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Cancer and myocardial injury in patients with suspected acute coronary syndrome

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Abstract

Background Cancer and cardiovascular diseases are the leading causes of mortality worldwide, as they share common risk factors and exacerbate cardiovascular outcomes when they coexist. This study aimed to assess the clinical characteristics and cardiovascular outcomes of patients with a history of cancer and myocardial injury (MI) presenting with suspected acute coronary syndrome (ACS) in an emergency setting.

Methods This retrospective cohort study included 3,626 patients admitted to the emergency department with suspected ACS between 2012 and 2013. Patients were categorized on the basis of their cancer history and the presence of MI. Clinical variables and the associations between cancer history and MI with all-cause mortality were analyzed over a four-year follow-up period via univariate and multivariate Cox regression models.

Results Of the cohort, 10.6% ($n=384$) had a history of cancer. Compared with other groups, cancer patients with MI were older, had more comorbidities, and presented a higher incidence of type 2 myocardial infarction (T2MI). At the four-year follow-up, all-cause mortality was significantly greater among cancer patients with MI (68.8%) than among cancer patients without MI (32.4%) and noncancer patients with or without MI (42.5% vs. 11.3%, respectively). Multivariate analysis identified cancer patients, particularly those with MI, as independent predictors of mortality.

Conclusions Patients who present to emergency departments with suspected ACS, a history of cancer, or the presence of MI face greater cardiovascular risk and mortality than other patients do. The higher prevalence of T2MI in this population underscores the need for tailored management strategies.

Keywords Cancer, Myocardial infarction, Acute coronary syndrome

Introduction

Cancer and cardiovascular diseases (CVD) are the leading causes of death worldwide [1]. The coexistence of cancer and CVD significantly worsens the prognosis of patients. Cancer and CVD share common risk factors and pathological mechanisms that exacerbate adverse outcomes [2]. Patients with both conditions have a greater risk of cardiovascular events and all-cause mortality than do those with either cancer or cardiovascular disease alone [3].

Cardiac troponin I (cTnI) is a biomarker of myocardial injury, and several nonischemic conditions are frequently observed in patients admitted to the emergency room,

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reflecting myocardial damage [4]. Elevated troponin in patients seen in the emergency department has important prognostic implications, whether for type 1 or type 2 myocardial infarction (T1MI or T2MI) or nonischemic myocardial injury (NIMI) [5–7]. Troponin elevation in cancer patients is a multifaceted phenomenon influenced by various factors. Cancer therapies, including chemotherapy and radiotherapy, are frequently cardiotoxic and can lead to elevated plasma troponin levels. The inflammatory milieu associated with both cancer and its treatments can further impact the cardiovascular system, promoting troponin release. Finally, cancer-related microvascular dysfunction, characterized by impaired blood flow at the microvascular level, may contribute to MI and subsequent troponin elevation [8]. In addition, the prognostic implications of patients with a history of cancer visiting the emergency department with chest pain and elevated cTnI levels are not known.

The aim of this study was to identify the clinical characteristics and prognostic implications of the combination of cancer and MI in patients who visit the emergency room and undergo cTnI testing due to suspected acute coronary syndrome.

Methods

Study population

This was an observational, retrospective cohort study of patients who were admitted to the University Hospital Joan XXIII emergency department between January 1, 2012, and December 31, 2013, and who underwent at least one cTnI test due to suspected acute coronary syndrome, following the chest pain protocol of our center. In our protocol, if the first troponin measurement is negative and the patient's symptoms have persisted for more than six hours, a second measurement is not necessary. However, in patients who were ultimately classified as T1MI, T2MI or NIMI on a single troponin measurement, the final diagnosis was made by consensus between two cardiologists after reviewing all available clinical information. In cases where more than one cTnI test was performed, we selected the highest cTnI value. For patients admitted to the emergency room multiple times, we included only the first admission episode. The exclusion criteria were age under 18 years, patients who had recovered from cardiac arrest, and patients living outside our reference area.

Cardiac troponin I assay

All cTnI measurements were performed in the same laboratory via a contemporary immunoassay technique (TnI-Ultra from Siemens, Advia Centaur). According to the manufacturer, the lower detection limit was 6 ng/L. The reference range for a positive cTnI test was > 39 ng/L, corresponding to the 99th percentile of a reference control group, with a coefficient of variation of < 10%. A cTnI level above the reference range was considered indicative of MI.

Categorization of the study population

Patients were categorized according to their present or past history of cancer, and the presence or absence of MI. We define cancer according to the National Cancer Institute as a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body [9]. Cancer status was defined according to the information in the patients' clinical records. Information was collected on the different treatments administered (surgery, chemotherapy, radiotherapy) and the years elapsed between diagnosis and the event prompting the emergency visit. Solid cancers were defined as those originating in a solid organ or tissue, whereas hematologic cancers were defined as those originating in blood-forming tissues, such as the bone marrow or lymphatic system.

