

Characteristics and outcomes of patients with cancer hospitalized with new onset acute heart failure

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Abstract

Aims Limited evidence exists regarding the outcomes of cancer patients hospitalized with new onset acute heart failure (AHF). We assessed the in-hospital mortality and 1 year outcomes of cancer patients admitted for new onset AHF, taking into account both past and active cancer status as well as cancer site.

Methods We examined administrative data of adult patients hospitalized with a first episode of AHF from 2003 to 2018 in Lombardy, Italy. Patients were categorized based on their cancer history. The primary endpoint was in-hospital mortality with secondary endpoints including 1 year all-cause mortality and 1 year re-hospitalization for AHF.

Results Among 283 144 patients AHF hospitalizations, 55 145 (19%) involved patients with a history of cancer (60% past cancer, 40% active cancer). Both in-hospital and 1 year mortality rates were higher among cancer patients compared with those without (9.3% vs. 6.4% and 34.9% vs. 22.3%, respectively; $P < 0.0001$). After adjustment, cancer patients exhibited increased risk of in-hospital mortality [odds ratio (OR) 1.40; 99% confidence interval (CI) 1.34–1.46] and 1 year mortality (HR 1.35; 99% CI 1.32–1.39), particularly among those with lung cancer. Patients with active and past cancer had a similar in-hospital mortality risk (OR 0.99; 99% CI 0.91–1.07) while 1 year mortality risk was higher among those with active cancer (HR 1.26; 99% CI 1.21–1.31).

Conclusions Cancer is a prevalent comorbidity in patients hospitalized with new onset AHF, and it is associated with a poorer prognosis. Mortality risk appears to vary based on cancer status and type.

Keywords acute heart failure; administrative database; cancer; in-hospital mortality; 1 year mortality

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Introduction

Advancements in cancer treatment have significantly decreased the morbidity and mortality associated with various neoplasms, leading to more than 80% of adult patients now surviving long-term.¹ Large observational studies have highlighted an elevated risk of cardiovascular diseases, particularly heart failure (HF), among cancer patients compared with control subjects.^{2,3} Recent findings indicate that cancer patients have a up to a 50% higher risk of incident HF compared with those without cancer.³ Shared risk factors between cancer and HF may contribute to this increased risk.^{4,5}

Additionally, cancer treatments, including chemotherapy, radiotherapy and newer targeted therapies, can induce cardiotoxicity.^{3–6} Some cancers also produce cardiotoxic substances that directly impact cardiac function, such as light-chain immunoglobulins in AL amyloidosis or vasoactive mediators in neuroendocrine tumours.⁷

There has been growing attention on the occurrence of cancer in individuals with existing HF^{8–10} and vice versa.^{3–7} Many studies have explored pharmacological strategies to prevent HF in cancer patients undergoing cardiotoxic treatments.^{11–14} However, few studies have investigated the mortality of cancer patients hospitalized for acute HF

(AHF),^{10,15–17} and none have specifically examined the prognostic impact of cancer, considering both past and active cancer status, and tumour site in a large cohort of patients hospitalized for their first episode (new onset) of AHF.

In this study, we utilized population-based administrative data from Lombardy, Italy's most populous region, to assess in-hospital mortality, 1 year mortality and 1 year re-hospitalization for AHF in cancer patients admitted for new-onset AHF. We compared these outcomes with those of new-onset AHF patients without cancer, while also analysing the impact of cancer status and site on these endpoints.

Methods

Data source

The present study used linkable administrative health databases of the Lombardy region in Italy, which include a population registry with demographic data of all residents and detailed information on hospital records and drug prescriptions. Data are available for about 10 million registered inhabitants of Lombardy from 2000 to 2019. Access to data is allowed within the agreement between the *Centro Cardiologico Monzino*, I.R.C.C.S, Milan, Italy, and Regional Health Ministry of Lombardy. Healthcare in Italy is publicly funded for all residents, irrespective of social class or employment, and everyone is assigned a personal identification number kept in the National Civil Registration System. All registered residents are assisted by general practitioners and are covered by the National Health System (NHS) with high levels of completeness regarding drug prescriptions, diagnosis and length of observation. The pharmacy prescription database contains the medication name and anatomic therapeutic chemical classification code (ATC) and date of dispensation of drugs reimbursed by the NHS. The hospital database contains information on date of admission, discharge, death, primary diagnosis and up to five co-existing clinical conditions and procedures performed during the hospitalization, regardless of the payer (NHS, insurance or out-of-pocket). The diagnoses, uniformly coded according to 9th International Code of Diseases (ICD-9-CM) and standardized for all Italian hospitals, are compiled by the hospital specialists directly in charge of the patients and are validated by hospitals against detailed clinical-instrumental data as they determine reimbursement from the NHS or any other payer. A unique identification code allows linkage of all databases. To ensure individual data protection, each identification code was automatically converted into an anonymous code before we received the dataset. In Italy, studies using retrospective anonymous data from administrative databases that do not involve direct access by inves-

tigators to identification data do not require ethics committee approval or notification nor patient informed consent signing.

