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CLINICAL RESEARCH

In-hospital outcomes and 5-year mortality following an acute myocardial infarction in patients with a history of cancer: Results from the French registry on Acute ST-elevation or non-ST-elevation myocardial infarction (FAST-MI) 2005 cohort

Évolution hospitalière et mortalité à 5 ans au décours d'un infarctus du myocarde chez des patients avec antécédents de cancer : résultats du registre français des infarctus du myocarde avec sus-décalage du segment ST 2005 (FAST-MI)

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Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; HR, hazard ratio; NSTEMI, non-ST-segment elevation myocardial infarction; OR, odds ratio; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

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KEYWORDS
Acute myocardial infarction;
Cancer;
In-hospital mortality;
Mortality

Summary
Background. — Cancer and acute myocardial infarction (AMI) have important prognostic consequences. Treatment of some cancers may affect coronary artery disease, myocardial function and/or AMI management. Whether the early and long-term mortality of patients with AMI differ according to their history of cancer remains questionable.
Aims. — To determine in-hospital outcomes and 5-year mortality following AMI according to patient history of cancer.
Methods. — The FAST-MI registry is a nationwide French survey collecting data on characteristics, management and outcomes of 3670 consecutive patients admitted for AMI during October 2005.
Results. — Overall, 246/3664 patients (6.7%) admitted for an AMI (47.6% with ST-segment elevation myocardial infarction [STEMI]; 52.4% with non-STEMI [NSTEMI]) had a history of cancer. In-hospital mortality was not significantly different for patients with versus without a history of cancer, overall (adjusted odds ratio [OR]: 1.15, 95% confidence interval [CI]: 0.68—1.94; $P = 0.61$) and in patients with STEMI (adjusted OR: 1.37, 95% CI: 0.69—2.71; $P = 0.37$) or NSTEMI (adjusted OR: 0.97, 95% CI: 0.41—2.28; $P = 0.95$). All-cause mortality at 5 years was higher among patients with a history of cancer (adjusted hazard ratio [HR]: 1.36, 95% CI: 1.08—1.69; $P = 0.008$), whereas 5-year cardiovascular mortality did not differ (adjusted HR: 1.17, 95% CI: 0.89—1.53; $P = 0.25$), regardless of whether the patients had STEMI or NSTEMI. Similar results were found in populations matched on a propensity score including baseline characteristics and early management.
Conclusion. — A history of cancer, per se, does not appear to be a risk factor for increased in-hospital mortality or long-term cardiovascular mortality in patients admitted for AMI.

MOTS CLÉS
Infarctus du myocarde ;
Cancer ;

Résumé
Contexte. — La prise en charge des patients atteints de cancer peut être marquée par des complications cardiovasculaires, notamment coronarienne. La mortalité d'origine cardiovasculaire à court et long terme des patients aux antécédents de cancer et admis en unité de soins intensifs pour un infarctus du myocarde (IDM) n'est pas clairement établie.

Mortalité hospitalière ; Mortalité

Objectifs. — L'objectif de cette analyse des données du registre FAST-MI 2005 était de décrire et de comparer la mortalité intra-hospitalière et la mortalité à 5 ans des patients admis en unité de soins intensifs pour un IDM avec et sans antécédents de cancer.
Résultats. — Au total, 3664 patients ont été inclus dans ce registre sur une période de 1 mois, 246 patients (6,7 %) présentaient un antécédent de cancer (47,6 % admis pour un IDM avec élévation du segment ST et 52,4 % admis pour un IDM sans élévation du segment ST). La mortalité intra-hospitalière des patients avec un antécédent de cancer n'était pas significativement différente des patients sans antécédents de cancer (OR ajusté : 1,15, IC95 % : 0,68—1,94 ; $p = 0,61$), que ce soit chez les patients admis pour un IDM avec sus-décalage du segment ST (OR ajusté : 1,37, IC95 % : 0,69—2,71 ; $p = 0,37$) ou sans décalage du segment ST (OR ajusté : 0,97, IC95 % : 0,41—2,28 ; $p = 0,95$). La mortalité toute cause à 5 ans était plus élevée chez les patients ayant un antécédent de cancer (HR : 1,36, IC95 % : 1,08—1,69 ; $p = 0,008$), alors que la mortalité cardiovasculaire à 5 ans ne différait pas (HR ajusté : 1,17, IC95 % : 0,89—1,53 ; $p = 0,25$), que les patients aient été admis pour un IDM avec ou sans sus-décalage du segment ST.
Conclusion. — Chez les patients admis en unité de soins intensifs pour un IDM avec ou sans sus-décalage du segment ST, un antécédent de cancer n'est pas associé à une majoration de la mortalité intra-hospitalière ni de la mortalité à long terme.

Background

Patients with cancer are exposed to an increased risk of coronary artery disease through multiple mechanisms [1—4]. Both conditions are associated with an aging population [5] and share common risk factors [6], and cancer management itself may have a deleterious effect and increase the risk of developing coronary artery disease [7]. However, the relationship between cancer status and cardiovascular outcomes following an acute coronary syndrome remains poorly described. There are only scarce data regarding the management of acute myocardial infarction (AMI) in patients with cancer [8—10]. This is an important issue, as cardiovascular disease and cancer represent two leading causes of death; and a recent report showed that a decline in cardiovascular mortality leads to a relative increase in death as a result of cancer [5]. Despite the growing and emerging field of cardio-oncology in the past few years, most of the research and publications focus on the description of cardiotoxicity or accelerated atherosclerosis as a result of chemotherapy or radiotherapy [11]. Epidemiological studies have shown that patients are exposed to an increased risk of coronary artery disease for up to 10 years following cancer diagnosis [7]. Moreover, patients with cancer and cardiovascular disease have worse survival rates compared with patients with cancer who are free of cardiovascular disease [12].

