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CLINICAL RESEARCH
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Incidence of sudden cardiac death after ventricular fibrillation complicating acute myocardial infarction: a 5-year cause-of-death analysis of the FAST-MI 2005 registry†

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Aims Limited data are available on long-term prognosis or causes-of-death analysis among survivors of acute myocardial infarction (MI) according to whether or not they developed ventricular fibrillation (VF) during the acute stage of MI.

Methods and results Among 3670 MI patients hospitalized in France in 2005 and enrolled in this prospective follow-up cohort study, we assessed in-hospital mortality and 5-year cause of death among those who survived to hospital discharge, according to whether they developed VF (116 cases) or not, during the acute stage. 94.5% of patients had complete follow-up at 5 years. In-hospital mortality was significantly higher among VF patients (adjusted OR 7.38, 95% CI 4.27–12.75, $P < 0.001$). Among 3463 survivors at hospital discharge, 1024 died during a mean follow-up of 52 ± 2 months. The overall survival rate at 5 years was 74.4% (95% CI 72.8–76.0). In Cox multivariate analysis, occurrence of VF during the acute phase of MI was not associated with an increased mortality at 5 years (HR 0.78, 95% CI 0.38–1.58, $P = 0.21$). The distribution of causes of death at 5 years did not statistically differ according to the presence or absence of VF, especially for sudden cardiac death (13.1% in VF group vs.12.9% in non-VF group), despite a very low rate of implantation of cardioverter defibrillator in both groups (Overall rate 1.2%).

Conclusion Patients developing VF in the setting of acute MI are at higher risk of in-hospital mortality. However, VF is not associated with a higher long-term all-cause or sudden cardiac death mortality.

Keywords Sudden death • Acute coronary syndrome • Ventricular fibrillation • Implantable cardioverter defibrillator • Prognosis

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Introduction

The prognosis following acute myocardial infarction (MI) has improved considerably in recent decades, principally due to the development of percutaneous coronary intervention and improved medical therapy, including thrombolytic agents.[1,2] However, despite these major advances, ventricular fibrillation (VF) or rapid ventricular tachycardia (VT) still occur during the acute phase of MI in 2–8% of cases.[3–6]

Several studies have shown that patients who develop VF during the acute phase of MI have a higher risk of death in the short-term.[4,5,7] In contrast, data on mid-to-long-term survival are limited and controversial.[8–13] In the long-term, the mode of death is poorly characterized, particularly the risk of sudden cardiac death (SCD). Despite this area of significant uncertainty, the European and North American guidelines in 2008 did not recommend early implantation of implantable cardioverter-defibrillators (ICD) in such patients, even though experts agreed on the particularly low level of evidence in the field (level of evidence C).[14] The main reasons behind those guidelines were the reversible nature of the arrhythmic trigger (acute myocardial ischaemia) and the presumed efficacy of current treatments (coronary revascularization) in preventing recurrences of VF. However, recent studies have questioned the dogma that such treatment of reversible causes of malignant arrhythmia can be sufficient to prevent later fatal event.[15–20] In this setting, data addressing long-term follow-up as well as specific causes of death in survivors of VF are necessary to assess whether such patients are at higher long-term risk of SCD.[21]

In the present analysis, we report the 5-year cause-of-death analysis of patients with MI, according to whether or not they developed VF during their index hospital stay.

Methods

Study setting and population

The methodology of the FAST-MI 2005 Registry has been described in detail elsewhere.[2,22,23] Briefly, the primary objective was to evaluate acute MI management in 'real life' practice, and to assess medium and long-term prognosis of patients admitted to intensive care units (ICUs) after acute MI. This registry comes from a prospective multicentre study (223 centres) including 3670 MI patients. Patients were recruited consecutively from ICU departments over a period of 1 month (October 2005), with an additional 1-month extension for diabetic patients. Participation in the study was offered to all French institutions, university teaching hospitals, general and regional hospitals, and private clinics with ICUs authorized to receive acute coronary syndrome emergencies. In each centre, a physician was in charge of the registry and provided a full list of all patients admitted to his/her unit. The study was conducted in compliance with Good Clinical Practice, French Law and the French data protection law. The protocol was reviewed by the Committee for the Protection of Human Subjects in Biomedical Research (CCPPRB) of Saint-Antoine University Hospital. Data file of the FAST-MI 2005 registry was declared to and authorized by the French data protection committee (Commission Nationale Informatique et Liberté, CNIL).