Study population

Patients 18 years and older with a first hospitalization due to AHF (new onset AHF) from 1 January 2003 to 31 December 2018 were included. Only hospitalizations in which AHF-associated ICD-9 code was listed as a primary diagnosis were analysed. Secondary AHF diagnoses, unscheduled outpatient visit and short-term monitoring in the emergency ward were not considered in the analysis. Patients were grouped according to history of cancer, including those with past or active cancer. Cancer records were extracted using available administrative data [ICD-9 codes, pharmacy prescription database (prior outpatient chemotherapy services), and the NHS care co-payment exemption codes]. The definition of past or active cancer was made considering co-payment exemption codes. In Italy, at the diagnosis of neoplastic disease, patients are given a co-payment exemption code lasting 5 years. After this time span, the co-payment exemption code is not renewed if the patient is considered disease-free and does not require further diagnostic tests or treatments. Patients with active cancer were considered to be those with a still valid exemption code while with past cancer were those with an exemption code that was no longer renewed. Patients with cancer were also stratified according to quartiles of time elapsed from the first oncologic diagnosis to the hospitalization for AHF.

Patients with a record of any cancer were also classified by cancer site (five most common cancers: haematological, lung, gastrointestinal, prostate and breast).

Study variables

The history of comorbidities of interest were retrieved using hospital (including up to six co-existing diagnosis and procedures) and out-of-hospital medical records. Exposure to cardiovascular medications before and after index hospitalization were also retrieved.

Study outcomes

The primary endpoint of the study was in-hospital mortality. One year cumulative all-cause mortality and re-hospitalization for AHF were considered as secondary endpoints. Patients were followed-up from the index admission date until death, migration or up to the end of 1 year follow-up.

Statistical analysis

Baseline characteristics were evaluated using descriptive statistics. Categorical variables were described using frequencies and percentages and compared using χ^2 test. Continuous variables were described using mean and standard deviation and compared using Student's *t*-test.

The association between cancer history, as well as its status and site, and in-hospital mortality was analysed using logistic model, and the results were reported as odds ratios (ORs) and 99% confidence intervals (CIs). The association between cancer history, its status and site and cumulative 1 year mortality was investigated applying Cox regression to competing risk of in-hospital mortality, by the Fine–Gray method. The association between cancer history, its status and site, and 1 year first hospital readmission for AHF was evaluated by Cox regression. The results were shown as hazard ratio (HR) and 99% CI. Multivariable models were fitted by including all baseline variables found to be significantly different between the compared groups. Therapies before admission were considered as adjustment covariates for the primary endpoint while those after hospital discharge were considered for the secondary endpoints.

Differences in cumulative 1 year survival were plotted using Kaplan–Meier curves according to cancer history and its status.

A two-sided *P* value less than 0.01 was required for statistical significance. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

During the considered study period (2003–2018), 283 414 patients with a first hospitalization for AHF as primary diagnosis were identified. Of them, 55 145 (19%) patients had a history of cancer, including 33 040 (60%) with past cancer [median time from cancer diagnosis to index hospitalization for AHF 8.5 (5.7–11.9) years] and 22 105 (40%) with active cancer [median time from cancer diagnosis to index hospitalization for AHF 2.8 (1.1–5.7) years]. Baseline clinical characteristics of the population, cardiovascular medications taken before admission and after hospital discharge and ward of hospitalization in the overall cohort of AHF patients and in patients grouped according to history of cancer (yes vs. no) are shown in *Table 1*. Compared with non-cancer patients, age and comorbidity burden were higher in cancer patients who were also more likely to be on chronic cardiovascular medications at the time of index hospitalization. Moreover, they were more frequently admitted to the internal medicine ward and less treated with cardiovascular medications after hospital discharge compared with patients without cancer. Furthermore, in the overall study population, only 1.5% of patients underwent percutaneous coronary intervention during the in-

dex hospitalization (1.6% in patients without cancer and 1.2% in those with cancer).

Primary and secondary endpoints rates in patients grouped according to their history of cancer are shown in *Figure 1*. Patients with cancer had a significantly higher in-hospital and 1 year mortality and a similar first re-hospitalization rate. One year cumulative AHF-readmission rate in patients with and without cancer is reported in *Figure S1* (left panel).

The adjusted risk of in-hospital and 1 year mortality was significantly higher in patients with cancer while the adjusted risk of 1 year first re-hospitalization for AHF was similar in the two groups (*Figure 2*). The coefficients for the covariates used for adjustment are reported in *Table S1*.