Clinical variables studied

The electronic medical records of all patients were reviewed. The demographic variables, cardiovascular risk factors, relevant cardiovascular and noncardiovascular history, physical examination at the initial emergency evaluation, electrocardiographic findings, and laboratory tests were included. The glomerular filtration rate was calculated via the formula MDRD-4 (diet modification in kidney disease). The primary diagnoses at discharge were also recorded. T1MI, T2MI and NIMI were defined by a consensus of two cardiologists, as previously reported [4].

Primary endpoint

The primary outcome of the study was all-cause mortality at the 4-year follow-up, categorized by cancer status and MI. The incidence of myocardial infarction or hospitalization due to heart failure was also analyzed, as were the combined events of death, myocardial infarction, or hospitalization for heart failure (Major Adverse Cardiovascular Events: MACE) occurring during the follow-up years. Follow-up events were obtained from patients' electronic medical records and death registries.

Statistical analysis

Data are presented as medians and interquartile ranges (IQRs) for continuous variables and as counts with percentages for categorical variables. The baseline characteristics of the patients were compared via the

Kruskal–Wallis test for continuous variables that did not meet normality assumptions, the Student's t test for independent samples for continuous variables that fulfilled normality criteria, and Pearson's chi^2 test for categorical variables. Continuous variables with more than two categories were analyzed via analysis of variance (ANOVA) after verifying the assumptions of normality and homogeneity of variance. In both cases, tests were performed a posteriori to identify any groups with nondiffering means or proportions via the Bonferroni technique. Survival analysis was performed via the Kaplan–Meier method, and group comparisons were made via the log-rank test. Cox proportional hazards regression analysis was used in the univariate and multivariate mortality analyses. Backward stepwise selection was used with an input p value < 0.05. The results are presented as hazard ratios (HRs) with confidence intervals (CIs) of 95%. The clinically relevant variables included in the multivariate Cox regression analysis were age, sex, hypertension status, diabetes mellitus status, hemoglobin status, glomerular filtration rate, history of myocardial infarction, heart failure, chronic renal disease, cerebrovascular disease, and atrial fibrillation. Differences were considered statistically significant at $p < 0.05$. IBM SPSS Statistics Version 29.0.2.0 (20) was used for all analyses.

Ethics approval and consent to participate

The study was approved by the Comitè Ètic d´Investigació Clínica, Hospital Universitari de Tarragona Joan XXIII (CEIC 82/2014). Written informed consent was not required because of the retrospective analyses of the data and the lack of intervention for the patients.

Results

The initial cohort consisted of 3,710 patients, of which those under 18 years of age, those with cardiac arrest, and those lost to follow-up were excluded, resulting in a total of 3,626 valid patients for the study. Among them, 10.6% ($n = 384$) had a history of cancer (Fig. 1). Elevated