The inclusion criteria were: (i) man or woman aged over 18 years; (ii) patient admitted within 48 h of symptom onset in an ICU for an acute MI characterized by the elevation of cardiac biomarkers associated with at least one of the following elements: symptoms compatible with myocardial ischaemia, onset of pathological Q waves, ST-T changes compatible with myocardial ischaemia (ST segment elevation or depression, T-wave inversion); and (iii) having agreed to take part in the study. The exclusion criteria were: (i) refusal to consent; (2) MI admitted > 48 h after symptoms; (3) iatrogenic MIs, defined as MIs occurring within 48 h of a therapeutic procedure (bypass surgery, coronary angioplasty, or any other medical or surgical intervention); (iv) acute coronary syndrome diagnosis later invalidated in favour of another diagnosis; (v) patients with unstable angina and no increase in cardiac biomarkers.

Definitions of acute MI and standard of care were established according to the current guidelines at the time of study initiation. Acute MI with ST elevation (STEMI) was defined as acute MI with ST elevation ≥ 1 mm in at least two contiguous leads in any location in the index or qualifying ECG; and non-ST-segment-elevation MI as acute MI without any ST-segment elevation in the index or qualifying ECG. Patients who died very early after admission and for whom cardiac biomarkers were not measured were included if they had compatible signs or symptoms associated with typical ST changes.

In the present analysis, we studied patients with MI according to whether or not they developed VF during the acute phase (defined by VF occurring after diagnosis of MI is made). Ventricular fibrillation was defined as irregular waves of inconsistent shape without distinct QRS complexes or T-waves. Ventricular fibrillation was classified as early VF if it occurred in the first 48 h of admission, and late VF if it occurred after the first 48 h but before hospital discharge. Patients who developed stable VT, even with haemodynamic compromise requiring urgent cardioversion, were not considered in the VF group. In an additional analysis, we considered patients who developed stable VT, defined as rapid (>120 b.p.m.) ventricular rate with no features for associated atrial tachycardia, lasting more than 30 s, with or without haemodynamic compromise requiring urgent cardioversion. We assessed the influence of VF on the 5-year follow-up, as well as the combined influence of VT associated to VF.

Annual follow-up and mode of death adjudication process

A modified Hinkle-Thaler system was used to classify deaths into SCD, non-SCD, and non-cardiovascular death.[24] Sudden cardiac death was assumed in patients who: (i) died suddenly and unexpectedly within 1 h of cardiac symptoms in the absence of progressive cardiac deterioration; (ii) died unexpectedly in bed during sleep; or (iii) died unexpectedly within 24 h after last being seen alive. Other cardiovascular deaths included MI, heart failure, acute aortic syndrome, and pulmonary embolism. Terminal arrhythmias associated with heart failure deaths were classified as non-sudden cardiovascular deaths. Deaths that could be attributed to non-cardiovascular reasons were classified as non-cardiovascular death (cancer, infectious disease, renal failure, respiratory failure). If available data were insufficient to make a reasonable identification of the cause of death, it was considered as unclassifiable. When no data were available, cause of death was adjudicated as unknown.

Local investigators notified deaths and their causes during the index hospital stay, using a predefined detailed form. A specific working group ensured annual follow-up of patients, using specific electronic Case Report Forms through contacts with the attending physicians, and/or the patients themselves for additional information. Follow-up focused particularly on vital status, specific mode, and cause of death, as well as significant medical events or interventions during follow-up (especially regarding modification of pharmacological treatment, hospitalization, or ICD implantation). If missing, vital status was obtained from the registries of the patients' birthplaces, and from French National Institute of Health and Medical Research–INSERM CépiDc Unit (Kremlin-Bicêtre, France). Overall, 3-year follow-up was completed in 97.8% of patients, and 5-year follow-up in 94.5% of patients.

A systematic review of all death notifications was performed, with central adjudication of all events, by two independent cardiologists

blinded to VF status. In cases of divergent opinion on the mode of death, a third expert was asked to arbitrate. Primary endpoints of the present analysis were overall mortality and cause-specific mortality among hospital survivors of acute MI according to whether or not they developed VF during the acute MI admission.