Status and site of cancer

Clinical characteristics and study endpoints of patients with past or active cancer are reported in *Table 2*. The adjusted risk of in-hospital mortality was similar in patients with past and active cancer (OR 0.99; 99% CI 0.91–1.07) while 1 year mortality risk was higher in patients with active cancer (HR 1.26; 99% CI 1.21–1.31). The adjusted risk of 1 year first re-hospitalization for AHF was similar in patients with past and active cancer (HR 0.82; 99% CI 0.57–1.17). One year cumulative AHF-readmission rate in patients with past and active cancer is reported in *Figure S1* (right panel). The coefficients for the covariates used for adjustment are reported in *Table S2*.

The adjusted Kaplan–Meier curves for cumulative 1 year survival in patients with and without cancer and in those with past or active cancer are shown in *Figures S2* and *S3*, respectively.

Patients with cancer were also stratified according to quartiles of time elapsed from oncologic diagnosis to the index hospitalization for AHF. Notably, in-hospital and 1 year mortality rate and adjusted risk significantly increased as this time interval reduced while 1 year first AHF re-hospitalization rate did not change over the periods considered (*Figure 3*).

Rates and adjusted risks of in-hospital mortality, 1 year cumulative mortality and 1 year first re-hospitalization for AHF according to cancer site are shown in *Figure 4*. Patients with lung and haematological cancer showed the worse prognosis.

Discussion

This study utilized data from the Lombardy Health Databases in Italy to examine the in-hospital and 1 year outcomes of cancer patients admitted for new-onset AHF between 2003 and 2018. Over this 15 year span, nearly 20% of all AHF hospitalizations involved patients with a current or previous cancer diagnosis. Cancer patients were more likely to be ad-

Table 1 Clinical characteristics of patients hospitalized with acute heart failure from 2003 to 2018.

| Variables | Overall study population | Patients with cancer | Patients without cancer |
|---|--------------------------|----------------------|-------------------------|
| | (n = 283 414) | (n = 55 145) | (n = 228 269) |
| Age (years) | 79 ± 11 | 80 ± 9 | 79 ± 11 |
| Gender (males) | 135 008 (48%) | 30 690 (56%) | 104 318 (46%) |
| History of comorbidities, n (%) | | | |
| Hypertension | 117 921 (42%) | 24 678 (45%) | 93 243 (41%) |
| Diabetes mellitus | 78 121 (28%) | 15 591 (28%) | 62 530 (27%) |
| Chronic IHD | 55 510 (20%) | 11 566 (21%) | 43 944 (19%) |
| Atrial fibrillation | 57 257 (20%) | 12 031 (22%) | 45 226 (20%) |
| Chronic renal disease | 28 920 (10%) | 68 883 (12%) | 22 037 (10%) |
| COPD | 37 161 (13%) | 8708 (16%) | 28 453 (12%) |
| Number of comorbidities, n (%) | | | |
| 0 | 89 290 (32%) | 14 987 (27%) | 74 303 (33%) |
| 1 | 94 706 (33%) | 19 038 (35%) | 75 668 (33%) |
| 2 | 64 133 (23%) | 13 507 (24%) | 50 626 (22%) |
| 3 | 27 242 (9.61%) | 5934 (10.76%) | 21 308 (9%) |
| >3 | 8043 (2.84%) | 1679 (3.04%) | 6364 (3%) |
| Medications of interest (before index AHF hospitalization), n (%) | | | |
| ACE-I/ARBs | 183 360 (65%) | 36 194 (66%) | 147 166 (64%) |
| Beta-blockers | 103 564 (37%) | 22 218 (40%) | 81 346 (36%) |
| Diuretics | 149 366 (53%) | 30 771 (56%) | 118 595 (53%) |
| Ca-antagonists | 94 521 (33%) | 19 545 (35%) | 74 976 (33%) |
| Lipid-lowering drugs | 79 359 (28%) | 16 134 (29%) | 63 225 (28%) |
| Antiplatelet drugs | 129 640 (46%) | 26 082 (47%) | 103 558 (45%) |
| Oral anticoagulant drugs | 57 274 (20%) | 11 771 (21%) | 45 503 (20%) |
| Medications of interest (after hospital discharge), n (%) | | | |
| ACE-I/ARBs | 156 825 (55%) | 25 947 (47%) | 130 878 (57%) |
| Beta-blockers | 121 636 (43%) | 22 525 (41%) | 99 111 (43%) |
| Diuretics | 196 155 (69%) | 36 731 (67%) | 159 424 (70%) |
| Ca-antagonists | 53 736 (19%) | 9663 (18%) | 44 073 (19%) |
| Lipid-lowering drugs | 72 240 (25%) | 12 402 (23%) | 59 838 (26%) |
| Antiplatelet drugs | 109 281 (38%) | 18 749 (34%) | 90 532 (40%) |
| Oral anticoagulant drugs | 71 042 (25%) | 12 175 (22%) | 58 867 (26%) |
| Ward of hospitalization, n (%) | | | |
| Cardiology | 70 254 (25%) | 11 758 (21%) | 58 496 (26%) |
| Intensive care unit | 21 146 (7%) | 3290 (6%) | 17 856 (8%) |
| Internal medicine | 192 014 (68%) | 40 097 (73%) | 151 917 (67%) |

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease.