Few studies have evaluated and described the management and early and late outcomes of patients with cancer admitted for an AMI. Current guidelines do not detail treatment options for patients with both cardiovascular disease and cancer [13—15]. Furthermore, patients with cancer are usually excluded from phase III trials evaluating new therapies in the field of acute coronary syndrome, and cancer is not always reported in registries.

We therefore used data from the French registry of acute ST-elevation or non-ST-elevation myocardial infarction (FAST-MI) to describe the management and evaluate the in-hospital outcomes and 5-year mortality of patients with a history of cancer admitted to an intensive care coronary unit for an AMI.

Methods

Population and patient selection

The methodology, population and main results of the FAST-MI programme have been described previously [16,17]. In summary, the FAST-MI registry is a nationwide prospective multicentre cohort including consecutive adult patients hospitalized for ST-segment elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) (with symptom onset $\leq$ 48 hours) during October 2005. Patients with AMI following cardiovascular procedures were excluded. Participation in the study was offered to all intensive care coronary units in French institutions (university teaching hospitals, general and regional hospitals and private clinics) with the capacity to receive acute coronary syndrome emergencies; 223 centres (60%) actually participated in the registry. Management was at the discretion of the physician in charge of the patient, independent of participation in the registry.

The protocol was reviewed by the committee for the protection of human subjects in biomedical research of Saint-Antoine University Hospital, and was approved by the French data protection authority. Patients gave informed consent for participation in the survey and late follow-up. The trial was registered at ClinicalTrials.gov (NCT00673036).

Data collection and follow-up

Data on baseline characteristics, including demographics (age, sex, body mass index), risk factors (hypertension, diabetes, current smoking, hypercholesterolaemia, family history of coronary artery disease) and medical history (history of cancer, coronary artery disease, myocardial infarction, stroke or transient ischaemic attack, heart failure, peripheral artery disease, previous percutaneous coronary intervention [PCI], coronary artery bypass graft, chronic renal failure and chronic obstructive pulmonary disease) were collected as described previously [16]. Information on the use of cardiac procedures, including PCI and medications (anticoagulants, antiplatelet agents, diuretics, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers and lipid-lowering agents) in the first 48 hours and at hospital discharge was collected.

All data were collected prospectively and recorded on computerized case report forms by dedicated research technicians who visited the site at least once each week. The follow-up was centralized at the French Society of Cardiology, with research technicians contacting both physicians and patients, after checking the patients' vital status in the municipal register.

Outcomes

In-hospital complications included recurrent myocardial infarction, ventricular fibrillation, bleeding or transfusion and stroke. We examined all-cause mortality as well as cardiovascular and non-cardiovascular mortality at 5-year follow-up. Cardiovascular mortality was defined as death of documented cardiac or vascular origin, including myocardial infarction, stroke, heart failure or aortic/peripheral artery disease. For the main analysis, cardiovascular mortality included deaths of documented cardiovascular origin and of unknown cause. In a sensitivity analysis, cardiovascular mortality only included death of documented cardiovascular origin. Non-cardiovascular mortality included documented non-cardiovascular deaths.

Statistical analysis

Continuous variables are described as means ± standard deviations; categorical variables are described using absolute and relative frequency distributions. Comparisons between groups used unpaired *t* tests or nonparametric Mann—Whitney tests for continuous variables, and Chi^2 tests for discrete variables.

Binary logistic regression analysis was used to determine whether history of cancer was an independent correlate of in-hospital management and discharge medications, using demographic characteristics, risk factors, previous (non-cancer) medical history and previous medications (i.e. before the index episode) as covariables.

Survival curves were generated using the Kaplan—Meier method, and were compared by the use of log-rank tests. Patients lost to follow-up were kept in the analyses and censored at the time they were last known to be alive.

We performed two types of analyses to describe the association between history of cancer and mortality: conventional multivariable analyses were used to seek an association with in-hospital and long-term mortality; and a propensity score-matched analysis was used in hospital survivors to analyse 5-year survival according to previous history of cancer.

The analyses were performed with IBM-SPSS software, version 23.0 (IBM, Armonk, NY, USA) and NCSS 10 software (NCSS, LLC, East Kaysville, UT, USA). For all tests, a value of $P < 0.05$ was considered significant.

Multivariable analyses of survival

Binary logistic regression analysis was used to determine whether history of cancer was an independent correlate of in-hospital mortality. Demographic variables, risk factors, history of coronary artery disease, co-morbidities, previous use of cardiovascular medications, type of myocardial infarction (STEMI or NSTEMI), presenting symptoms, Killip class on admission and presence of atrial fibrillation on first electrocardiogram were used as covariables.

In hospital survivors, a backward Cox multivariable analysis was used to assess predictors of 5-year mortality, with a value of $P = 0.05$ for inclusion and $P = 0.10$ for exclusion. The cumulative hazard functions for each covariable were computed to assess proportionality; collinearity was verified by calculating variance inflation factors. The candidate variables included in the multivariable analyses were selected ad hoc on the basis of their clinical relevance and potential to be associated with mortality: demographic variables; risk factors; history of coronary artery disease, co-morbidities, type of myocardial infarction (STEMI or NSTEMI), presenting symptoms, Killip class on admission and presence of atrial fibrillation on first electrocardiogram; early (within 48 hours of admission) use of aspirin, clopidogrel, low-molecular-weight heparin or glycoprotein IIb/IIIa inhibitors; in-hospital complications; coronary artery disease extent; coronary angiography, PCI and coronary artery bypass graft during initial hospital stay; and discharge medications. A time-dependent Cox multivariable analysis was also used to assess whether non-cardiovascular mortality differed in the first year versus longer-term follow-up between patients with and without a history of cancer.