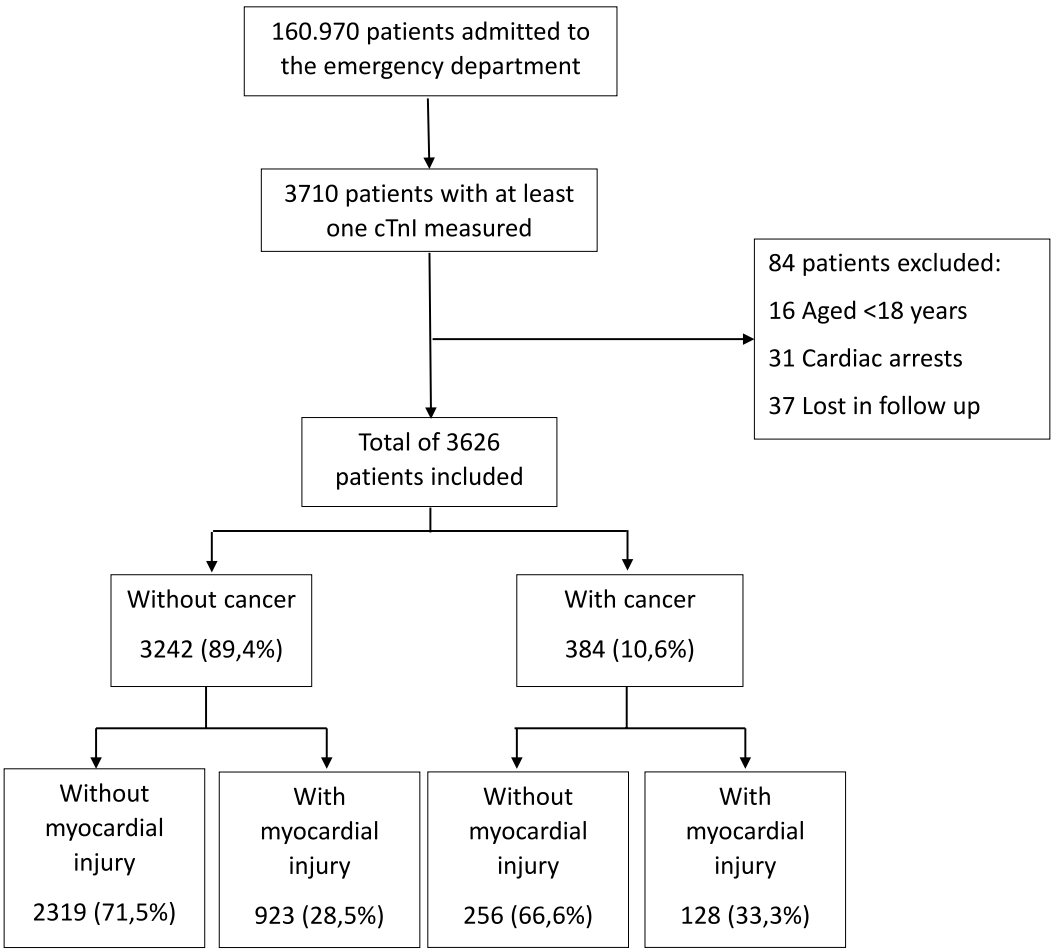

Fig. 1 Flow diagram of patient selection. The distribution of patients according to cancer status is depicted. cTnI: Cardiac troponin I

cTnI was detected in 30% of the total population (33.3% of patients with cancer and 28.5% of patients without cancer, $p=0.039$).

Baseline characteristics

Compared with the other groups, cancer patients with MI were older and had a higher incidence of hypertension, chronic kidney disease, and chronic obstructive pulmonary disease. These patients presented to the emergency department more frequently with dyspnea than with chest pain. Additionally, cancer patients with MI have worse oxygen saturation, a greater heart rate, more severely reduced kidney function and lower hemoglobin levels. On electrocardiographic examination, cancer patients with MI presented a greater incidence of atrial fibrillation, right bundle branch block (RBBB), and left or right bundle branch block (LBBB) (Table 1).

Within the cancer group ($N=384$), 40 patients had hematologic cancer, and 344 had solid tumors. Among solid tumors, prostate, breast, and colorectal cancers were the most common. Fifty-eight percent of the patients had been diagnosed with cancer within the last 5 years of data collection, 10% had more than one type of cancer, 9% had metastasis, and 65% were in complete remission at the time of data collection (Supplementary Material, Table 1S).

Clinical diagnosis

The primary diagnoses of cancer patients were very similar to those of noncancer patients, except for

Table 1 Clinical characteristics of patients with and without a history of cancer according to myocardial injury status