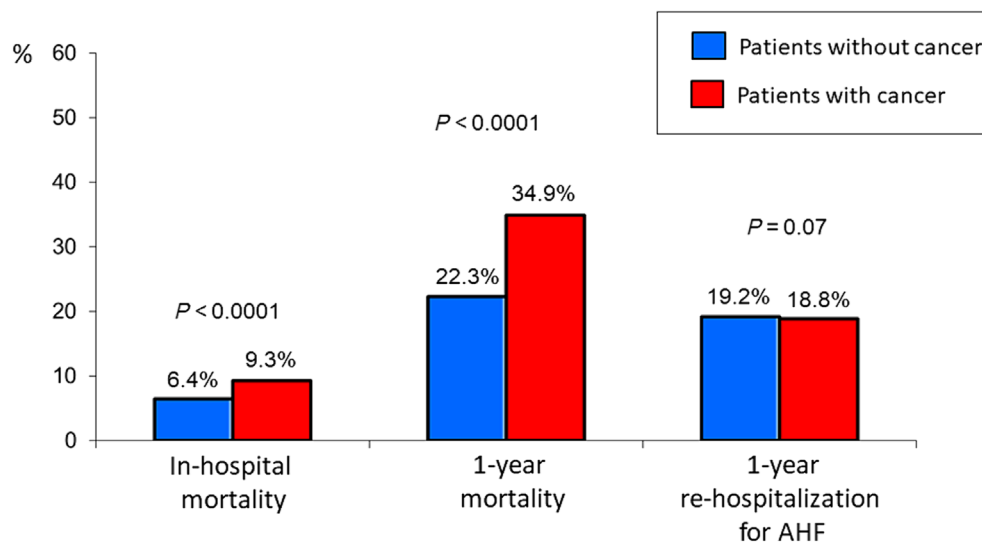
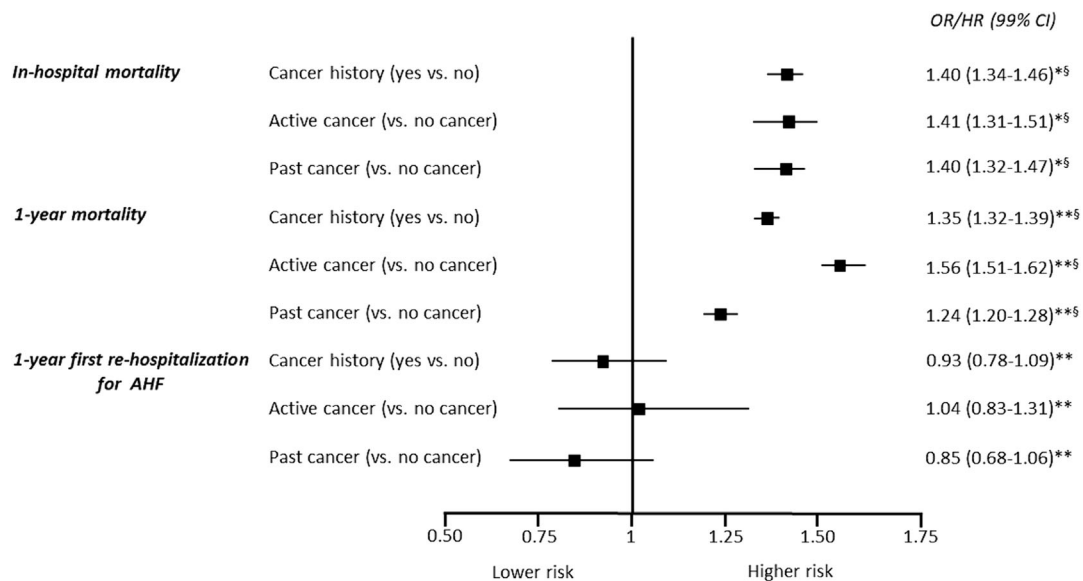
Figure 1 Primary and secondary endpoint rates in patients hospitalized with new-onset acute heart failure (AHF), grouped according to cancer history.

Figure 2 Adjusted risk of the primary and secondary endpoints associated with cancer history and status in patients hospitalized with new-onset acute heart failure (AHF). Patients without cancer have been considered as a reference. CI = confidence interval; HR = hazard ratio (calculated by competing risks); OR = Odds ratio. *data presented as OR; **data presented as HR. [§]*P* value <0.01.



mitted to internal medicine wards, received cardiovascular medications less frequently upon hospital discharge and experienced a 40% higher in-hospital mortality rate and a 35% higher 1 year mortality rate compared with patients without a history of cancer.