Propensity score-matched analyses

A second type of analysis was undertaken using propensity scores to match each patient with a history of cancer to two patients without a history of cancer. The propensity score was calculated from a multivariable binary logistic regression analysis using the same baseline characteristics as for the Cox analysis.

Results

Baseline patient characteristics

Of the 3670 patients included in the FAST-MI registry, information on cancer history was not recorded for six patients, and 246/3664 (6.7%) had a documented history of cancer. Overall, 117 patients with a history of cancer (47.6%) were admitted for a STEMI and 129 (52.4%) for an NSTEMI.

Patients with a history of cancer were older, had a lower mean body mass index, more frequently had hypertension,

Table 1 Baseline characteristics and initial management of patients presenting with acute myocardial infarction, according to history of cancer.

Characteristic/management	No history of cancer ($n = 3418$)	History of cancer ($n = 246$)	P
Age (years)	67 ± 14	74 ± 11	< 0.001
Female	1086 (31.8)	67 (27.2)	0.14
Body mass index (kg/m^2)	27.2 ± 4.8 [3033]	26.3 ± 4.2 [205]	< 0.001
Risk factors			
Hypertension	2017 (59.0)	167 (67.9)	0.006
Diabetes	1221 (35.7)	92 (37.4)	0.60
Current smoking	1016 (29.7)	48 (19.5)	0.001
Hypercholesterolaemia	1661 (48.6)	111 (45.1)	0.29
Family history of cardiovascular disease	789 (23.1)	36 (14.6)	0.002
Medical history			
Coronary artery disease	1039 (30.4)	100 (40.7)	0.001
Myocardial infarction	612 (17.9)	52 (21.1)	0.20
PCI	483 (14.1)	34 (13.8)	0.89
CABG	195 (5.7)	15 (6.1)	0.80
Stroke or transient ischaemic attack	270 (7.9)	32 (13.0)	0.005
Peripheral artery disease	333 (9.7)	35 (14.2)	0.023
Heart failure	187 (5.5)	27 (11.0)	< 0.001
Chronic kidney disease	185 (5.4)	25 (10.2)	0.002
Chronic obstructive pulmonary disease	158 (4.6)	21 (8.5)	0.006
Previous medications			
Antiplatelet agents	1116 (32.7)	86 (35.0)	0.46
Statins	958 (28.0)	71 (28.9)	0.78
ACE inhibitors or ARBs	1192 (34.9)	99 (40.2)	0.09
Beta-blockers	847 (24.8)	73 (29.7)	0.09
Current episode			
STEMI	1764 (51.6)	117 (47.6)	0.22
Typical chest pain	2563 (75.0)	178 (72.4)	0.52
Resuscitated cardiac arrest	55 (1.6)	4 (1.6)	0.98
Time to first call ≤ 120 minutes	1850 (54.1)	134 (54.5)	0.91
MICU transportation	1604 (46.9)	111 (45.1)	0.58
Admission to PCI centre	2563 (75.0)	188 (76.4)	0.62
Left bundle branch block	149 (4.4)	10 (4.1)	0.83
Atrial fibrillation on first electrocardiogram	246 (7.2)	28 (11.4)	0.016
Shock at admission	65 (1.9)	3 (1.2)	0.45
GRACE score	148 ± 37	165 ± 33	< 0.001
Anaemia on admission	719 (21.8) [3303]	107 (46.1) [232]	< 0.001
Haemoglobin on admission (g/dL)	13.8 ± 1.9 [3303]	12.6 ± 2.1 [232]	< 0.001
Creatinine on admission (mg/L)	12 ± 7 [3322]	13 ± 9 [238]	< 0.001
C-reactive protein (mg/L)	27 ± 51 [2162]	47 ± 63 [161]	< 0.001

Data are expressed as mean ± standard deviation or number (%); values in square brackets denote the total number of patients in whom a given characteristic was recorded. ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; CABG: coronary artery bypass graft; GRACE: Global Registry of Acute Coronary Events; MICU: mobile intensive care unit; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

were less frequently current smokers and had a higher mean Global Registry of Acute Coronary Events (GRACE) score (Table 1). Co-morbidities were more commonly observed in patients with cancer, with higher proportions of history of coronary artery disease, previous stroke or transient ischaemic attack and peripheral artery disease compared with patients without cancer. Clinical presentation, time to first call and mobile intensive care unit use were similar between the two groups, but there were significant differences in concentrations of haemoglobin and creatinine at admission.

The rates of patients lost to follow-up were < 1% at 1 year, 3% at 3 years and 5% at 5 years.

Early management by cancer status

There were significant differences in some of the medications administered within the first 48 hours of admission between patients with and without a history of cancer (Table 2 and Table 3). However, after adjustment, only clopidogrel was used significantly less often in patients with a history of cancer (adjusted odds ratio [OR]: 0.69,

Table 2 Initial management of patients presenting with acute myocardial infarction, according to history of cancer.

