] Apart from baseline comorbidities, certain characteristics of AMI may also favor the occurrence of VF; TIMI (Thrombolysis in Myocardial Infarction) flow 0 or 1, anterior infarction, acute heart failure signs, and the absence of prior angina were associated with VF in a Danish cohort.[29] Interestingly, we observed an inverse association between hypertension and prior myocardial infarction and the occurrence of VF, both in the total population and in men. In women, no significant relationship was found between prior myocardial infarction and VF, probably because of lack of power (few women presented with VF and a history of MI). The finding that several cardiovascular risk factors and comorbidities might protect against malignant arrhythmias in the AMI context, described as the risk factor paradox, has already been noted in previous studies.[25,30] In this study, we did not find an independent, inverse association between age and the occurrence of VF. Still, women presenting with VF were significantly younger than those without VF. This lack of association may be explained by the fact that younger women have fewer cardiovascular comorbidities and risk factors. Thus, low cardiovascular risk rather than age itself may influence susceptibility to the ischemia–reperfusion mechanism. It has been hypothesized that several prior transient ischemia–reperfusion episodes,

occurring in patients with multiple cardiovascular risk factors, might reduce the incidence of ventricular arrhythmias induced by ischemia.[31] Another explanation to this risk factor paradox could be a genetic predisposition to ischemia-related rhythm disorders, such as 21q21 locus or a variant of *SCN5A*, which were identified as mutations leading to increased susceptibility to ischemia-induced arrhythmias.[32,33]

In-hospital death was similar in both sexes in the VF subgroup but significantly higher in female patients without VF. At 1 year after AMI complicated with VF, the crude death rate was higher in women. However, 1-year survival did not differ after adjustment on age, type of MI, survey period, PCI, and other confounders. The increased in-hospital death rate in women with AMI, irrespective of the occurrence of VF, has already been highlighted in prior studies.[12,13] This higher death rate has been related to a lack of systematic invasive investigation and revascularization in women presenting with AMI either with or without sudden cardiac arrest.[34–36] Of note, in-hospital mortality in women who had PCI was lower than in men with PCI (17.5% versus 22.0%), whereas the reverse trend was observed in patients without PCI (65.9% in women versus 54.3% in men). Another factor that could influence postdischarge survival is how well patients have been put on optimal medical therapy. Piccini et al showed that failure to prescribe β-blockers in the first 24 hours after ventricular arrhythmias during AMI significantly affects survival.[37] The relative deficiency in secondary prevention treatments in women with AMI is also well-known and must be corrected.[38,39] Overall, these disparities in the in-hospital management of women, both in terms of revascularization and medical treatment, need to be addressed to improve short- and long-term survival of these patients with VF during AMI.

The large size of our cohort, rigorous data collection with central adjudication of all events, and highly representative data on the management and outcomes of patients hospitalized for AMI in France are the main strengths of this study. However, we acknowledge limitations. First, the FAST-MI program is an observational cohort; hence, conclusions about causal relationships between patient characteristics, management, and outcomes cannot be readily drawn. Second, because the study population was recruited from cardiac intensive care units, patients with AMI with out-of-hospital cardiac arrest, admitted to general intensive care units instead of cardiac intensive care units, or older individuals with AMI who may have been admitted to geriatric units or general wards may have been missed, with some scope for error in calculation of VF incidence. Third, the study was limited to patients developing VF during their hospital stay with information about the precise timing of VF being unavailable in the earlier periods. Analyses according to the timing of VF and, more specifically, according to the occurrence of VF during, before, or after revascularization were therefore not performed. Also, in spite of the size of the cohort, the number of patients with VF was small, particularly in women, limiting statistical power to document potential associations with VF occurrence and outcomes. Last, the present data reflect French clinical practice and caution should be exercised when generalizing results to other countries with different health systems.

CONCLUSIONS

Women are at lower risk of developing VF during AMI compared with men. However, they are less likely to receive cardiac interventions than men, possibly contributing to missed opportunities of improved outcomes. Closing the sex gap in terms of provision of timely intervention and adequate secondary prevention drug therapy may help further improve the long-term outcomes of women presenting with VF at the acute stage of MI.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Data S1

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SUPPLEMENTAL MATERIAL

Table S1. Procedural Code for ICM Insertion

Procedure	ICD-9	ICD-10	CPT
Insertion of loop recorder	37.79	0JH602Z or 0JH632Z	33282 or 33285

Table S2. Annual Normalized Procedural Rates

Year	***2013***	***2014***	***2015***	***2016***	***2017***	***2018***
Enrollees available	*n=18,141,621*	*n=18,603,133*	*n=14,205,816*	*n=13,754,924*	*n=13,339,401*	*n=12,348,839*
Procedure Rate per Million Enrollees: Annual Rate (% of 2013 Mean Rate)						
ICM implant	5.5 (100)	8.4 (154)	13.1 (239)	12.4 (227)	12.5 (229)	11.1 (203)
Syncope diagnoses	10,083 (100)	10,477 (104)	10,028 (99)	10,791 (107)	10,829 (107)	11,064 (109)
Holter Monitor	2,634 (100)	2,585 (98)	2,453 (93)	2,536 (96)	2,607 (99)	2,650 (101)
CEM/MCOT	1,058 (100)	1,015 (95)	930 (88)	962 (91)	987 (93)	986 (93)
Implantable Cardiac Defibrillator/Pacemaker insertion	21.9 (100)	18.3 (84)	20.8 (95)	21.1 (97)	21.2 (97)	21.4 (98)