In recent years, there has been a growing interest in understanding the connection between cancer and HF. Emerging evidence highlights several shared risk factors between these two conditions, including age, obesity, sedentary lifestyle, diabetes, smoking and alcohol consumption.⁴⁻⁸ Moreover, advancements in anticancer therapies have led to a rising number of cancer survivors.¹⁸ However, this population exhibits a heightened cardiovascular morbidity and mortality compared with the general population.²⁻⁹ Their increased cardiovascular risk stems from a combination of factors, including cancer-related pathophysiological processes, comorbidities and the cardiotoxic effects of anticancer treatments.⁸ Notably, AHF is the most prevalent cardiovascular reason for hospital admissions among patients with cancer, with approximately 13% of cancer patients requiring hospitalization for AHF, a figure that has been progressively increasing over time.¹⁶ Concurrently, the prevalence of a history of cancer among patients hospitalized with AHF ranges between 12% and 20%, with the present large-scale observational study reporting a rate of 19%.

There is limited evidence regarding the outcomes of cancer patients hospitalized with new-onset AHF, primarily because they are often excluded or underrepresented in clinical trials. Consequently, much of the available evidence stems from registries and administrative databases, where patients with both past and active cancer are frequently

grouped together.^{10,15-17,19} For instance, a retrospective population-based cohort study conducted in England from 2012 to 2018, involving 12 867 cancer patients hospitalized for AHF, reported a comparable in-hospital mortality rate between patients with and without cancer (5.9% vs. 5.0%). However, the median survival after hospital discharge was notably lower in cancer patients (1.6 vs. 2.6 years).¹⁵ Notably, this study considered both past and active cancer patients as part of the cancer cohort, regardless of the time of cancer diagnosis preceding hospitalization. Similarly, Kobo et al.¹⁶ analysed data from the Nationwide Inpatient Sample in the United States spanning from 2004 to 2017. They found an average in-hospital mortality rate of 5.7% among patients with any record of cancer and hospitalized with AHF. However, they did not differentiate between patients with past and active cancer. Additionally, their analysis included all hospitalizations for AHF, including both first episodes and recurrences, without directly comparing in-hospital mortality rates between patients with and without cancer.¹⁶

To the best of our knowledge, our study represents the first endeavour to specifically investigate the prognostic implications of cancer history, status (active vs. past) and site in a large population of patients hospitalized with their first episode of AHF. Consistent with prior findings, cancer patients exhibited a greater prevalence of comorbidities and were less frequently admitted to cardiology wards.¹⁵⁻¹⁷ Furthermore, they were less likely to receive guideline-recommended therapies upon discharge from the hospital. The in-hospital mortality rate was 1.4 times higher and the 1 year mortality rate was 1.6 times higher in patients with a history of cancer com-

Table 2 Clinical characteristics of patients with past and active cancer hospitalized with acute heart failure from 2003 to 2018.

| Variables | Patients with past cancer | Patients with active cancer |
|---|---------------------------|-----------------------------|
| | (n = 33 040) | (n = 22 105) |
| Age (years) | 82 ± 9 | 78 ± 9 |
| Gender (males) | 17 723 (54%) | 12 967 (59%) |
| History of comorbidities, n (%) | | |
| Hypertension | 14 608 (44%) | 10 070 (46%) |
| Diabetes mellitus | 9440 (29%) | 6151 (28%) |
| Chronic IHD | 6703 (20%) | 4863 (22%) |
| Atrial fibrillation | 7120 (22%) | 4911 (22%) |
| Chronic renal disease | 4304 (13%) | 2579 (12%) |
| COPD | 5334 (16%) | 3374 (15%) |
| Number of comorbidities n (%) | | |
| 0 | 9092 (28%) | 5895 (27%) |
| 1 | 11 392 (34%) | 7646 (35%) |
| 2 | 8020 (24%) | 5487 (25%) |
| 3 | 3506 (11%) | 2428 (11%) |
| >3 | 1030 (3%) | 649 (3%) |
| Medications of interest (before index AHF hospitalization), n (%) | | |
| ACE-I/ARBs | 21 572 (65%) | 14 622 (66%) |
| Beta-blockers | 12 730 (39%) | 9 488 (43%) |
| Diuretics | 18 832 (57%) | 11 939 (54%) |
| Ca-antagonists | 11 992 (36%) | 7553 (34%) |
| Lipid-lowering drugs | 9329 (28%) | 6805 (31%) |
| Antiplatelet drugs | 15 998 (48%) | 10 084 (46%) |
| Oral anticoagulant drugs | 6929 (21%) | 4842 (22%) |
| Medications of interest (after hospital discharge), n (%) | | |
| ACE-I/ARBs | 15 122 (46%) | 10 821 (49%) |
| Beta-blockers | 12 694 (38%) | 9929 (44%) |
| Diuretics | 21 308 (64%) | 15 420 (70%) |
| Ca-antagonists | 5825 (18%) | 3838 (17%) |
| Lipid-lowering drugs | 7099 (21%) | 5303 (24%) |
| Antiplatelet drugs | 11 347 (34%) | 7401 (35%) |
| Oral anticoagulant drugs | 6983 (21%) | 5191 (24%) |
| Ward of hospitalization, n (%) | | |
| Cardiology | 6722 (20%) | 5036 (23%) |
| Intensive care unit | 1910 (6%) | 1380 (6%) |
| Internal medicine | 24 408 (74%) | 15 689 (71%) |
| Study endpoints, n (%) | | |
| In-hospital mortality | 3368 (10%) | 1788 (8%) |
| 1 year mortality | 10 225 (34%) | 7233 (36%) |
| 1 year re-hospitalization for AHF | 5660 (19%) | 3745 (18%) |