Statistical analysis

This report was prepared in compliance with the STROBE checklist for observational studies.[25] Normality assumption was checked for continuous variables, and continuous variables were presented as mean ± standard deviation, and discrete variables were presented as percentages. Comparisons between groups (patients with or without VF) were made with χ^2 or Fisher's exact tests for discrete variables, and with unpaired *t*-tests or one-way ANOVA for continuous variables. In-hospital survival was described as percentages and comparisons analysed using χ^2 test. Factors associated with occurrence of VF were identified using multivariate backward stepwise logistic regression analysis.

Overall as well as specific mortality rates were calculated. Survival curves over the 5-year follow-up period were estimated using the Kaplan–Meier estimation. Cox proportional hazards regression analysis was used to assess variables independently associated with overall mortality. The cumulative hazard functions for each covariable were computed to assess proportionality. Variables with a value of $P < 0.10$ in univariate analyses were included in the final multivariate model, including demographic characteristics, comorbidities (cardiovascular risk factors including body mass index, heart failure, stroke history, cancer, chronic kidney disease, anaemia), chronic cardiovascular medications before the acute event, MI characteristics (STEMI vs. non-STEMI), 12 lead-ECG at admission (left bundle block branch, atrial fib illation), revascularization procedures at admission (medical, percutaneous coronary intervention, coronary artery bypass), anti-thrombotic during the first 48 h (low-molecular weight heparin, glycoprotein IIb/IIIa antagonists), extent of coronary artery disease, left-ventricular ejection fraction, discharge medications, heart rate, and systolic blood pressure at discharge. A backward stepwise selection was applied to obtain a final model that included covariates with $P \leq 0.05$. All tests were two-tailed, and values of $P < 0.05$ were considered significant. Statistical analysis was performed using SPSS 18.0 software (SPSS, Inc., Chicago, IL, USA).

Results

Incidence of VF and associated factors

Among the 3670 enrolled patients, 116 developed VF during the acute phase of MI, giving an incidence rate of 3.2% (95% CI 2.6–3.8), among MI patients alive at hospital admission. This group included 92 early VF (79.3%) and 24 late VF (20.7%). The mean time from MI diagnosis to occurrence of VF was 1.8 days (95% CI 1.4–2.2).

Table 1 shows baseline characteristics of patients, especially medical history and previous treatments, according to VF occurrence during the acute phase of MI. Patients with VF were younger, presented with less frequent history of systemic arterial hypertension (47.4 vs. 60%,

Table 1 Baseline characteristics by occurrence of VF

Baseline characteristics	VF (n = 116)	No VF (n = 3554)	*P*-value
Age, year (SD)	63.3 (14.4)	67.4 (13.9)	0.002
Male sex, *n* (%)	88 (75.9)	2427 (68.3)	0.084
BMI, kg/m^2 (SD)	27.3 (5.0)	27.2 (4.8)	0.76
Medical history			
Diabetes mellitus, *n* (%)	34 (29.3)	1282 (36.1)	0.135
Hypertension, *n* (%)	55 (47.4)	2132 (60.0)	0.007
Hyperlipidaemia, *n* (%)	45 (38.8)	1729 (48.6)	0.037
Current smoker, *n* (%)	45 (38.8)	1020 (28.7)	0.018
COPD, *n* (%)	5 (4.3)	174 (4.9)	0.77
Chronic kidney disease, *n* (%)	4 (3.4)	205 (5.8)	0.286
Prior MI, *n* (%)	19 (16.4)	647 (18.2)	0.616
Prior CABG, *n* (%)	4 (3.4)	206 (5.8)	0.284
Prior PCI, *n* (%)	13 (11.2)	505 (14.2)	0.361
Prior stroke, *n* (%)	11 (9.5)	188 (5.3)	0.051
Prior transient ischaemic attack, *n* (%)	4 (3.4)	131 (3.7)	0.89
Prior peripheral vascular disease, *n* (%)	9 (7.8)	359 (10.1)	0.403
Prior congestive heart failure, *n* (%)	5 (4.3)	209 (5.9)	0.474
Previous treatment			
Beta-blockers, *n* (%)	24 (20.7)	897 (25.2)	0.266
Aspirin, *n* (%)	23 (19.8)	911 (25.6)	0.158
Clopidogrel, *n* (%)	9 (7.8)	470 (13.2)	0.085
Statin, *n* (%)	26 (22.4)	1005 (28.3)	0.167
ACE-inhibitor or ARB, *n* (%)	28 (24.1)	1265 (35.6)	0.011
Amiodarone, *n* (%)	3 (2.6)	124 (3.5)	0.601

ACE, angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; VF, ventricular fibrillation.

