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Original Article

Temporal trends, ethnic determinants, and short-term and long-term risk of cardiac death in cancer patients: a cohort study

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ABSTRACT

Background: We evaluated the risk of cardiac death in patients with prior cancer diagnoses and compared risk by cancer type and ethnicity in a large US population.
Method: Utilizing the Surveillance, Epidemiology, and End Results database, data on patients with a cancer diagnosis between 2000 and 2014 were obtained. We calculated the standardized mortality ratio (SMR) of cardiac death after a cancer diagnosis and the excess risk per 10,000 person-years. We stratified the analysis according to the time interval between cancer and cardiac events, cancer site, cancer stage, and race.
Results: A total of 4,671,989 patients with a cancer diagnosis were included, of which 163,255 died due to cardiac causes within 10 years of diagnosis. We found a significantly higher rate of cardiac death for cancer patients [SMR=1.16, 95% confidence interval (CI) 1.15−1.16] compared to the general population. When observed for each cancer site, the highest SMR was after a diagnosis of hepatocellular carcinoma (SMR=2.58, 95% CI 2.45−2.72), pancreatic cancer (SMR=2.36, 95% CI 2.25−2.47), and lung cancer (SMR=2.30, 95% CI 2.27−2.34). Patients with metastatic disease had a higher rate of cardiac death (SMR=2.16, 95% CI 2.13−2.19). When stratified by ethnicity, SMR for cardiac death was 1.76, 2.28, 3.68, 2.65, and 1.84 for whites, blacks, American Indians/Alaska Natives, Asians/Pacific Islanders, and Hispanics, respectively.
Conclusions: Cancer patients are more vulnerable to cardiac death than the general population, especially those with nonwhite ethnicity; liver, lung, and pancreatic cancers; and history of metastasis. Healthcare providers should be aware of this risk and pay particular attention to the highest-risk groups.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality worldwide [1]. Cancer is ranked second with an incidence of 1,735,350 cases and 609,640 attributable deaths in the United States alone in 2018 [2]. Interestingly, both of these causes of death have numerous interactions. Several risk factors for CVD, such as smoking and obesity, significantly increase the risk of cancer as well [3,4]. Moreover, many modern cancer treatments have detrimental effects on cardiac function. For example, radiotherapy for chest tumors such as lung cancer, breast cancer, and Hodgkin's lymphoma can result in valvular insufficiency, restrictive cardiomyopathy, and radiation-induced constrictive pericarditis [5,6]. Similarly, chemotherapy can cause cardiac complications, such as cardiomyopathy (with adriamycin/doxorubicin and trastuzumab), arrhythmias (with paclitaxel), and coronary vasospasm (with 5-fluorouracil) [7,8]. The sequelae of such treatments may persist for months or even years after cancer remission [9]. Accordingly, oncologists now often screen and monitor chemotherapy patients for systolic dysfunction [10].

Cancer-related cardiac complications and mortality have been studied for decades; however, most studies have been limited in size. Also, it appears that cardiac risk varies widely depending on cancer type, stage, and underlying patient characteristics. In this study, we used data from a large US population in the Surveillance, Epidemiology, and End Results (SEER) database to assess future cardiac mortality risk after a cancer diagnosis and to better understand which cancers and which patient subgroups are most vulnerable.

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2. Methods

2.1. Data source

Access to the SEER program was granted by the National Cancer Institute (NCI). We used the SEER*stat software (version 8.3.4) to access the SEER18 registries (2016 submission) which cover approximately 27.8% of the U.S. population (based on the 2010 census) from 2000 to 2014 in 14 states to represent cancer incidence for the entire United States as intended by the NCI. Mortality data of the general population used in the study were collected by the National Vital Statistics System/National Center for Health Statistics between the years 1969 and 2014 and represent the same population of the SEER 18 registries. It was accessed with SEER*Stat software [11,12]. Due to the anonymized nature of patient information provided in the SEER program, institutional review board approval was waived for the current study.

2.2. Study design and population

The study was a retrospective cohort study conducted according to the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology Statement checklist [13]. We included all cancer patients diagnosed with histological confirmation between 2000 and 2014 and followed them for death due to cardiac causes within 10 years of cancer diagnosis (using the SEER Cause of Death Recode 1969+ variable). In patients in whom the event of interest occurred, we assessed the following variables: age at the time of cancer diagnosis, sex, race, location (by state), marital status, cancer site, and cancer stage. Patients' races were first grouped into Hispanics and non-Hispanics. The non-Hispanics group was further subdivided into white, black, American Indian/Alaska Native, and Asian or Pacific Islander, e.g., patients in the whites group are not Hispanics, and this applies to other groups.