Management	No history of cancer ($n = 3418$)	History of cancer ($n = 246$)	P
Medications within first 48 hours			
Aspirin	3189 (93.3)	229 (93.1)	0.90
Clopidogrel	2963 (86.7)	189 (76.8)	< 0.001
Glycoprotein IIb/IIIa inhibitor	1271 (37.2)	63 (25.6)	< 0.001
Low-molecular-weight heparin	2161 (63.2)	140 (56.9)	0.048
Statin	2550 (74.6)	167 (67.9)	0.020
Beta-blocker	2373 (69.4)	162 (65.9)	0.24
ACE inhibitor or ARB	1827 (53.5)	124 (50.4)	0.36
Reperfusion and procedures during hospital stay			
Time from first call to reperfusion ≤ 120 minutes in patients with STEMI	590/1109 (53.2)	23/60 (38.3)	0.033
Reperfusion therapy in patients with STEMI	1113 (63) [1764]	60 (51.3) [117]	0.01
Type of reperfusion therapy in patients with STEMI			
Fibrinolysis	497 (28.2)	18 (15.4)	0.003
Primary PCI	616 (34.9)	42 (35.9)	0.84
Coronary angiography	2915 (85.3)	183 (74.4)	< 0.001
PCI	2207 (64.6)	127 (51.6)	< 0.001
CABG	135 (3.9)	9 (3.7)	0.82
Multivessel coronary artery disease	1318 (45.2) [2915]	96 (52.5) [183]	0.056
LVEF (%)	52 ± 13 [2631]	51 ± 13 [169]	0.28
LVEF $\leq 40\%$ or missing	1381 (40.4)	120 (48.8)	0.009

Data are expressed as number (%) or mean $\pm$ standard deviation; values in square brackets denote the total number of patients in whom a given characteristic was recorded. ACE: angiotensin-converting enzyme; ARB: angiotensin II receptor blocker; CABG: coronary artery bypass surgery; LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.

95% confidence interval [CI]: 0.48—0.99; $P = 0.043$). The use of low-molecular-weight heparin, beta-blockers, statins, angiotensin-converting enzyme inhibitors and aldosterone receptor blockers did not differ between patients with or without a history of cancer (Table 3).

Among patients with STEMI, the use of reperfusion therapy — particularly primary PCI — did not differ according to cancer status; in contrast, intravenous fibrinolysis was less used (Tables 2 and 3).

Among patients with NSTEMI, coronary angiography was performed significantly less frequently among patients with cancer, but the difference was no longer significant after adjustment (adjusted OR: 0.82, 95% CI: 0.50—1.34; $P = 0.42$). PCI was used less frequently among patients with NSTEMI with cancer, but the difference did not reach statistical significance after adjustment (adjusted OR: 0.69, 95% CI: 0.45—1.04; $P = 0.079$).

More procedures were performed using balloon angioplasty alone among patients with NSTEMI with versus without a history of cancer (12.2% vs 5.7%; $P = 0.06$) as well as in patients with STEMI with versus without a history of cancer (11.5% vs 6.7%; $P = 0.11$).

In-hospital outcomes

In-hospital complications did not differ according to history of cancer, with the exception of recurrent myocardial infarction and major bleeding and/or transfusion. The rate of major bleeding and/or transfusion was significantly higher among patients with a history of cancer, mainly related to more frequent use of transfusion (6.9% vs 3.9%; $P = 0.024$) (Table 4). However, the difference was no longer significant after adjustment (adjusted OR: 1.33, 95% CI: 0.73—2.44; $P = 0.34$). Notably, the rates of minor and major bleeding were similar in the two groups (Table 4).

The in-hospital mortality rates for the whole AMI population were 8.9% among patients with a history of cancer and 5.4% among those with no history of cancer, giving a crude OR of 1.73 (95% CI: 1.09—2.74) and an adjusted OR of 1.15 (95% CI: 0.68—1.94; $P = 0.606$) (Fig. 1). Similarly, after adjustment, there was no significantly increased risk of in-hospital mortality in patients with STEMI or NSTEMI according to cancer status (Fig. 1).

Overall, 16/184 in-hospital deaths (9%) were considered not to be related to a cardiovascular origin in patients without history of cancer, compared with 3/22 (14%) in those with a history of cancer ($P = 0.72$).

Five-year mortality rates

Among all patients, regardless of hospital survivor status, the 5-year mortality rate was 52.8% in patients with and 28.1% in patients without a history of cancer. Among hospital survivors, 5-year all-cause death was significantly higher

Table 3 Management in patients with a history of cancer.

Management	Crude OR[a] (95% CI)	*P*	Adjusted OR[a] (95% CI)	*P*
Medications in first 48 hours				
Aspirin	0.97 (0.58–1.61)	0.90	1.34 (0.74–2.43)	0.30
Low-molecular-weight heparin	0.77 (0.59–1.00)	0.048	0.99 (0.74–1.32)	0.95
Glycoprotein IIb/IIIa inhibitor	0.58 (0.43–0.78)	< 0.001	0.79 (0.57–1.08)	0.79
Clopidogrel	0.51 (0.37–0.70)	< 0.001	0.69 (0.48–0.99)	0.043
Statin	0.72 (0.54–0.95)	0.020	0.88 (0.64–1.21)	0.44
Beta-blocker	0.85 (0.65–1.12)	0.24	1.18 (0.85–1.63)	0.32
ACE inhibitor or ARB	0.88 (0.68–1.15)	0.36	0.88 (0.66–1.18)	0.40
Procedures				
Reperfusion therapy (in patients with STEMI)	0.61 (0.42–0.89)	0.010	0.79 (0.52–1.20)	0.27
Primary PCI (in patients with STEMI)	1.04 (0.70–1.54)	0.84	1.19 (0.78–1.81)	0.42
Coronary angiography	0.50 (0.37–0.68)	< 0.001	0.73 (0.50–1.06)	0.097
PCI	0.59 (0.45–0.76)	< 0.001	0.73 (0.54–0.99)	0.041
CABG	0.92 (0.46–1.84)	0.82	1.00 (0.47–2.11)	1.00
Transfusion	1.80 (1.07–3.04)	0.027	1.33 (0.73–2.44)	0.34