$P = 0.007$) and hyperlipidaemia (38.8 vs. 48.6%, $P = 0.037$), and were more often current smokers (38.8 vs. 28.7%, $P = 0.018$). Previous treatment with angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blocker (ARB) was less frequent in the VF group (24.1 vs. 35.6%, $P = 0.011$). Conversely, previous treatment by beta-blockers did not differ according to VF occurrence (20.7 vs. 25.2%, $P = 0.266$). Other treatments, such as antiplatelet agents or antiarrhythmics, did not differ between groups. Overall, 518 patients (14.1%) presented a history of percutaneous coronary intervention at baseline. Characteristics of MI and details on management are summarized in *Table 2*. In patients undergoing percutaneous coronary intervention, 89% in the VF group and 79% in the non-VF group had TIMI 3 flow at the end of the procedure ($P = 0.14$). Among patients who underwent percutaneous coronary intervention, 48 (41.4%) and 1270 (35.7%) had single-vessel disease ($P = 0.46$), in the VF and non-VF groups, respectively. Anterior MI (vs. non-anterior) was significantly associated to the occurrence of VF in univariate analysis (37.9% in VF vs. 20.1% in non-VF, $P < 0.001$).

In multivariate analysis, independent factors associated with early occurrence of VF were STEMI (OR 2.4, 95% CI 1.5–3.6, $P < 0.001$), age <60 years (OR 1.7, 95% CI 1.1–2.5, $P = 0.01$), history of stroke (OR 2.4, 95% CI 1.2–4.7, $P = 0.01$), and atrial fibrillation on first ECG (OR 2.5, 95% CI 1.4–4.4, $P = 0.003$).

In-Hospital mortality and cause-of-death analysis

Overall, 207 deaths occurred during the hospital stay, giving a mortality rate of 5.6% (95% CI 4.8–6.4). In-hospital mortality rates according to the occurrence of VF are shown in *Figure 1*. In-hospital mortality was higher among patients with VF than in patients without VF (25.0 vs. 5.0%, $P < 0.001$). After adjustment by age, sex, type of MI, cardiovascular risk factors, history of stroke, history of chronic kidney disease, heart rate, blood pressure, atrial fibrillation at admission, medications used before entry, and use of coronary angiography during the hospital stay, in-hospital mortality remained higher among patients with VF than patients without VF (adjusted OR 7.38, 95% CI 4.27–12.75, $P < 0.001$). When considering VF timing, in-hospital mortality was significantly higher in the late VF group than in the early VF group (33.3 vs. 22.8%, $P < 0.001$) (*Figure 1*).

Table 3 summarizes causes of in-hospital death. Causes of deaths significantly differed between VF and non-VF patients ($P < 0.001$). Whereas cardiogenic shock represented 37.9% of in-hospital causes of death in the non-VF group (similar than SCD), cardiogenic shock was the predominant cause of death among non-VF patients (55.1%). When considering only in-hospital SCD, most of the deaths in the VF group (81.8%) were arrhythmia-related with unsuccessful resuscitation, whereas 61.5% of such deaths in the non-VF group were related to non-arrhythmic SCD, principally cardiac rupture and tamponade.

Long-term outcome of patients alive at hospital discharge

Treatments at hospital discharge are described in *Table 4*. Treatments were not statistically different between VF patients and non-VF patients regarding beta-blockers, aspirin, clopidogrel, statin, and aldosterone blockers. In contrast, patients from the VF group were

Table 2 Characteristics of MI and in-hospital management by occurrence of VF

Characteristics of MI	VF ($n = 116$)	No VF ($n = 3554$)	P-value
Clinical characteristics			
Symptom onset to call <3 h, *n* (%)	93 (80.2)	2097 (59.5)	<0.001
Killip class > 1, *n* (%)	42 (36.2)	835 (23.6)	0.002
Systolic blood pressure, mmHg (SD)	126.2 (31.8)	140.4 (28.5)	<0.001
Heart rate, b.p.m. (SD)	83.7 (24.8)	80.1 (20.2)	0.067
ECG			
STEMI, *n* (%)	84 (72.4)	1788 (50.3)	<0.001
Left bundle branch block, *n* (%)	4 (3.4)	155 (4.4)	0.635
Anterior MI, *n* (%)	44 (37.9)	713 (20.1)	<0.001
Atrial fibrillation on first ECG, *n* (%)	15 (12.9)	259 (7.3)	0.023
Paraclinical			
Admission glycaemia, g/L, mean (SD)	1.8 (0.9)	1.6 (0.8)	0.015
Admission LDL, g/L, mean (SD)	1.1 (0.5)	1.2 (0.4)	0.378
White blood cell count, 10^9/L, mean (SD)	12.5 (4.4)	10.3 (3.8)	<0.001
GRACE score, mean (SD)	110.9 (32.6)	115.9 (32.4)	0.117
In-hospital course			
PCI, *n* (%)	83 (71.6)	2253 (63.4)	0.072
CABG, *n* (%)	2 (1.7)	144 (4.1)	0.328
ICD implantation during hospital phase, *n* (%)	4 (3.4)	8 (0.2)	<0.001
Length of hospital stay, days (SD)	12.3 (15.2)	9.3 (8.1)	<0.001