Patients who died of cardiac causes were determined using "SEER Cause of Death Recode: Disease of Heart." The "SEER Cause of Death Recode" has been based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)—WHO since 1999. The SEER database lists one cause of death per patient. The classification "diseases of heart" includes ischemic heart diseases, hypertensive heart disease, rheumatic heart diseases, pulmonary heart disease, and other forms of heart disease. It does not include cerebrovascular diseases; diseases of arteries, arterioles, and capillaries; and diseases of veins, lymphatic vessels, and lymph nodes [14–16]. The SEER and the National Vital Statistics System/National Center for Health Statistics databases use the ICD-10—WHO to define diseases of heart.

2.3. Outcomes

We calculated the standardized mortality ratios (SMRs) of cardiac death following a cancer diagnosis. SMRs were defined as the observed over expected ratios were "observed" represented the number of cases that died due to cardiac causes and "expected" represented the number of cases expected to die due to a cardiac cause in a demographically similar population within the same time period (using data from the National Center for Health Statistics as stated in the "data source" section). Expected event numbers were adjusted for age, sex, and race. The SMR represented the change in cardiac death risk following a cancer diagnosis when compared to the general US population. We assessed the SMRs of cardiac death within 1 year and 10 years of cancer diagnosis.

2.4. Statistical analysis

Data were summarized as mean and standard deviation for continuous variables and number and percentage for categorical variables. We used the Multiple Primary Standardized Mortality Ratios (MP-SMR) session of the SEER*stat software (version 8.3.4) to calculate the SMR with 95% confidence interval (CI). A significant increase in risk was defined as the number of observed cardiac death cases being greater than the number of expected cardiac death cases in the general population with a P value <.05. All statistical tests were two-sided.

3. Results

3.1. Baseline characteristics

We reviewed 4,671,989 cancer patients, of which 2,022,536 died of any cause and 163,255 died of cardiac causes within 10 years of cancer diagnosis. Median time to cardiac death was 36 months (IQR 10–76 months). The mean age of cancer diagnosis was 75.5±11.1 years. Most patients were males (59.8%), non-Hispanic whites (77.8%), aged 65–84 years (62.3%), and married (45.8%) when they were diagnosed with cancer. Most patients had only one malignancy, while 8.9% had multiple malignancies. A total of 24,617 (15.1%) patients received chemotherapy, and 34,342 (21.0%) received radiotherapy. Table 1 summarizes the baseline characteristics of the included patients.

3.2. Risk of cardiac death within 1 year following cancer diagnosis

We found the risk of cardiac death to be significantly higher among cancer patients within 1 year of their cancer diagnosis when

Table 1
Baseline characteristics of cancer patients who died due to cardiac causes within 10 years of cancer diagnosis

Baseline characteristics	Cases, *N* (%)
Overall	163,255 (100)
Age	
<18	35 (<0.1)
18–40	721 (0.4)
41–64	25,838 (15.8)
65–84	101,712 (62.3)
>84	34,949 (21.4)
Sequence	
Only one malignancy	148,722 (91.1)
Multiple malignancies	14,533 (8.9)
Cancer stage	
Localized/regional	114,913 (70.4)
Metastatic	24,277 (14.9)
Sex	
Male	97,573 (59.8)
Female	65,682 (40.2)
Ethnicity	
Non-Hispanic white	127,088 (77.8)
Non-Hispanic black	19,123 (11.7)
Non-Hispanic Asian or Pacific Islander	6598 (4.0)
Non-Hispanic American Indian/Alaska Native	476 (0.3)
Hispanic (all races)	9970 (6.1)
Marital status	
Married	74,852 (45.8)
Single	17,821 (10.9)
Widowed	43,541 (26.7)
Divorced	13,033 (8.0)
Separated	1273 (0.8)
Unknown	12,735 (7.8)
State	
California	61,057 (37.4)
Connecticut	8468 (5.2)
Michigan	11,952 (7.3)
Hawaii	2575 (1.6)
Iowa	7397 (4.5)
New Mexico	2688 (1.6)
Washington	7226 (4.4)
Utah	2673 (1.6)
Georgia	16,077 (9.8)
Kentucky	10,868 (6.7)
Louisiana	10,408 (6.4)
New Jersey	21,866 (13.4)

compared to the general population; SMR was 1.86 (95% CI 1.84–1.87), and the excess risk was 59.58 per 10,000 person-years. The increase in risk was higher in cancer cases with distant metastasis; SMR was 3.41 (95% CI 3.35–3.46), and excess risk was 169.02 per 10,000 person-years. Localized/regional cases showed a less marked but still significant increase in SMR (O/E 1.28, 95% CI 1.27–1.30) with an excess risk of 19.08 per 10,000 person-years.