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CABG: coronary artery bypass graft; CI: confidence interval; OR: odds ratio; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.
[a] ORs for getting medications or procedures in patients with versus without cancer.

Table 4 In-hospital complications in patients presenting with acute myocardial infarction, according to cancer status.

In-hospital complications	No history of cancer ($n = 3418$)	History of cancer ($n = 246$)	*P*
Recurrent myocardial infarction	74 (2.2)	0	0.02
Stroke	32 (0.9)	2 (0.8)	0.85
Ventricular fibrillation	72 (2.1)	3 (1.2)	0.34
Killip class ≥ 2	942 (27.6)	81 (32.9)	0.07
Shock	212 (6.2)	11 (4.5)	0.27
Major bleeding and/or transfusion	139 (4.1)	19 (7.7)	0.006
Major bleeding	71 (2.1)	8 (3.3)	0.22
Transfusion	135 (3.9)	17 (6.9)	0.02
Minor bleeding	35 (1.0)	3 (1.2)	0.77
Duration of stay in ICCU (days)	5.1 ± 5.1	4.9 ± 3.9	0.55
Duration of stay in hospital (days)	9.3 ± 8.3	10.1 ± 10.1	0.15

Data are expressed as number (%) or mean $\pm$ standard deviation. ICCU: intensive coronary care unit.

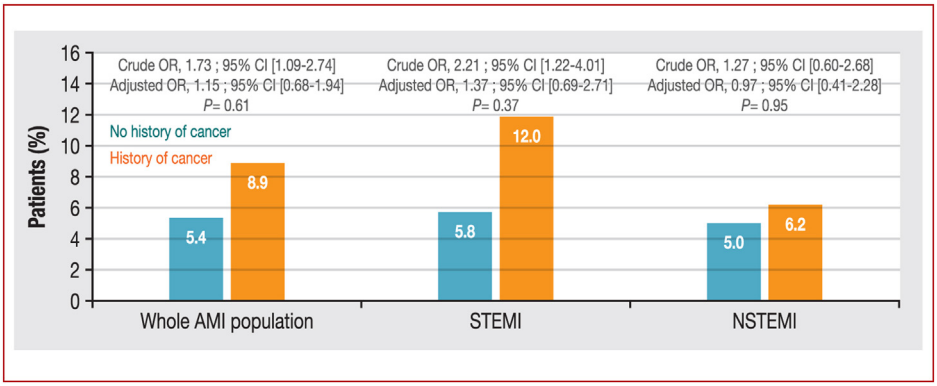

Figure 1. In-hospital mortality in all patients hospitalized with an AMI, according to their history of cancer, and in patients according to the type of myocardial infarction and their history of cancer. AMI: acute myocardial infarction; CI: confidence interval; NSTEMI: non-ST-segment elevation myocardial infarction; OR: odds ratio; STEMI: ST-segment elevation myocardial infarction.