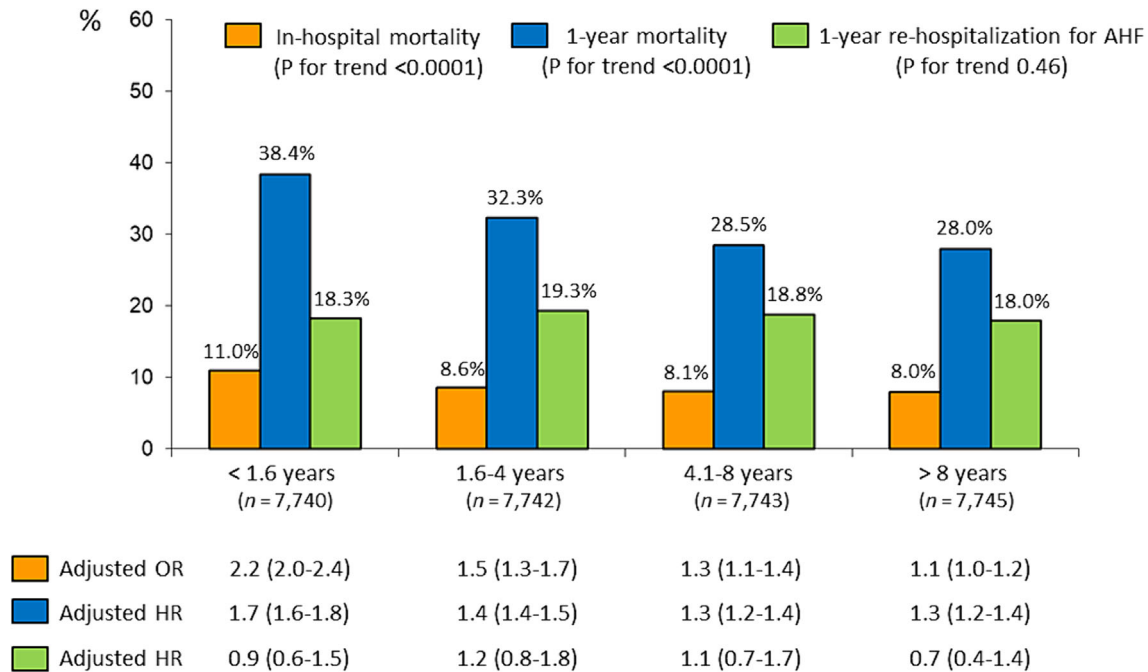
Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blockers; COPD, chronic obstructive pulmonary disease; IHD, ischaemic heart disease.

pared with those without. Similarly, after adjusting for relevant factors, the risk of mortality remained significantly elevated in cancer patients. Importantly, even after accounting for comorbidities and cardiovascular therapy following hospitalization, the risk of 1 year mortality remained higher in cancer patients. This suggests that beyond the burden of comorbidities and underutilization of pharmacological treatments, the presence of cancer itself and its associated complications contribute to the poorer prognosis observed in patients with cancer experiencing AHF. Furthermore, cancer is linked to chronic inflammation, which can also contribute to HF by inducing myocardial structural alterations, impairing cardiac function and promoting adverse cardiac remodelling.²⁰

Our study's strength lies in its focused examination of cancer status and site. We separately assessed outcomes for patients with past or active cancer, revealing distinct overall

prognoses based on cancer status. Specifically, patients with past and active cancer demonstrated similar in-hospital mortality risks. However, those with active cancer exhibited a heightened 1 year mortality risk compared with those with past cancer. Recognizing that the 5 year period used to differentiate past and active cancer may lead to some degree of patient misclassification, we delved further into the prognostic impact of the time interval between cancer diagnosis and AHF hospitalization. We observed an inverse relationship between this time interval and mortality. As the time from cancer diagnosis to index AHF hospitalization increased, the elevated risk of in-hospital death among cancer patients gradually diminished. Notably, this risk equalled that of patients without cancer when the time since oncologic diagnosis exceeded 8 years. However, while 1 year mortality progressively decreased with an increasing time interval between cancer diagnosis and index AHF hospitalization, it re-