The most common and morbid cancer sites in the United States were examined, and therefore, we stratified the SMR for cardiac death for each of these sites. We found the highest increases in cardiac death risk to be following hepatocellular carcinoma, lung cancer, pancreatic cancer, leukemias, oropharyngeal tumors, colorectal cancers, renal cancers, non-Hodgkin's lymphoma (NHL), bladder cancers, and uterine corpus cancers (SMR=4.03, 3.42, 3.10, 2.66, 2.19, 2.10, 2.10, 1.99, 1.59, and 1.57, respectively) (Table 2, Fig. 1). Patients with melanoma, breast cancer, and prostate cancer appeared to have less than expected rates of cardiac death, SMR<1.0. (Table 2, Fig. 1).

3.3. Risk of cardiac death within 10 years following cancer diagnosis

Risk of cardiac death remained significantly higher than the general population within 10 years following a cancer diagnosis; SMR was 1.16, 95% CI 1.15–1.16, and the excess risk was 11.66 per 10,000 person-years. This increase in risk was more pronounced in patients with metastatic disease; SMR 2.16, 95% CI 2.13–2.19, and excess risk was 77.02 per 10,000 person-years. However, patients with localized/regional cancers no longer showed a significant increase in long-term risk of cardiac death after they survived the first

Table 2
Risk of cardiac death among cancer patients (stratified by age, cancer site, and ethnicity)

	Within 10 years				Within 1 year			
	Cancer patients	Cardiac deaths	SMR (95% CI)	Excess risk[a]	Cancer patients	Cardiac deaths	SMR (95% CI)	Excess risk[a]
Age group								
<18	50,633	35	9.07* (6.32–12.62)	1.15	50,633	15	21.89* (12.25–36.11)	3.10
18–40	294,778	721	2.31* (2.14–2.48)	2.61	294,778	187	5.31* (4.58–6.13)	5.67
41–64	2,002,370	25,838	1.32* (1.30–1.34)	6.78	2,002,370	7446	2.53* (2.48–2.59)	26.11
65–84	2,026,009	101,712	1.07* (1.06–1.07)	8.46	2,026,009	28,427	1.91* (1.89–1.93)	85.46
>84	298,199	34,949	1.36* (1.34–1.37)	166.48	298,199	13,126	1.51* (1.49–1.54)	245.86
Cancer site								
Breast cancer	705,837	18,827	0.91* (0.90–0.93)	−4.61	705,837	2859	0.91* (0.88–0.95)	−4.23
Prostate cancer	736,411	32,889	0.76* (0.75–0.77)	−24.29	736,411	4390	0.73* (0.71–0.75)	−23.20
Lung cancer	572,446	17,265	2.30* (2.27–2.34)	107.82	572,446	9575	3.42* (3.36–3.49)	199.02
Colorectal cancer	453,774	23,435	1.25* (1.23–1.27)	25.27	453,774	7430	2.10* (2.05–2.15)	102.81
Urinary bladder	185,026	12,701	1.22* (1.20–1.24)	27.86	185,026	3115	1.59* (1.53–1.65)	70.91
Uterine corpus	140,728	3567	1.08* (1.04–1.11)	3.65	140,728	844	1.57* (1.46–1.67)	24.03
Melanoma	193,228	5467	0.88* (0.86–0.90)	−7.27	193,228	933	0.87* (0.82–0.93)	−7.85
Thyroid cancer	126,302	1090	0.77* (0.73–0.82)	−4.77	126,302	215	1.04 (0.90–1.19)	0.67
Kidney and renal pelvis cancers	143,648	5357	1.37* (1.34–1.41)	24.28	143,648	1524	2.10* (2.00–2.21)	66.27
NHL	195,361	7401	1.25* (1.22–1.28)	18.07	195,361	2291	1.99* (1.91–2.07)	71.08
Oral cavity and pharynx cancers	110,182	3959	1.54* (1.49–1.59)	31.77	110,182	1225	2.19* (2.07–2.32)	70.13
Pancreatic cancer	119,194	1911	2.36* (2.25–2.47)	103.58	119,194	1458	3.10* (2.94–3.26)	173.68
Leukemias	130,238	4964	1.56* (1.52–1.61)	38.18	130,238	1904	2.66* (2.54–2.78)	119.14
Liver cancers	74,100	1359	2.58* (2.45–2.72)	76.65	74,100	882	4.03* (3.77–4.30)	161.45
Ethnicity								
Non-Hispanic white	3,397,048	127,088	1.13* (1.12–1.13)	10.09	3,397,048	36,886	1.76* (1.74–1.78)	57.27
Non-Hispanic black	501,039	19,123	1.36* (1.35–1.38)	27.45	501,039	6458	2.28* (2.22–2.33)	90.73
American Indian/Alaska Native	19,040	476	2.33* (2.13–2.55)	39.05	19,040	156	3.68* (3.13–4.31)	75.48
Asian/Pacific Islander	296,019	6598	1.44* (1.41–1.48)	17.57	296,019	2351	2.65* (2.54–2.76)	61.08
Hispanic	458,843	9970	1.05* (1.03–1.07)	2.65	458,843	3350	1.84* (1.78–1.91)	41.60

[a] Excess risk per 10,000 person-years.
* *P* value <.05.