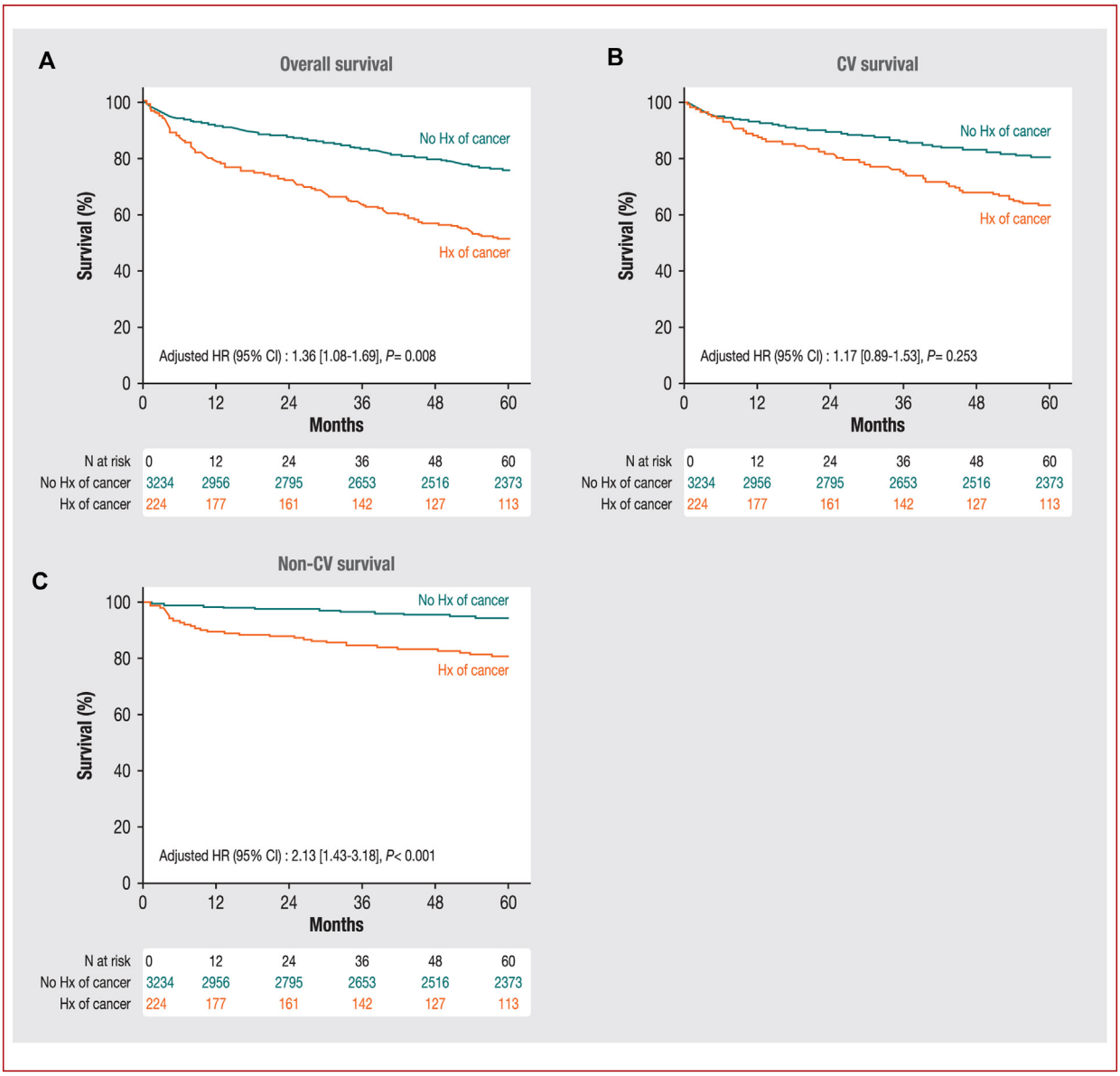

Figure 2. Five-year cumulative survival among hospital survivors. A. Overall survival. B. Cardiovascular survival. C. Non-cardiovascular survival. CI: confidence interval; CV: cardiovascular; HR: hazard ratio; Hx: history.

among those with versus without cancer among all patients with AMI (Fig. 2A) and among those with STEMI, but the difference was not quite significant among those with NSTEMI (Table 5). However, 5-year cardiovascular mortality did not differ significantly by cancer status among all patients with AMI (Fig. 2B) or in the STEMI or NSTEMI populations (Table 5). The results were similar whether cardiovascular death was defined as death of documented cardiovascular origin or unknown cause, or as death of documented cardiovascular origin (Table 5). Morbidity follow-up at 1 year was available in 90% of the patients; hospitalization for heart failure was observed in 7.8% of patients with versus 6.0% of patients without a history of cancer ($P = 0.24$).

Five-year mortality from non-cardiovascular causes was higher among hospital survivors with a history of cancer in the overall AMI population (Fig. 2C) as well as in the STEMI and NSTEMI populations (Table 5).

Most of the excess in non-cardiovascular mortality was observed during the first 12 months following the index AMI; although a numerical excess in non-cardiovascular deaths persisted after 1 year, it was no longer statistically significant. In a time-dependent analysis set at 12 months after the index episode, the hazard ratio (HR) for non-cardiovascular death before 12 months was 5.08 (95% CI: 2.84–9.09; $P < 0.001$), but was no longer significant beyond 1 year (HR: 1.59, 95% CI: 0.89–2.85; $P = 0.12$).

Using a 2:1 matching procedure, the propensity score-matched cohorts comprised 190 patients with and 380 without a history of cancer. Model fits were satisfactory (Hosmer-Lemeshow, $P = 0.30$) and the discriminatory power of the model was acceptable (C-statistic = 0.72) for the overall population model. Baseline characteristics and early management were similar in the two cohorts (Table 6). All-cause mortality at 5 years was higher among hospital

Table 5 Five-year mortality rates among hospital survivors, according to cancer status.

Outcome	5-year mortality rates in patients with versus without a history of cancer (%)	Adjusted HR (95% CI)	*P*
All-cause death			
Overall population	48 vs 24	1.36 (1.08—1.69)	0.008
STEMI	39 vs 16.5	1.59 (1.09—2.32)	0.016
NSTEMI	56 vs 32	1.32 (1.00—1.74)	0.051
CV death (documented or cause unknown)			
Overall population	32 vs 19	1.17 (0.89—1.53)	0.25
STEMI	22 vs 14	1.25 (0.77—2.02)	0.37
NSTEMI	41 vs 25	1.21 (0.86—1.69)	0.27
Documented non-CV death			
Overall population	16.5 vs 5	2.13 (1.43—3.18)	< 0.001
STEMI	20 vs 11	2.93 (1.56—5.52)	0.001
NSTEMI	31 vs 20	1.71 (1.03—2.83)	0.038
Documented CV death			
Overall population	26 vs 15	1.19 (0.88—1.60)	0.25

CI: confidence interval; CV: cardiovascular; HR: hazard ratio; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

survivors with versus without a history of cancer (48% vs 38%; adjusted HR: 1.37, 95% CI: 1.05—1.78; $P = 0.019$) as a result of increased non-cardiovascular mortality (16% vs 8%; adjusted HR: 2.34, 95% CI: 1.41—3.88; $P = 0.001$), whereas there was no significant increase in cardiovascular mortality (26% vs 25%; adjusted HR: 1.12, 95% CI: 0.80—1.55; $P = 0.50$) (Fig. 3). Among patients who had died by 5 years, the cardiovascular death rates were 66% in patients with and 79% in patients without a history of cancer ($P = 0.003$).