CABG, coronary artery bypass graft; ICD, implantable cardioverter-defibrillator; MI, myocardial infarction; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST elevation myocardial infarction; VF, ventricular fibrillation.

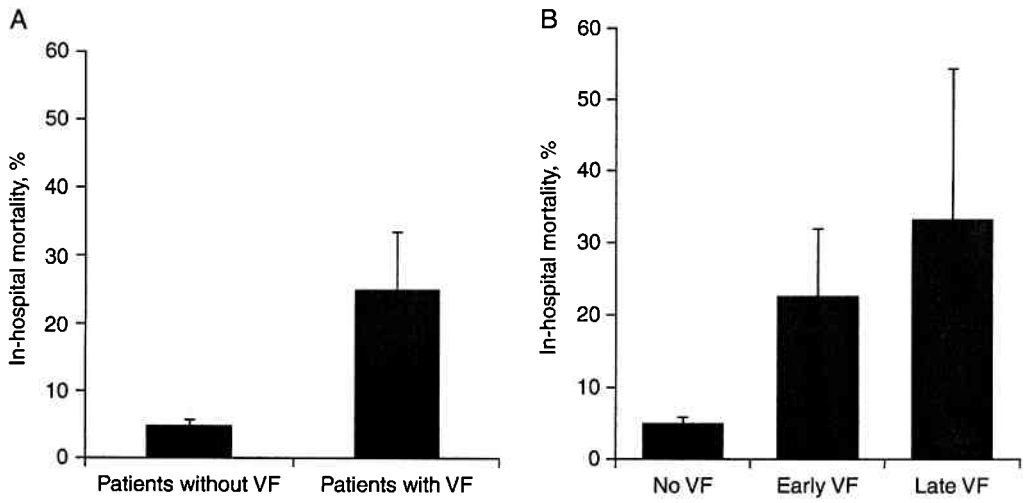

Figure 1 In-hospital mortality according to occurrence of ventricular fibrillation.

Table 3 Cause-specific death during hospitalization according to occurrence of VF

	VF (29/116)	No VF (178/3554)	*P*-value
			<0.001
Sudden cardiac death, *n* (%)	11 (37.9)	52 (29.2)	
Arrhythmic SCD, *n* (%)	9/11 (81.8)	20/52 (38.5)	
Non-arrhythmic SCD, *n* (%)	2/11 (18.2)	32/52 (61.5)	
Cardiogenic shock, *n* (%)	11 (37.9)	98 (55.1)	
Other cardiovascular, *n* (%)	1 (3.5)	12 (6.7)	
Non-cardiovascular death, *n* (%)	6 (20.7)	16 (9.0)	

VF, ventricular fibrillation.

Table 4 Treatments at hospital discharge among survivors by occurrence of VF

	VF (*n* = 87)	No VF (*n* = 3376)	*P*-value
Beta-blockers, *n* (%)	72 (84.7)	2582 (77.9)	0.134
Aspirin, *n* (%)	81 (93.1)	3089 (92.2)	0.745
Clopidogrel, *n* (%)	72 (82.8)	2707 (80.9)	0.667
Statins, *n* (%)	73 (84.9)	2788 (83.9)	0.802
ACE-inhibitor or ARB, *n* (%)	69 (81.2)	2318 (70.4)	0.031
Aldosterone blocker, *n* (%)	6 (6.9)	164 (4.9)	0.32
Oral anticoagulant, *n* (%)	7 (8)	183 (5.4)	0.333
Amiodarone, *n* (%)	12 (13.8)	251 (7.4)	0.027