		Without cancer		With cancer		
	Total	**Without MI**	**With MI**	**Without MI**	**With MI**	***p***
	3626	**2319**	**923**	**256**	**128**	
Age, years	68[55–79]	65 [51–76][a]	74 [60–83][b]	75 [65–80][b]	80 [72–85][c]	0.001
Male sex	2072 (57.1)	1261 (54.4)[a]	563 (61.0)[b]	161 (62.9)[a,b]	87 (68.0)[b]	0.001
Female sex	1554 (42.9)	1058 (45.6)[a]	360 (39.0)[b]	95 (37.1)[a,b]	41 (32.0)[b]	0.001
Risk factors and comorbidities						
Hypertension	2195 (60.6)	1247 (53.8)[a]	672 (72.8)[b]	175 (68.4)[b]	101 (78.9)[b]	0.001
Smoker	1216 (33.5)	701 (30.2)[a]	380 (41.2)[b]	87 (34.0)[a,b]	48 (37.5)[a,b]	0.001
Diabetes	925(25.5)	466 (20.1)[a]	288 (31.2)[b]	60 (23.4)[a,b]	38 (29.7)[a,b]	0.001
Prior myocardial infarction	719 (19.8)	392 (16.9)[a]	242 (26.2)[b]	45 (17.6)[a]	40 (31.3)[b]	0.001
Congestive heart failure	257 (7.1)	109 (4.7)[a]	117 (12.7)[b]	14 (5.5)[a]	17 (13.3)[b]	0.001
Stroke	284 (7.8)	124 (5.3)[a]	113 (12.2)[b]	27 (10.5)[b]	20 (15.6)[b]	0.001
Kidney disease	296 (8.2)	84 (3.6)[a]	159 (17.2)[b]	20 (7.8)[c]	33 (25.8)[b]	0.001
COPD	651 (18.0)	367 (15.8)[a]	199 (21.6)[b]	51 (19.9)[a,b]	34 (26.6)[b]	0.001
Symptoms						
Chest pain	1894 (52.2)	1255 (54.1)[a]	458 (49.6)[a]	122 (47.7)[a]	59 (46.1)[a]	0,02
Dyspnea	606 (16.7)	284 (12.2)[a]	238 (25.8)[b]	41 (16.0)[a]	43 (33.6)[b]	0.001
Syncope	245 (6.8)	162 (7.0)[a]	56 (6.1)[a]	20 (7.8)[a]	7 (5.5)[a]	0.001
Other symptoms	1205 (33.2)	830 (35.8)[a]	248 (26.9)[b]	96 (37.5)[a,c]	31 (24.2)[a,b]	0.001
Exploration						
Heart rate (bmp)	79[67–95]	77 [66–90][a]	83 [68–105][b]	76 [65–93][a]	87 [70–108][b]	0.001
Systolic blood pressure (mmHg)	138[121–155]	138 [123–153][a]	137 [120–159][a]	138 [120–156][a]	134 [115–154][a]	0.191
Oxygen saturation (%)	98 [96–100]	99 [97–100][a]	97 [94–99][b]	98 [96–100][a]	97 [91–98][c]	0.001
Electrocardiogram						
Atrial fibrillation	574 (16.7)	281 (12.8)[a]	218 (24.7)[b]	41 (17.7)[a,b]	34 (27.4)[b]	0.005
RBBB or LBBB	529 (15.4)	270 (12.3)[a]	190 (21.5)[b,c]	35 (15.1)[a,c]	34 (27.4)[b]	0.004
Pacemaker stimulation	76 (2.2)	36 (1.6)[a]	27 (3.1)[a]	3 (1.3)[a]	10 (8.1)[b]	0.006
Blood test						
Glucose (mg/dl)	111[95–147]	106 [93–131][a]	133 [104–187][b]	114 [98–140][a]	128 [100–174][b]	0.001
Glomerular filtration rate (ml/min/m2)	81[60–100]	85 [69–105][a]	65 [45–90][b]	78 [59–93][c]	53 [36–74][d]	0.001
Hemoglobin (g/dl)	13.4[12.1–14.7]	13.6 [12.4–14.9][a]	13.2 [11.6–14.6][b]	13.3 [11.7–14.4][b]	12 [10.8–13.3][c]	0.001

Each superscript letter indicates a subset of the 4 groups analyzed for which the means or proportions showed no difference at a significance level of 0.05

MI Myocardial injury, *COPD* Chronic obstructive pulmonary disease, *LBBB* Left bundle branch block, *RBBB* Right bundle branch block

bradyarrhythmia, respiratory pathology, renal failure, and infections, which were slightly more common in cancer patients. The incidence of T1MI and NIMI was similar between the two groups, but patients with cancer had significantly greater T2MI. The high rate of anemia as a cause of T2MI among cancer patients is noteworthy (Table 2).

Events in the follow-up

Hospital admission and in-hospital mortality rates were similar between patients with MI, with or without cancer. During follow-up, the overall mortality rate was 817 (22.5%): 171 (44.5%) cancer patients and 646 (19.9%) patients without cancer, $p < 0.001$. Patients with cancer and MI experienced higher mortality from any cause, as well as more rehospitalizations for heart failure and more MACE (Table 3). Among the surviving patients, the median follow-up was 1461 days (4 years), and 90% of these patients had a follow-up period longer than 1148 days (3.14 years). Figure 2 shows the Kaplan–Meier survival curves for patients with and without cancer, based on the presence or absence of MI. Within the cancer group, patients diagnosed with cancer within the last 5 years had higher mortality than those diagnosed more than 5 years ago (51% vs. 38%, $p = 0.018$). Similarly, cancer patients in complete remission had lower mortality rates than did those without complete remission (42.8% vs. 66.1%, $p = 0.001$). In Table 4, the univariate and multivariate models for predicting mortality according to the four groups are

Table 2 Principal diagnosis of patients with and without a history of cancer according to myocardial injury