Discussion

The two main results from this analysis, based on the nationwide 2005 FAST-MI registry, were as follows. Firstly, after adjustment for baseline characteristics, patient management was quite similar between those with and without a history of cancer, except for the use of invasive strategies (other than primary PCI for patients with STEMI), which was significantly lower in patients with a history of cancer. Secondly, we found that cardiovascular death is the leading cause of death in patients with AMI with or without cancer, but that a history of cancer, per se, was not significantly associated with an increased risk of early or long-term cardiovascular death, regardless of whether their index episode was STEMI or NSTEMI. In contrast — and as expected — non-cardiovascular mortality was increased approximately two-fold among patients with a history of cancer, and was five-fold higher during the first year following AMI. This analysis suggests the potential benefit of guideline-recommended cardiovascular therapies for patients admitted for a STEMI and a previous history of cancer in terms of cardiovascular outcomes, despite the fact that these patients remain at high non-cardiac risk, mostly related to their cancer disease.

Patients with cancer are exposed to an increased risk of thrombosis through multiple and cumulative mechanisms, represented by prothrombotic mechanisms caused by increased platelet activation, increased procoagulant state, and endothelial injury resulting from oncological treatment, such as radiotherapy or molecular-targeted agents [18,19]. The extent to which these abnormalities translate into an increased risk of developing coronary heart disease and/or an AMI remains poorly described [20]. Zoller et al. [7], who performed a nationwide follow-up study in Sweden, found that most types of cancer were associated with an increased risk of coronary heart disease during the 6 months after cancer diagnosis, and that this risk was related to the presence of metastasis, suggesting a potential role and impact of oncological management on cardiovascular prognosis.

Few reports describe the management and outcomes of patients with cancer. However, our results from a prospective registry are in line with those from Hess et al. [8], who used an administrative database. The authors studied patients with cancer, 67% of whom were treated with PCI for an acute coronary syndrome, and reported that neither cancer status nor oncological treatment was associated with worse long-term cardiovascular mortality compared with patients without cancer.

Our analysis of an unselected consecutive population has identified other important findings not previously described. The clinical presentation and way of admission of patients with a history of cancer — as well as usual care — did not differ from those patients free from cancer. The proportion of STEMI, time to first call ≤ 120 minutes and mobile intensive care unit use were similar, as was admission to a PCI centre. However, among patients presenting with a STEMI, patients with a history of cancer received fibrinolytic treatment less frequently than those with a cancer history, but had a similar rate of primary PCI. This suggests that there was no bias in terms of the decision to give reperfusion therapy, but that a history of cancer was probably considered to represent a contraindication to the use of fibrinolytic treatment.

Table 6 Characteristics of patients with and without a history of cancer, after matching.

	No history of cancer ($n = 380$)	History of cancer ($n = 190$)
Age (years)	73 ± 12	73 ± 11
Body mass index (kg/m^2)	26.5 ± 4.4	26.3 ± 4.3
Risk factors		
Hypertension	249 (65.5)	121 (63.7)
Diabetes	148 (38.9)	66 (34.7)
Current smoking	71 (18.7)	37 (19.5)
Hypercholesterolaemia	173 (45.5)	84 (44.2)
Family history of cardiovascular disease	66 (17.4)	30 (15.8)
Previous medical history		
Myocardial infarction	76 (20.0)	41 (21.6)
PCI	51 (13.4)	28 (14.7)
CABG	24 (6.3)	12 (6.3)
Stroke or transient ischaemic attack	41 (10.8)	20 (10.5)
Peripheral arterial disease	53 (13.9)	27 (14.2)
Heart failure	36 (9.5)	18 (9.5)
Chronic kidney disease	36 (9.5)	19 (10.0)
Chronic obstructive lung disease	25 (6.6)	14 (7.4)
Previous medications		
Antiplatelet agents	135 (35.5)	72 (37.9)
Statins	117 (30.8)	58 (30.5)
ACE inhibitors or ARBs	161 (42.4)	79 (41.6)
Beta-blockers	124 (32.6)	59 (31.1)
Current episode		
Typical chest pain	304 (80.0)	149 (78.4)
Resuscitated cardiac arrest	6 (1.6)	3 (1.6)
Time to first call ≤ 120 minutes	194 (51)	98 (51.6)
MICU transportation	183 (48.2)	86 (45.3)
Admission to PCI centre	267 (70.3)	152 (80.0)
Left bundle branch block	21 (5.5)	8 (4.2)
Atrial fibrillation on first electrocardiogram	40 (10.5)	18 (9.5)
GRACE score	158 ± 35	162 ± 30
Anaemia on admission	95 (25)	80 (42.1)
Haemoglobin on admission (g/L)	13.6 ± 2.0 [372]	12.8 ± 2.0 [181]
Creatinine on admission, (mg/L)	12.6 ± 0.73	12.8 ± 0.72
C-reactive protein (mg/L)	31 ± 51 [245]	43 ± 63 [119]
Management in first 48 hours		
Aspirin	350 (92.1)	181 (95.3)
Clopidogrel	302 (79.5)	154 (81.1)
Glycoprotein IIb/IIIa inhibitor	131 (34.5)	60 (31.6)
Low-molecular-weight heparin	222 (58.4)	112 (58.9)
Statin	275 (72.4)	136 (71.6)
Beta-blocker	245 (64.5)	132 (69.5)
ACE inhibitor or ARB	157 (41.3)	86 (45.3)
LVEF > 40%	208 (54.7)	108 (56.8)
Discharge medications[a]		
Aspirin	319 (88.9)	160 (89.9)
Clopidogrel	268 (74.7)	135 (75.8)
Oral anticoagulant	29 (8.1)	15 (8.4)
Statin	293 (81.6)	136 (76.4)
Beta-blocker	168 (44.2)	132 (69.5)
ACE inhibitor or ARB	245 (68.2)	117 (65.7)
Aldosterone antagonist	15 (4.2)	8 (4.5)