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; VF, ventricular fibrillation.

more often discharged with amiodarone (13.8 vs. 7.4%, $P = 0.027$) and ACE-inhibitor/ARB (81.2 vs. 70.4%, $P = 0.031$) than patients without VF. Left-ventricular ejection fraction was lower at discharge among VF patients than non-VF patients (46.6 vs. 52.0%, $P < 0.001$). The rate of ICD implantation during in-hospital course was low (0.3% in the overall population), but higher in the VF group (3.4 vs. 0.2%, $P < 0.001$). After 3 years of follow-up (available in 97.8% of patients), pharmacological therapies no longer differed between the two groups, including antiarrhythmic medications, particularly amiodarone ($P = 0.22$). An additional 35 patients received an ICD during the first 3 years of follow-up, all of these in the non-VF group, giving an overall ICD implantation rate of 1.2%, not significantly different between VF (3.4%) and non-VF (1.2%) groups.

Among 3463 survivors at hospital discharge, 1024 died during a mean follow-up of 52 ± 2 months, giving an overall survival rate at 5 years of 74.4% (95% CI 72.8–76.0%). Survival rates were 81.3% (95% CI 73.1–89.5%) in the VF group compared with 74.2% (95% CI 72.6–75.8%) in the non-VF group (*Figure 2*). In multivariate analysis, after adjustment for other prognostic factors, occurrence of VF during the acute phase of MI was not associated with any increase in mortality at 5 years (HR for mortality 0.78, 95% CI 0.38–1.58, $P = 0.21$), in both STEMI and non-STEMI patients. When considering timing of VF, neither early VF (OR 0.5, 95% CI 0.2–1.1, $P = 0.09$) nor late VF (OR 1.9, 95% CI 0.6–5.9, $P = 0.30$) was associated significantly with long-term mortality. When we consider the additional 75 cases of VT to the VF group, in multivariate analysis, after adjustment for other prognostic factors, occurrence of sustained ventricular arrhythmias (VT and VF considered together) during the acute phase of MI was not associated with significant increase in mortality at 5 years (HR 0.95, 95% CI 0.64–1.42, $P = 0.81$). Comparatively to patients without any sustained ventricular arrhythmias, neither patients with VT only (HR 1.29, 95% CI 0.79–2.11, $P = 0.31$) nor