		Without cancer		With cancer		
	Total	Without MI	With MI	Without MI	With MI	*p*
	3626	2319	923	256	128	
Heart failure	237 (6.5)	87 (3.8)[a]	120 (13.0)[b]	12 (4.7)[a]	18 (14.1)[b]	0.001
Tachyarrhythmia	219 (6.0)	129 (5.6)[a]	67 (7.3)[a]	18 (7.0)[a]	5 (3.9)[a]	0.186
Bradyarrhythmia	60 (1.7)	29 (1.3)[a]	19 (2.1)[a]	9 (3.5)[a]	3 (2.3)[a]	0,196
Hypertensive crisis	52 (1.4)	42 (1.8)[a]	6 (0.7)[a]	4 (1.6)[a]	0[a]	0,041
Myocarditis	66 (1.8)	43 (1.9)[a]	20 (2.2)[a]	2 (0.8)[a]	1 (0.8)[a]	0.399
Syncope	197 (5.4)	155 (6.7)[a]	23 (2.5)[b]	16 (6.3)[a]	3 (2.3)[a,b]	0.001
Chest pain	957 (26.4)	853 (36.8)[a]	27 (2.9)b	70 (27.3)[c]	7 (5.5)[b]	0,001
Cerebrovascular disease	70 (1.9)	41 (1.8)[a]	24 (2.6)[a]	3 (1.2)[a]	2 (1.6)[a]	0.337
Respiratory pathology	298 (8.2)	165 (7,1)[a]	91 (9.9)[a,b]	24 (9.4)[a,b]	18 (14.1)[b]	0.004
Pulmonary embolism	27 (0.7)	10 (0.4)[a]	14 (1.5)[b]	1 (0.4)[a,b]	2 (1.6)[a,b]	0.007
Gastrointestinal bleeding	22 (0.6)	11 (0.5)[a]	6 (0.7)[a,b]	2 (0.8)[a,b]	3 (2.3)[b]	0.065
Gastrointestinal pathology	286 (7.9)	233 (10.0)[a]	30 (3.3)[b]	22 (8.6)[a]	1 (0.8)[b]	0.001
Renal failure	23 (0.6)	4 (0.2)[a]	13 (1.4)[b]	1 (0.4)[a,b]	5 (3.9)[b]	0,001
Anemia	37 (1.0)	22 (0.9)[a]	8 (0.9)[a]	5 (1.0)[a]	2 (1.6)[a]	0.405
Sepsis	22 (0.6)	6 (0.3)[a]	11 (1.2)[b,c]	0[a,c]	5 (3.9)[b]	0.001
Other infections	53 (1.5)	28 (1.2)[a]	15 (1.6)[a]	6 (2.3)[a]	4 (3.1)[a]	0.168
Other diagnoses	1000(27.6)	461(19.9)	429(46.5)	61(23.8)	49(28.3)	
Type of myocardial injury						
Type 1 myocardial infarction	379 (10.5)		342 (10.5)		37 (9.6)	0.58
Type 2 myocardial infarction	193 (5.3)		160 (4.9)		33 (8.6)	0.003
Non ischemic MI	479 (13.2)		421 (13.0)		58 (15.1)	0.246
Type 2 myocardial infarction:						
Anemia	55 (28.5)		40 (25.0)		15 (45.5)	0.032
Shock	13 (6.7)		10 (6.3)		3 (9.1)	0,469
Bradycardia	22 (11.4)		19 (11.9)		3 (9.1)	0.772
Respiratory insufficiency	30 (15.5)		22 (13.8)		8 (24.2)	0.183
Tachycardia	38 (19.7)		36 (22.5)		2 (6.1)	0.031
Severe heart failure	35 (18.1)		33 (20.6)		2 (6.1)	0.05

Each superscript letter indicates a subset of the 4 groups analyzed for which the proportions showed no difference at a significance level of 0.05

MI Myocardial injury

Table 3 Clinical outcomes at the 4-year follow-up of patients with and without a history of cancer according to myocardial injury

		Without cancer		With cancer		
	Total	Without MI	With MI	Without MI	With MI	
	3626	2319	923	256	128	*p*
Hospitalization						
Hospital admission	1186 (32.7)	394 (17.0)[a]	648 (70.2)[b]	56 (21.9)[a]	88 (68.8)[b]	0.001
Coronariography	392(10.9)	63(2.7)[a]	300(32.5)[b]	4(1.6)[a]	25(19.5)[c]	0.001
In-hospital mortality	103 (2.8)	23 (1.0)[a]	71 (7.7)[b]	0[a]	9 (7.0)[b]	0.001
4-year follow-up						
Rehospitalization for myocardial infarction	177 (4.9)	66 (2.8)[a]	83 (9.0)[b]	15 (5.9)[a,b]	13 (10.2)[b]	0.001
Rehospitalization for HF	274 (7.6)	104 (4.5)[a]	126 (13.7)[b]	18 (7.0)[a]	26 (20.3)[b]	0.001
All-cause death	817 (22.5)	263 (11.3)[a]	383 (41.5)[b]	83 (32.4)[b]	88 (68.8)[c]	0.001
MACE	1044 (28.8)	384 (16.6)[a]	465 (50.4)[b]	102 (39.8)[c]	93 (72.7)[d]	0.001