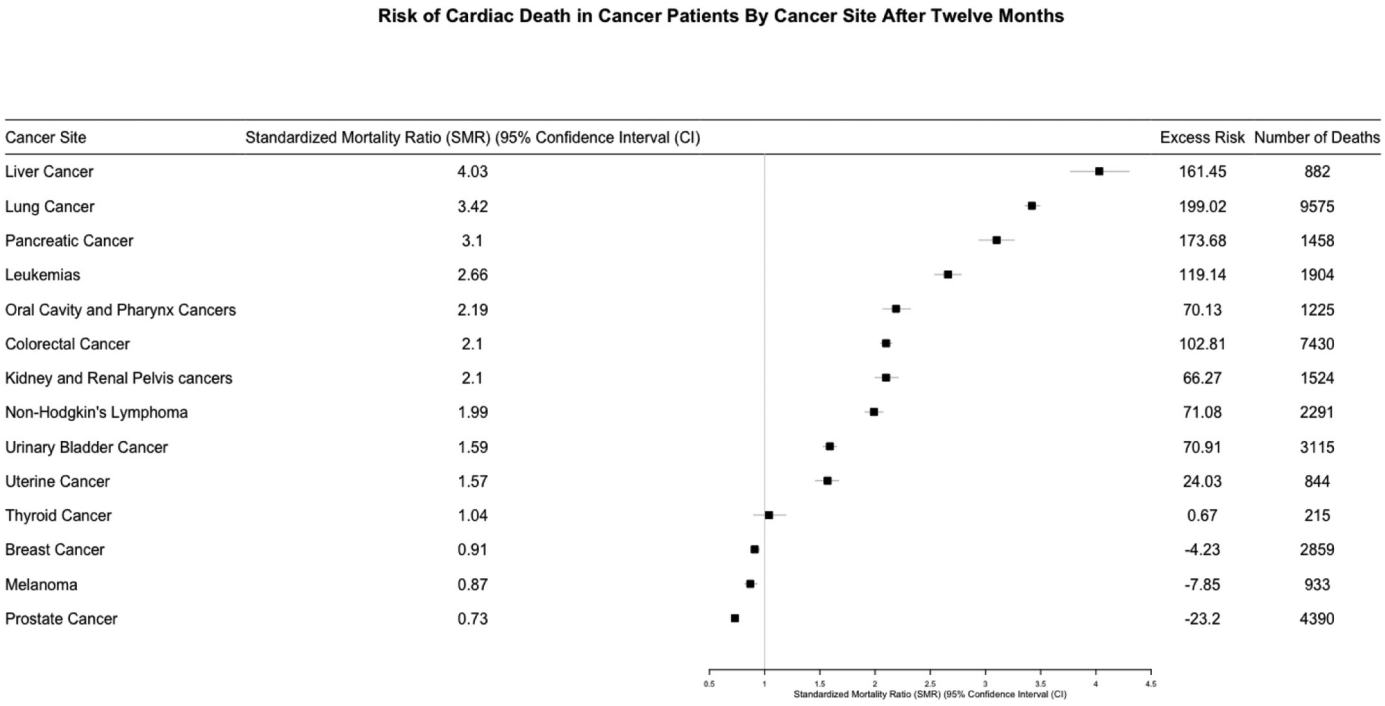

Fig. 1. Risk of cardiac death in cancer patients by cancer site after 12 months. Legend: SMR of cardiac death in the 12 months following a cancer diagnosis according to cancer site.

year of follow-up; SMR was 0.99, 95% CI 0.99–1.00, for cardiac death within 10 years of cancer diagnosis.

When stratifying by cancer site, the highest increase in cardiac death risk was following hepatocellular carcinoma, pancreatic cancers, lung cancers, leukemias, oropharyngeal tumors, renal cancers, non-Hodgkin's lymphoma, colorectal cancers, bladder cancers, and uterine corpus cancers (SMR=2.58, 2.36, 2.30, 1.56, 1.54, 1.37, 1.25, 1.25, 1.22, and 1.08, respectively) (Table 2, and Fig. 2). As for melanoma, breast cancer, and prostate cancer, cardiac death rates within 10 years of diagnosis were again lower than expected (Table 2 and Fig. 2).

3.4. Ethnic and racial disparities in the risk of cardiac death following cancer diagnosis

When cardiac death risk was calculated according to ethnicities, all groups showed a statistically significantly higher risk of cardiac death within 1 year following cancer diagnosis compared to the general population even after adjustment for other patient characteristics (SMR=1.76 [1.74–1.78], 2.28 [2.22–2.33], 3.68 [3.13–4.31], 2.65 [2.54–2.76], and 1.84 [1.78–1.91] for non-Hispanic whites, blacks, American Indian/Alaskan Natives, Asian/Pacific Islanders, and Hispanics, respectively) (Table 2 and Fig. 3).