Figure 3 In-hospital mortality, 1 year mortality, and 1 year first re-hospitalization for acute heart failure (AHF) rate and adjusted risk associated with quartiles of time from the initial diagnosis of cancer to index hospitalization in the overall study population. Patients without cancer have been considered as a reference. HR = hazard ratio; OR = Odds ratio. P for trend <0.001 for both endpoints. Data presented as OR/HR and 99% confidence interval.



mained significantly elevated beyond this 8 year threshold. This suggests that the proximity of the patient to a cancer diagnosis greatly influences mortality risk in AHF. The underlying reasons for this mortality risk pattern cannot be definitively determined from our data and necessitate further investigation. It is plausible that factors such as the toxicity of anti-cancer therapies and the residual frailty of patients recovering from recent illness may play pivotal roles in this phenomenon. It is important to note that while our analysis reveals a temporal relationship between cancer duration and decreased mortality rates following AHF hospitalization, it does not establish a causal link and a cautious interpretation of the results is necessary. We therefore emphasize the need for future research aimed at addressing data limitations, minimizing misclassification bias and unravelling the causal pathways linking cancer duration to cardiovascular outcomes following AHF hospitalization. By undertaking such efforts, we can deepen our understanding of this complex relationship and develop more precise interventions to improve outcomes for this vulnerable patient population.

Additionally, our study revealed that patients with lung cancer exhibited the highest mortality risk within our cohort. This finding aligns with recent observations and is not unexpected.¹⁵ Patients with lung cancer commonly present with a high prevalence of cardiovascular risk factors and comorbidities, notably smoking and coronary artery disease. Furthermore, they often have diminished pulmonary func-

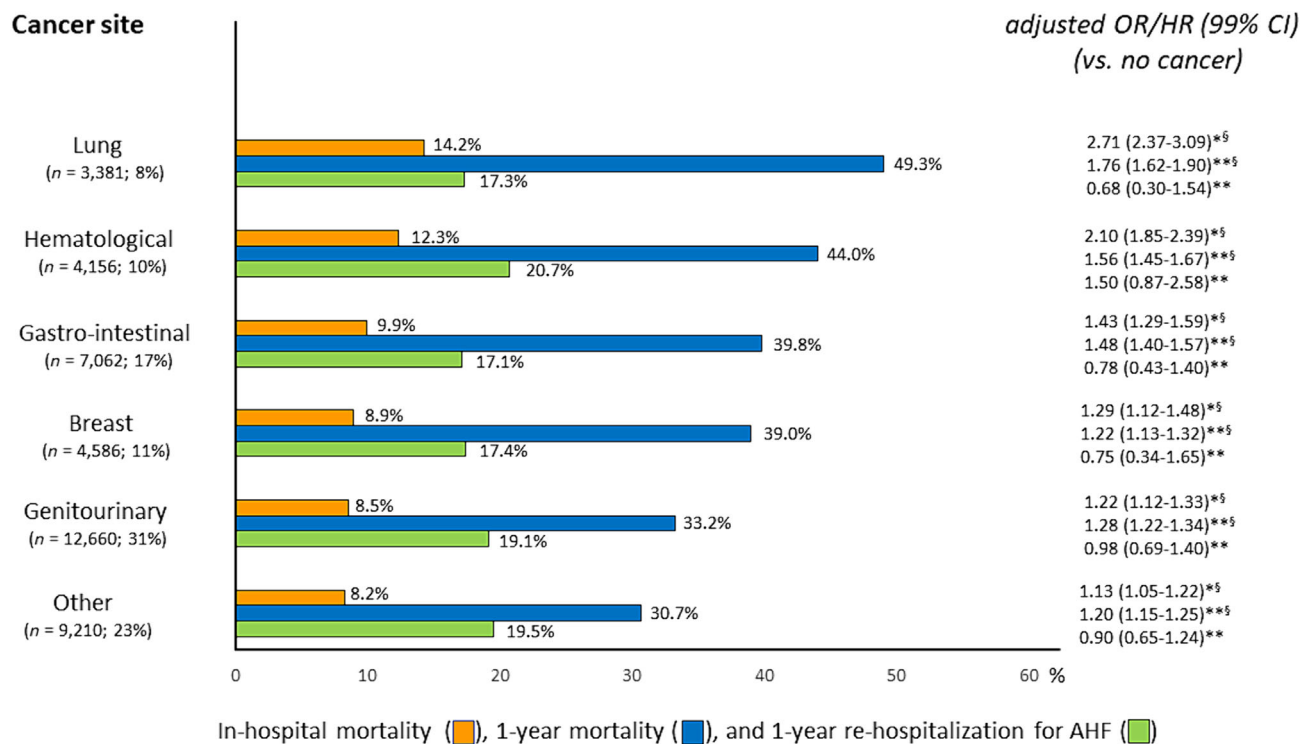
tional reserve.²¹ These factors collectively contribute to the heightened mortality risk observed in this patient population.