Data are expressed as mean ± standard deviation or number (%); values in square brackets indicate the numbers of patients with available data for variables for which data were not available for all patients. ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CABG: coronary artery bypass graft; GRACE: Global Registry of Acute Coronary Events; LVEF: left ventricular ejection fraction; MICU: mobile intensive care unit; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction.
[a] No history of cancer: $n = 359$; history of cancer, $n = 178$.

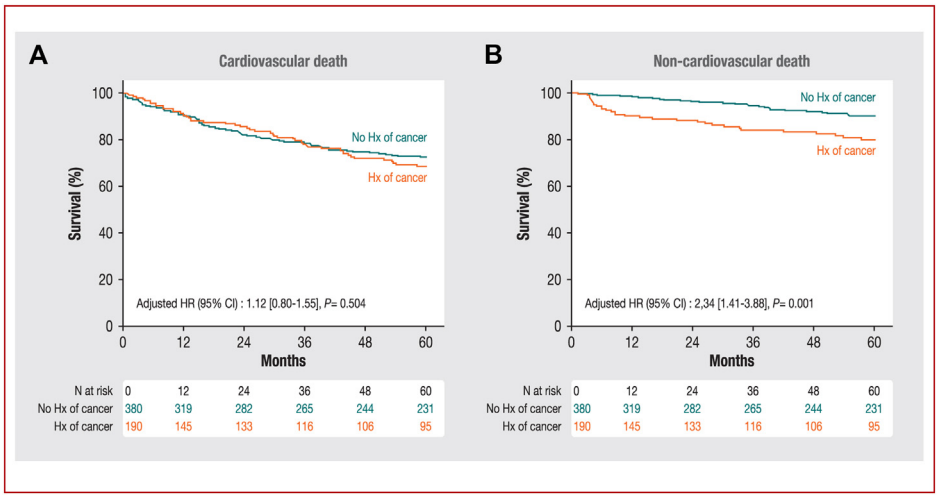

Figure 3. Five-year cumulative death among hospital survivors in the whole acute myocardial infarction population using a matched propensity score. A. Cardiovascular death. B. Non-cardiovascular death. CI: confidence interval; HR: hazard ratio; Hx: history.

In crude analyses, patients with a history of cancer received less antithrombotic medication (except aspirin) than those without cancer. After adjustment, however, the differences were no longer significant, except for clopidogrel, a finding in line with the less frequent use of PCI in these patients. Several factors, such as the perceived risk of bleeding, creatinine clearance at admission or the proportion of cancer patients with anaemia, could — at least in part — explain these results. We cannot exclude that other variables — particularly those defining patients with cancer — were not captured in this registry, such as general physical condition, performance status, presence of metastases, perceived adverse short-term prognosis and/or bleeding risk. These variables could have influenced the final decision about whether to perform an invasive strategy. Our findings also differ from those described by Velders et al. [10], who found a similar level of clopidogrel use in patients with and without cancer. However, potential differences in initial management did not translate into a higher risk of major and minor bleeding during the hospital stay in the two populations. Among patients with STEMI, the lower use of fibrinolytic therapy — resulting in an overall lower use of reperfusion at the acute stage despite similar rates of primary PCI — did not result in an altered long-term cardiovascular outcome for patients with cancer. In a registry of consecutive patients undergoing primary PCI for a STEMI, Velders et al. [10] found that patients with cancer were less likely to receive stents. Interestingly, our observations were similar, with 11.5% of patients with STEMI with a history of cancer treated with balloon angioplasty alone, compared with 6.7% of those without a history of cancer.

Study limitations and strengths

As with all observational studies, our study has several limitations. The item ''history of cancer'' might have been under-reported as it was based on either self-declaration or hospital records, which might attenuate the difference between groups. However, the frequency of cancer in our registry (6.7%) was of a similar magnitude to the 3.3% observed by Hess et al. [8] and the 6% reported in a Dutch registry [10]. Also, precise information on the nature, location, duration and specific treatment of cancer was not recorded, nor was the presence of metastases. We were unable to investigate in both groups the impact of performance status, previous venous thromboembolism/pulmonary embolism, infections and haemorrhagic risk on management; as such information was not captured in the FAST-MI registry. Similarly, in patients without a history of cancer, information on the risk of developing neoplasia during follow-up was not available.

Conversely, FAST-MI can be considered highly representative of the management and outcomes of patients hospitalized for an AMI in France, with a high overall participation rate, all major institutions participating in the survey and the totality of the metropolitan French territory covered. Also, the snapshot nature of the registry allows comprehensive data collection and monitoring.

Conclusion

Overall, there was little difference in the management of patients with AMI according to history of cancer. A history of cancer, per se, does not appear to be a risk factor for increased in-hospital mortality or long-term cardiovascular mortality in patients admitted for AMI.

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The other authors declare that they have no competing interest.

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