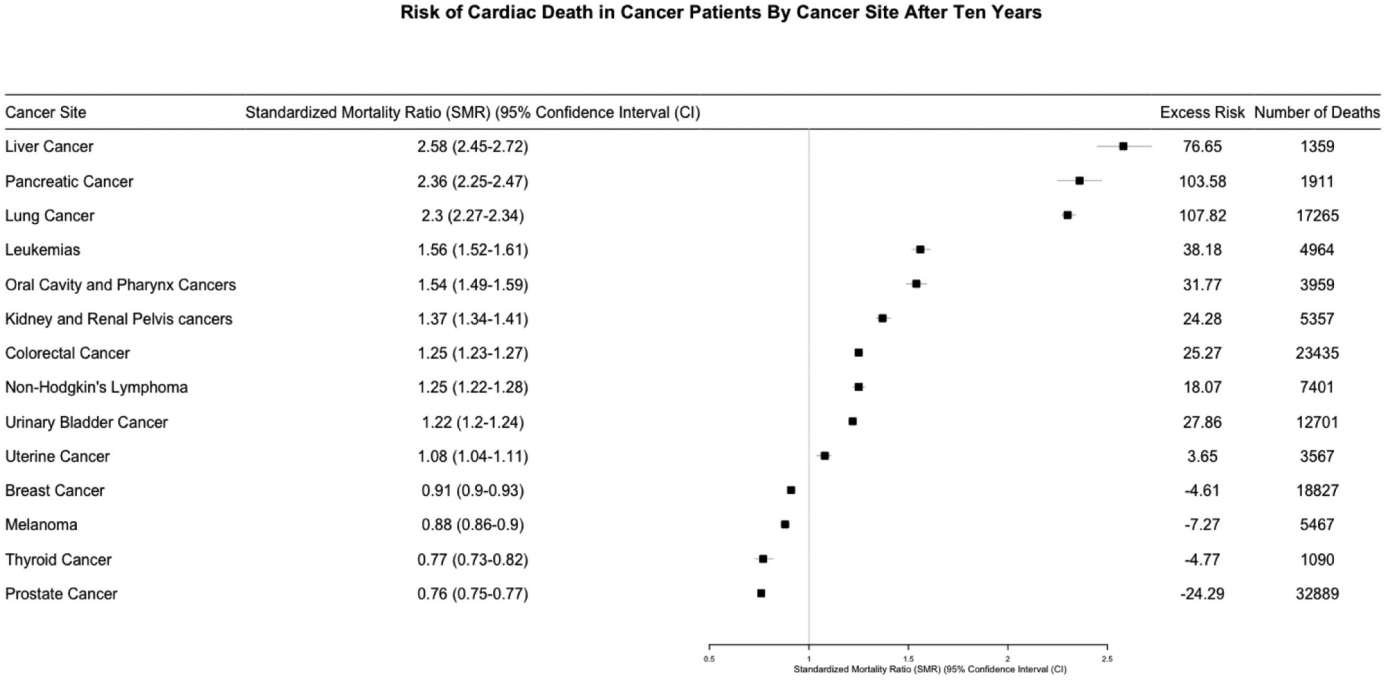

Fig. 2. Risk of cardiac death in cancer patients by cancer site after 10 years. Legend: SMR of cardiac death in the 10 years following a cancer diagnosis according to cancer site.

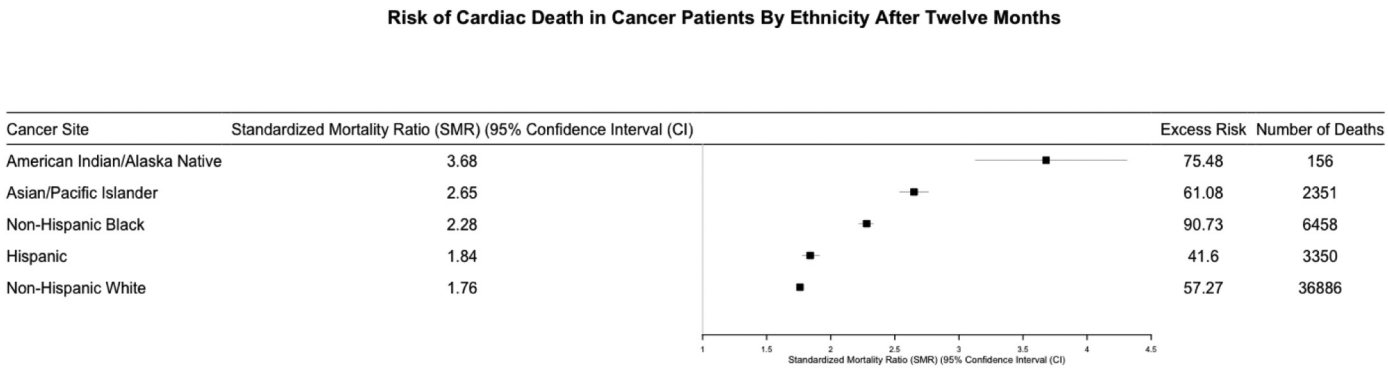

Fig. 3. Risk of cardiac death in cancer patients by ethnicity after 12 months. Legend: SMR of cardiac death in the 12 months following a cancer diagnosis according to ethnicity.