Each superscript letter indicates a subset of the 4 groups analyzed for which the proportions showed no difference at a significance level of 0.05

MI Myocardial injury, *HF* Heart failure, *MACE* Major adverse cardiovascular events

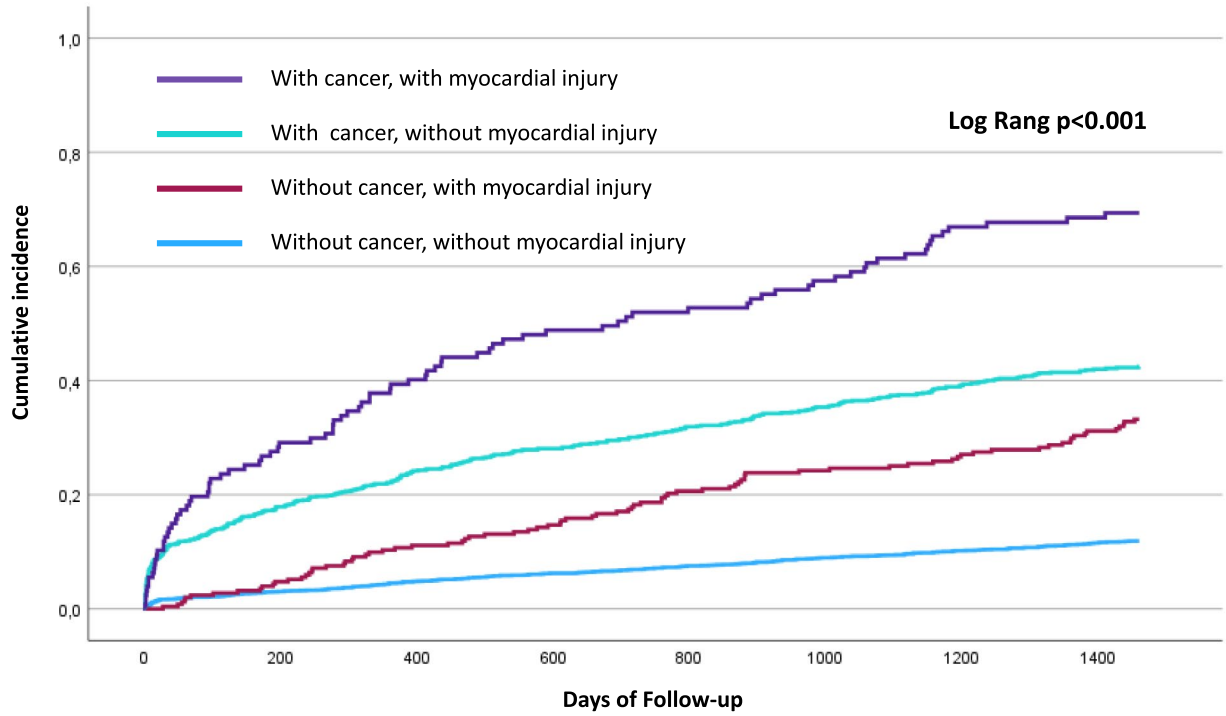

Fig. 2 Kaplan–Meier survival curves for patients with and without cancer stratified by the presence or absence of myocardial injury

presented. MI, cancer without MI, and especially cancer with MI were variables associated with mortality.

Discussion

Our study revealed that cancer patients who presented with suspected acute coronary syndrome in the emergency room experienced more MI and were often diagnosed with type 2 myocardial infarction (T2MI), which was primarily secondary to anemia. Additionally, cancer patients tend to be older and have more comorbidities, factors that contribute to higher all-cause mortality, and increased rates of rehospitalization for myocardial infarction and heart failure at the four-year follow-up.

Table 4 Univariate and multivariate Cox regression analyses for total mortality

	Univariate				Multivariate			
	HR	95,0% CI		p	HR	95,0% CI		*p*
		Inferior	Superior			Inferior	Superior	
Age	1.076	1.069	1.082	0.001	1.055	1.048	1.063	0.001
Gender	1,005	0,875	1,154	0,07				
Hypertension	2.574	2.178	3.047	0.001				
Diabetes	1.816	1.52	2.098	0.001	1.21	1.041	1.412	0.013
Smoker	1.070	0.927	1.235	0.357				
Hemoglobin	0.785	0.763	0.807	0.001	0.903	0.872	0.936	0.001
Glomerular filtration rate	0.976	0.975	0.979	0.001	0.994	0.991	0.997	0.001
Prior MI	1.748	1.503	2.032	0.001	1.197	1.020	1.406	0.028
Congestive heart failure	3.353	2.793	4.025	0.001	1.599	1.311	1.949	0.001
Stroke	2.504	2.072	3.026	0.001	1.303	1.062	1.598	0.011
Sepsis	5.482	3.231	9.301	0.001	2.070	1.126	3.806	0.019
Atrial fibrillation	2,359	2,018	2,758	0,001				
Without cancer and without MI	Ref							
With cancer and without MI	3.067	2.396	3.925	0.001	2.154	1.653	2.807	0.001
Without cancer and with MI	4.549	3.888	5.323	0.001	2.790	2.346	3.328	0.001
With cancer and with MI	9.355	7.343	11.918	0.001	3.999	3.075	5.200	0.001