Our study unveils a notable variation in mortality risk among cancer patients, directly linked to disease status and site. This finding may hold promise for refining early risk stratification strategies for cancer patients hospitalized with AHF and enhancing both in-hospital therapeutic interventions and post-discharge management for those deemed at higher risk. Consequently, it is imperative for physicians caring for AHF patients to meticulously collect information on cancer history, including its status (active or past) and site. Furthermore, current prognostic risk scores utilized in HF patients typically do not incorporate cancer as a contributing factor.^{22,23} Given its significant prognostic impact, it is important that future studies explore whether incorporating this variable, along with its specific characteristics, can enhance mortality discrimination among AHF patients. Such investigations hold the potential to refine risk assessment tools and ultimately improve patient outcomes in the context of HF management.

Study limitations

Several limitations of the study should be considered. While administrative databases offer a reliable tool of delineating outcomes within large cohorts, reflecting real-world clinical

Figure 4 In-hospital mortality, 1 year mortality, and 1 year first re-hospitalization for acute heart failure (AHF) rate and adjusted risk associated with cancer site. Data on cancer site were available on 41,055 patients. Patients without cancer have been considered as a reference. CI = confidence interval; HR = hazard ratio; OR = Odds ratio. *data presented as OR; **data presented as HR. [§]P value <0.01.



care scenarios due to their standardized data collection and cost-effectiveness, they are susceptible to systematic biases contingent upon coding accuracy. Specifically, our analyses relied on precise coding of AHF and other pertinent conditions, with potential biases stemming from underreporting, alterations in diagnosis or coding practices over time, or challenges in validating AHF, especially pertinent in patients with lung cancer who may exhibit similar symptoms. However, the endpoints examined in our study are less likely to be affected by coding errors. Additionally, certain clinical variables and laboratory tests crucial for AHF prognosis assessment, such as left ventricular ejection fraction, renal function, natriuretic peptide levels and in-hospital pharmacologic therapy, were not accessible for analysis. Although our study endeavoured to mitigate the influence of numerous confounding variables, we recognize the presence of unmeasured or unaddressed factors, including socioeconomic status, lifestyle choices or access to healthcare resources. These factors may have impacted our findings and constrained their applicability to broader populations.

Similarly, owing to the considered study timeframe, we were unable to explore the influence of recent HF medications, such as angiotensin receptor–neprilysin inhibitors and sodium-glucose transporter 2 inhibitors, on 1 year outcomes. Consequently, the mortality risk associated with cancer in

AHF may have evolved with the introduction of these newer HF medications. Additionally, concerning cancer patients, pivotal variables including cancer stage, timing and modality of cancer treatment and functional capacity were not captured. Furthermore, the aetiology of AHF was not documented, and information regarding the cause of 1 year death was unavailable. Lastly, patients with a prior history of cancer may have potentially gained a ‘survival benefit’ by surviving until the occurrence of index AHF hospitalization, in contrast to individuals with active cancer or without cancer history. This circumstance might have, to some extent, influenced the interpretation of our findings, potentially artificially skewing survival estimates among patients previously diagnosed with cancer.

In conclusion, our study shows that cancer is a prevalent comorbidity among patients admitted with new-onset AHF, correlating with poorer in-hospital and 1 year prognosis. Furthermore, the mortality risk among AHF patients with cancer appears to be linked to the status and location of their oncological condition. Despite this heightened risk, substantial gaps still persist in real-world healthcare provision, as indicated by lower admission rates to cardiology departments and reduced prescription rates for cardiovascular medications following hospitalization for AHF among patients with cancer.

Acknowledgements

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Conflict of interest

None declared.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. The coefficients for the covariates used for risk adjustment of in-hospital mortality, 1-year mortality, and 1-year first re-hospitalization for acute heart failure (AHF) in patients with cancer versus those without cancer.

Table S2. The coefficients for the covariates used for risk adjustment of in-hospital mortality, 1-year mortality, and 1-year first re-hospitalization for acute heart failure (AHF) in patients with past cancer versus active cancer.

Figure S1. Mean cumulative function for accurate heart failure re-hospitalization in patients with and without cancer (left panel) and in those with active or past cancer (right panel).

Figure S2. Adjusted Kaplan–Meier curves for cumulative 1-year survival in patients with or without cancer.

Figure S3. Adjusted Kaplan–Meier curves for cumulative 1-year survival in patients with past or active cancer.

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