The risk within 10 years following cancer diagnosis was also significantly higher for all ethnic groups (Table 2). American Indian/Alaska Native patients consistently had the highest increase in risk when compared to a demographically similar population, whether within 1 year or 10 years of their cancer diagnosis (SMR=2.33, with an excess risk of 39.05 per 10,000 person-years within 10 years), followed by Asian/Pacific Islander and black patients (Fig. 4).

3.5. Temporal trends in cardiac death

In order to ensure that results were not driven by a single aberrancy in annual cardiac death rates, we plotted the temporal trends for observed vs. expected cardiac death over the entire 14-year duration of the study. Pancreatic and lung cancer had persistently higher SMRs for cardiac death for the entire duration of the study, with even greater separation in rates during the latter years. Patients with metastatic disease also had persistently higher SMRs for cardiac death throughout the study with even a progressively widening separation in rates toward the end of the study. Finally, with regards to ethnicity, American Indian/Alaskan Natives had persistently higher SMRs when compared to white cancer patients throughout the study. Asian/Pacific Islander and black patients appeared to develop higher rates of cardiac death from 2009 onwards when compared to white cancer patients, and the trend seems to persist as time progresses (Fig. 5).

4. Discussion

Our results from over 4.6 million US cancer patients over the past two decades show that cancer patients are at an increased risk of long-term cardiac death when compared to the general population. However, the risk is not uniform in all patients. Rather, it depends on the location of the primary tumor, the extent of metastasis, and the patient ethnicity. Those with pancreatic or lung cancer; metastatic disease; and Native American, Asian, or Black ethnicity had more than twice the rate of cardiac death compared to expected rates for their counterparts without cancer in a demographically similar population. Moreover, these disparities appear to have persisted over the entire 14-year study duration. This raises critical questions regarding whether minority patients are at higher risk due to biological, genetic, clinical, or environmental causes.

To our knowledge, this is the largest study of long-term cardiac death risk following a cancer diagnosis and the first to report extensive detailed observations in risk based on cancer site and ethnicity alongside temporal trends compared to prior large-scale cohort studies [17]. While there was higher risk seen for certain cancers and advanced malignancy throughout the study duration, the disparity for Asian/Pacific Islander and black patients, in particular, appears to have started in 2009 with a persistently higher rate from there on out.

Multiple studies have evaluated the differences between various ethnicities receiving cancer treatment in the United States. Disparities in access to cancer treatment as well as the availability of chemotherapy have been widely reported [18,19]. Affordability of health care has also been reported as a concern for minorities that limits their access to high-volume specialized medical centers [18]. However, disparities in access alone cannot explain the difference in our results since all patients in this study had a histological diagnosis of cancer, subsequently survived their cancer diagnosis, and later died of noncancer (in this case cardiac) causes. Although that does not guarantee that they had high-quality access to care, it means they had at least some access to oncological care. Hence, differences in access or cancer treatments alone cannot explain the discrepancies in noncancer outcomes.

Some data show that minority populations generally have worse long-term survival than white patients even after adjusting for socioeconomic status and access to healthcare facilities [20]. Whether the ethnic disparities in cardiac risk observed here are primarily based on social factors or genetic factors remains unclear.

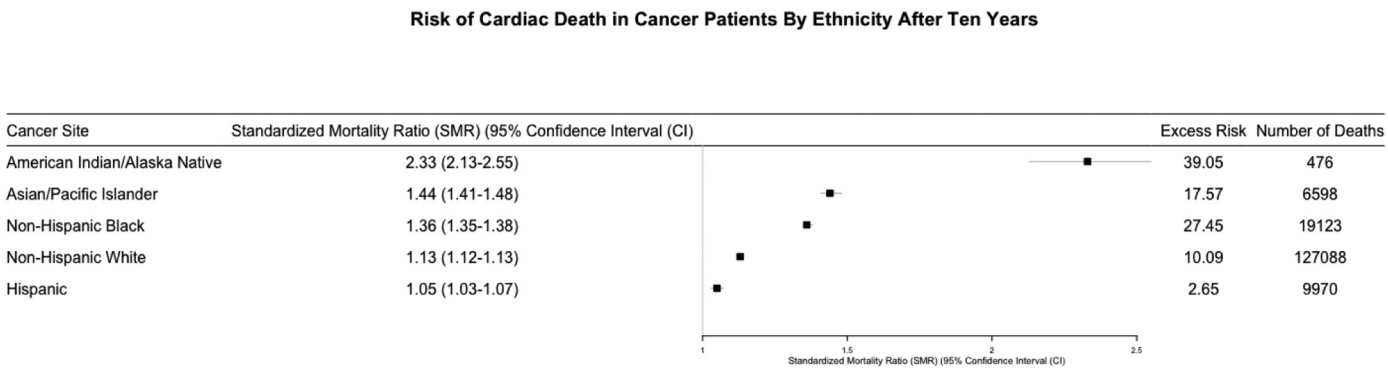

Fig. 4. Risk of cardiac death in cancer patients by ethnicity after 10 years. Legend: SMR of cardiac death in the 10 years following a cancer diagnosis according to ethnicity.