HR Hazard ratio, *CI* Coefficient interval, *MI* Myocardial injury

Cancer and cardiovascular diseases are the leading causes of death in most first-world countries. Both conditions share common risk factors, such as age, smoking, diabetes, obesity, and a sedentary lifestyle [10]. Owing to advances in cancer treatments, cancer survival rates have increased in recent years [11]. Consequently, cancer survivors are older and present with more comorbidities [12, 13]. In cancer patients, chest pain and elevated cardiac troponins may arise from either cardiac or noncardiac causes. Among the causes of cardiac disease, coronary artery disease and heart failure are the most common. Non cardiac causes include imbalances in oxygen demand and supply unrelated to acute coronary atherothrombosis (T2MI) or NIMI. In this group, elevated troponins may result from conditions such as anemia, pulmonary embolism, pleuritis, pulmonary and bone metastasis, or cancer therapies, among others [14]. A retrospective analysis of the National Inpatient Sample dataset in the US, which examined cancer patients diagnosed with T2MI, revealed that cancer patients experienced T2MI more frequently than patients without T2MI because of acute respiratory failure, acute pulmonary embolism, major bleeding, and renal failure [15].

Cancer treatment may decompensate or worsen an underlying cardiovascular disease or even result in a new heart disease. In the literature, an important number of papers have shown the relationship between cancer treatment and cardiovascular worsening of acute coronary syndrome, acute pericardial disease and effusion, acute heart failure, left ventricle dysfunction, acute cardiomyopathy, including myocarditis, acute arrhythmia and venous thrombosis, among others [14]. Most chemotherapy drugs and radiotherapy are treatments related mostly to cardiovascular complications [14, 16] and can accelerate coronary artery diseases [17]. Before the initiation of cancer treatment, cardiovascular risk assessment via cardiac imaging and biomarkers is recommended [10]. If there is a suspicion of a causal relationship between cancer treatment and cardiovascular disease, cancer therapy should be temporally interrupted [10].

There are several reviews and meta-analyses showing that high-sensitivity cardiac troponins could serve as predictors of cancer therapy-related cardiac dysfunction [18, 19]. A meta-analysis demonstrated that higher troponin levels after treatment were associated with a greater risk of left ventricle dysfunction [19]. Another meta-analysis revealed that elevated high-sensitivity cardiac troponin T at 3–6 months after cancer treatment has high early diagnostic value for cancer treatment-related cardiac dysfunction [20].

A study of 930 patients referred to initiate systemic therapies in a cardio-oncology unit revealed that high-sensitivity cardiac troponin T could identify patients at high risk of mortality with a cutoff of 7 ng/L. Additionally, an increase in high-sensitivity cardiac troponin T levels at the start of chemotherapy or during follow-up,

even with initially negative troponins, was associated with increased all-cause mortality [21]. Another retrospective study evaluated 3,666 cancer patients and a matched group of 3,666 noncancer patients who underwent cardiac catheterization. The findings revealed that cancer patients with coronary artery disease, elevated high-sensitivity troponin T, elevated NT-pro-BNP, or reduced left ventricular ejection fraction had increased all-cause mortality at the 5-year follow-up. NT-pro-BNP demonstrated a stronger predictive value for mortality than high-sensitivity troponin T did in both groups, with additional predictors of increased mortality, including comorbidities such as diabetes and age [22].

A retrospective study assessed the prognostic value of cardiac troponin I in cancer patients visiting the emergency department. A total of 9,135 cancer patients were included, excluding those with known coronary disease or who required coronary angiography. The samples were divided into four groups on the basis of troponin I level: < 0.006 ng/ml, 0.007–0.039 ng/ml, 0.040–0.129 ng/ml, and ≥ 0.130 ng/ml, with mortality evaluated at 180 days. At 180 days, 35% of patients had died, with higher all-cause, cardiovascular, and noncardiovascular mortality observed as troponin I levels increased [23].