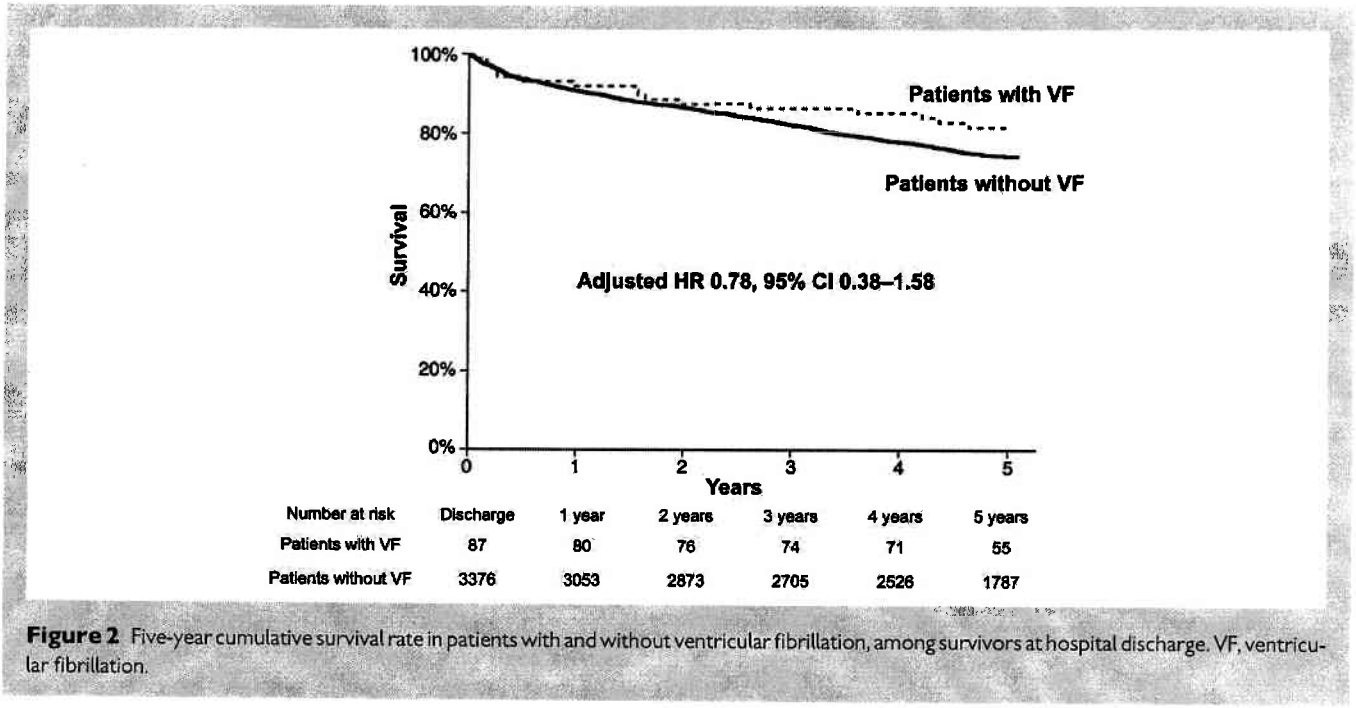

Figure 2 Five-year cumulative survival rate in patients with and without ventricular fibrillation, among survivors at hospital discharge. VF, ventricular fibrillation.

patients with VF only (HR 0.65, 95% CI 0.32–1.33, $P = 0.24$) had increased 5-year mortality.

Causes of deaths in the two groups (VF and non-VF) are reported in *Table 5*. Overall, causes of death were determined in 718 patients during the 5-year follow-up (70.1%). The frequency of unknown or unclassifiable causes of death was not statistically different between the two groups (30.4 vs. 29.8%). Among overall ascertained deaths, most were from cardiovascular causes (65%), including SCD (28% of deaths from cardiovascular cause) and non-SCD (72% of deaths from cardiovascular cause). No significant difference was found in the distribution of causes of death in the VF and non-VF groups ($P = 0.71$). The proportion of deaths related to SCD was 13.1% in the VF group compared with 12.9% in the non-VF group ($P = 0.71$), with respective annual incidence rates of 0.68% (95% CI 0.18–1.74) and 0.76% (95% CI 0.64–0.90).

Table 5 Cause-specific deaths at 5 years among survivors at discharge, by occurrence of VF

	VF (23/87)	No VF (1001/3376)	*P*-value
			0.71
Sudden cardiac death, *n* (%)	3 (13.1)	129 (12.9)	
Non-sudden cardiac death, *n* (%)	5 (21.7)	331 (33.1)	
Non-cardiovascular death, *n* (%)	8 (34.8)	242 (24.2)	
Unknown or unclassifiable, *n* (%)	7 (30.4)	299 (29.8)	

VF, ventricular fibrillation.

Discussion

From this multicentre and unselected cohort of more than 3500 MI patients carried out in the modern era of reperfusion therapy, we report, to the best of our knowledge, the first long-term cause-of-death analysis according to the development of VF during the acute stage. We have confirmed the classical predictors of VF and the high rate of in-hospital mortality among patients who developed VF, especially from SCD. However, our results suggest that among patients discharged alive from hospital after MI, the survival rate at 5 years did not differ significantly between VF and non-VF patients. Furthermore, incidence rate of SCD was low, and remarkably similar in both groups.

Coronary heart disease remains the most common cause underlying SCD in the western world, responsible for approximately 75% of cases.[26] The leading cause of VF is myocardial ischaemia,[27] and it has been demonstrated that the absolute risk of fatal arrhythmic event after MI is greatest within the weeks immediately after the event and declines significantly thereafter, reaching a steady state after approximately one year.[28,29] Considering these epidemiological findings, several studies have evaluated the potential benefit of ICD in primary prevention shortly after MI, and found no evidence for benefit.[30–32] In contrast, whereas patients developing VF at the acute phase of MI might seem at highest risk of recurrence of VF, no RCTs have evaluated the potential interest of ICD in such patients. In the setting of secondary prevention, the low-risk profile of patients who develop VF or haemodynamically unstable VT in the acute setting of ischaemia (<48 h) on one hand, as well as the high-risk profile of patients who develop such arrhythmias with no recent (<40 days) MI and no recent coronary revascularization (<3 months), has been demonstrated. In contrast, there is an important grey zone regarding patients in between these time periods. This has been recently underlined in the 2013 ACCF/HRS/AHA/ASE/HFSA/SCAI/SCCT/SCMR Appropriate Use Criteria for Implantable Cardioverter-Defibrillators and Cardiac Resynchronization Therapy Report.[33]