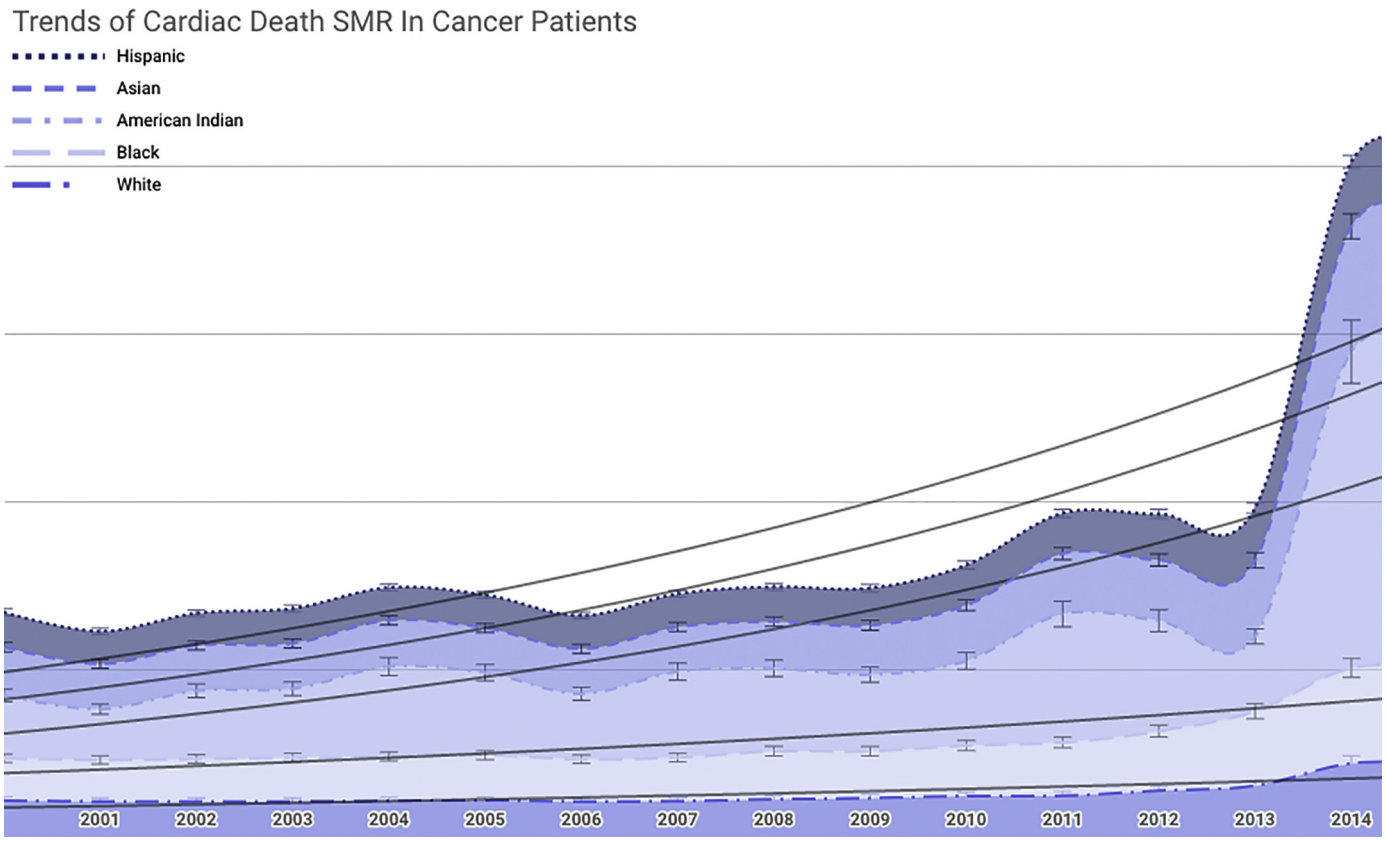

Fig. 5. Cumulative temporal trends of cardiac death in cancer patients. Legend: The risk of cardiac death in cancer patients over the study duration is increasing in every ethnicity, with an overall cumulative increase in all ethnicities; however, the increase in the risk was disproportionate between different races/ethnicities. *X*-axis shows years included in the study. *Y*-axis shows cumulative SMR of each ethnicity with CIs and a trend line.