Bima et al. conducted a multicenter, international prospective study of 8,267 patients who presented with nontraumatic acute chest pain in the emergency department and were divided into cancer (711, 8.6%) and noncancer (7,556, 91.4%) groups. Similar to our findings, cancer patients were generally older and had more comorbidities and cardiovascular risk factors. Acute myocardial infarction was more common in the cancer group (27% vs. 21%, $p < 0.001$), with higher rates of both T1MI (18% vs. 13%) and T2MI (5% vs. 3%) myocardial infarctions. Anemia was the primary cause of type 2 cases. Cancer patients also presented increased levels of high-sensitivity cardiac troponin T (8 ng/L vs. 17 ng/L) and NT-pro-BNP (1772 vs. 571 pg/ml). At the five-year follow-up, cancer patients had higher all-cause mortality (34% vs. 9%, $p < 0.001$) and cardiovascular mortality (15% vs. 8%, $p < 0.001$) rates. While this study did not perform a multivariable analysis, it noted that chest pain presentations in cancer patients were more frequently associated with thoracic cancers (e.g., esophageal and lung) and testicular cancer. The study also evaluated the diagnostic accuracy of high-sensitivity cardiac troponins in ESC algorithms and reported that while chronic cardiac disease increased troponin levels and reduced algorithm efficacy, it did not impact safety [24].

Detecting myocardial injury in cancer patients presents both diagnostic and therapeutic challenges. On the one hand, it may be necessary to determine the specific cause of myocardial injury in each patient. If the patient exhibits ischemic symptoms, a coronary angiography should be considered. However, our data indicate that among patients with both cancer and myocardial injury, coronary angiography is performed less frequently than in those with myocardial injury but without cancer. We believe that this difference may be attributed to the higher incidence of type 2 myocardial infarction among cancer patients, in whom coronary angiography is typically not indicated. Moreover, the use of other multimodal imaging techniques to investigate and characterize potential cardiac involvement in cancer patients may be particularly appropriate for those presenting with myocardial injury [25, 26]. Finally, further research is needed to evaluate the cost-effectiveness of these imaging techniques in patients with cancer and myocardial damage.

Limitations

Our study has several limitations. First, this was a single-center study; however, it included a large cohort, so our conclusions could serve as a working hypothesis. Second, although we collected general data on cancer treatment, we do not have detailed information on the specific chemotherapies and immunotherapies used or on whether the surgeries involved only tumor resection or lymphadenectomy. Third, It is crucial to consider the potential presence of significant confounding factors that may account for the increased mortality risk observed in the cohort of cancer patients. Since the cause of death (cancer vs. cardiovascular disease vs. other) was not specified, it is not possible to determine conclusively what led to these deaths. The higher mortality rate among patients with active cancer suggests that cancer may have been the primary cause of death, rather than cardiovascular disease, as might be inferred from the troponin analysis. Additionally, patients with active cancer who are not responding to treatment may receive less aggressive management of their cardiovascular conditions, introducing another variable that could affect the study's results and their interpretation. Fourth, our study was conducted using cardiac troponin I. It has been described that cardiac troponin T is more frequently elevated in patients with certain cancers compared to troponin I [27]. These differences in cancer patients need to be clarified because they may have therapeutic implications. And fifth, as a retrospective study, there may be selection bias, as cancer status was defined on the basis of patients' medical records from our regional health system, without access to clinical records from private medical centers or hospitals in other parts of Spain.

Conclusions

A history of cancer affects the prognosis of patients presenting with suspected acute coronary syndrome in the emergency room. Cancer patients tend to have more MI

upon arrival, which likely contributes to increased mortality. Furthermore, many cancer treatments, as well as the current status of the disease, impact the cardiovascular system, either by exacerbating preexisting cardiac conditions or by causing new cardiovascular illnesses. Therefore, it is essential to inquire about cancer therapies and assess cancer staging to provide the most appropriate management strategies and implement secondary prevention measures. These findings highlight the importance of integrating oncology and cardiology care to improve outcomes in this vulnerable population.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
Conceptualization, A.B.; methodology, A.B., G.C., A.C.; software, G.C.; validation, A.B., O.M.P.; formal analysis, A.B., O.M.P.; investigation, M.S.T., G.C. A. C.; resources, A.B.; data curation, A.B.,; writing—original draft preparation, M.S.T..; writing—review and editing, A.B.; visualization, A.B.; supervision, J.L.F.; project administration, J.L.F. All the authors have read and agreed to the published version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study was approved by our Institutional Review Board (Comité Ético de Investigación con Medicamentos del Institut d'Investigació Sanitària Pere Virgili) and conducted in accordance with the Declaration of Helsinki. The approval registry number is CEIC 82/2014. The ethics committee determined that individual patient written informed consent was not required because of the retrospective analyses of the data and the lack of intervention for the patients.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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