In this study, we identified several previously described factors associated with the occurrence of VF, such as STEMI,[5] younger age,[9,34] AF at initial presentation.[35] Our finding of a higher risk of in-hospital mortality among patients with VF in the setting of acute MI is also consistent with the literature.[5,7–9,11,34–36] Accordingly, current guidelines advocate close monitoring (continuous ECG) for at least 24 h after MI, and for up to 72 h in high-risk patients (especially patients with severe arrhythmias).[37] Our results support the importance of close monitoring during hospital stay. According to our findings, increased early mortality in VF patients cannot be explained by less frequent adequate revascularization, as judged by post-procedure TIMI flow. Interestingly, we observed that SCD resulted from non-arrhythmia-related causes in an important proportion of cases in patients without VF, in agreement with the findings of Pouleur *et al.*[38] Our results also emphasize the more unfavourable in-hospital outcomes of late VF when compared with early VF, consistent with previous studies.[4,10,36] Taken together, our results are very consistent with the existing literature regarding predictors of VF occurrence as well as short-term mortality.

We report, to the best of our knowledge, the first long-term cause-of-death analysis according to the development of VF during the acute stage. To the best of our knowledge, only three previous studies have reported long-term follow-up after VF complicating MI.[8,13,35] Two of those studies included patients from the pre-reperfusion era, before widespread use of thrombolytic and PCI treatments, elements that have undoubtedly changed the prognosis of MI.[8,34,39] They reported an increased short-term mortality but suggested no prognostic impact up to 3 years. However, the only cause-of-death analysis available to date was recently reported by Piccini *et al.*,[11,21] describing specific mortalities at 30 days of 228 subjects.

Despite the paucity of data regarding delayed cause-specific death, it is usually considered that patients with VF at the acute phase of MI do not have increased long-term risk of SCD. However, clinical, epidemiological, and genetic studies recently add substantial evidence that patients are not equal concerning the risk of developing VF during ischaemia,[15,16,18,19] and that patients who have developed VF during the acute phase of MI could be at higher long-term risk of further malignant arrhythmia and SCD. At this time, occurrence of VF resulting from reversible trigger (especially, ischaemia at the acute phase of MI) does not currently represent an indication for ICD implantation,[40] with a very low level of evidence. In this context, our results provide substantial data, first because of the 5-year follow-up (longest available to date in such a setting). Moreover, because comparable overall mortality rates could conceal significant differences in modes of death (especially arrhythmic death) during follow-up, our cause-of-death analysis is of particular interest. In this study, we report that patients with VF during the acute phase of MI present with very similar incidence rates of later SCD, despite comparable treatments during follow-up, including ICD implantation (in only a minority of cases, around 1%). This adds substantial evidence to the legitimacy of current guidelines in discouraging ICD implantation in the setting of VF occurring during the acute phase of MI.

Until now, most studies that evaluated short- or mid-term prognosis of MI patients according to the occurrence of early ventricular arrhythmias have merged sustained VT and VF.[4,6,7,12] However, VF is most often triggered by acute myocardial ischaemia,[41] whereas VT (although triggered by acute myocardial ischaemia) usually involves a structural substrate.[42,43] Furthermore, prognostic values of these arrhythmias seem different, when they occur in the setting of acute MI.[11] Thus, we decided to include only patients with VF, in order to respect pathophysiological specificities, possibly prognostic, of this arrhythmia.

We acknowledge some limitations. First, our data are observational. However, this study includes patients from different centres, avoiding selection bias inherent in randomized controlled trials. Secondly, initial treatment modalities could vary from one centre to another, and this study reflects real daily clinical practice. Thirdly, cause of death could only be determined in 70% of deaths. Considering the long follow-up (5 years, with very few patients lost to follow-up), the report of causes of deaths and the similar proportion of undetermined cause of death in VF and non-VF groups, our data can be regarded as robust.

In conclusion, in this long-term follow-up of a large cohort of MI patients treated according to contemporary medical therapy, occurrence of VF in the initial phase was associated with higher in-hospital mortality. In contrast, long-term outcome (especially incidence of SCD) was not different between VF and non-VF patients. This reinforces the crucial importance of close monitoring during the hospitalization of such patients, but also emphasizes the limited utility of early ICD implantation in such patients.

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