Further research is desperately needed to answer these questions related to ethnic disparities in cancer outcomes.

With regards to the increased cardiac death risk after metastatic disease, this can be explained by the fact that smaller more localized tumors are often treated with surgical resection, while more advanced, metastatic tumors are more frequently treated with radiation or chemotherapy [21], which have well-documented adverse cardiac effects [7,8,22].

As for cancer site, our study showed that patients with prior pancreatic, lung, and colorectal cancer were at greatest risk for future cardiac death. Currently, prostate and breast cancers are the most common cancers in men and women, respectively, followed by lung cancer and colorectal cancer [2,23]. Pancreatic cancer is not among the common cancers but is the fourth leading cause of cancer deaths in the United States [2]. Our analysis shows that while the risk of cardiac death was not increased in prostate and breast cancers, it was significantly increased after liver, lung, and pancreatic cancer diagnoses.

Multiple lung cancer treatments have been implicated in cardiotoxicity, ranging from radiotherapy to systematic chemotherapeutic agents, including doxorubicin and paclitaxel [22,24]. Interestingly, there is considerable overlap between the agents used for breast and lung cancer treatments [5,25]. This raises questions about why the risk is increased with one cancer but not the other. This difference may be attributable to the etiology of lung cancer and cardiovascular mortality since multiple risk factors, especially smoking, are shared between the two which may confound the risk analysis [3,26]. Likewise, colorectal [27] and pancreatic cancers [4,28] share CVD risk factors such as obesity and smoking, while cardioprotective medications such as aspirin may be protective against colorectal cancer as well [29].

With regards to breast cancer, different investigators have previously reported conflicting results, showing an increase, decrease, or no change in risk of cardiac death following a breast cancer diagnosis [24,30]. Several prior reports associated the use of radiotherapy and chemotherapy (with anthracyclines or monoclonal HER-2 antibodies as trastuzumab) for breast cancer treatment with the development of cardiomyopathies, congestive heart failure, or valvular diseases [5,6,8,9]. Interestingly, the results of our study did not show higher rates of cardiac death following breast cancer, which is in line with results from some prior authors [31,32].

Regarding the cardiac death risk following prostate cancer, reports have categorized risk based on the received hormonal therapy [33]. As for skin cancers, while malignant melanoma is one of few cancers that can metastasize to the heart, that complication is quite rare [34]. Studies have associated the use of protein kinase inhibitors for the treatment of melanoma with the development of cardiomyopathy and congestive heart failure [35]. However, our results showed that patients with melanoma have no increased risk of cardiac death as compared to the general population. This can be explained by the relatively recent introduction of protein kinase inhibitors and the fact that nonmetastatic melanoma patients may not be started on chemotherapy [35].

This study has some limitations. First, the retrospective design cannot control for sources of bias. Also, important factors such as the patients' baseline cardiac status, comorbidities, functional status, and antitumor therapy used were missing from the SEER database. Another limiting factor is that the database does not capture the environmental exposures or individual lifestyle habits of patients. This limits our ability to adjust for every potential confounder, and so we cannot establish causality between the studied variables and outcome of interest. Having said that, the

outcome of interest was a hard outcome (cardiac death), and the difference in event rates differed significantly based on cancer type and ethnicity. Other than basic demographics, the lack of information regarding comorbidities, established cardiovascular risk factors, onset of their cardiac disease and temporal trend between cardiac disease and cancer diagnosis, patients' socioeconomic status, and education level/health literacy limited the ability to adjust or study potential confounders [36]. Death cannot be refuted — a patient is either deceased or not, irrespective of whether cancer type, cancer treatment, genetics, ethnicity, or other confounders were causative. So, the persistent and significantly higher rates of cardiac death in certain patient subgroups are alarming irrespective of the mechanistic causes and warrant heightened attention and further investigation. Especially since overlap exists between cardiac and cancer risk factors, it is now more important than ever to understand the role of long-term lifestyle changes on future CVD risk in cancer. Yet, determining cause of death can be quite complex, cardiac death is intricate to classify, and the SEER database lacked certain information about detailed cause of death such as a cardiac ischemic event or end-stage heart failure, for example.

In addition to these limitations, there are important strengths. First, this study is based on a large, multiethnic cohort of men and woman from 12 different states, which makes the data reflective and generalizable across the US population. Second, this study included hard outcomes of cardiac death adjudicated by the National Center for Health Statistics. Third, it included comprehensive data on cancer site and ethnicity, measures which were not reported to such a large degree previously. Finally, the results were not driven by isolated discrepancies over a 1- or 2-year period. Rather, the temporal trends show that the differences observed have persisted throughout the study duration. Further studies are needed to confirm whether minority patients and those with prior lung and pancreatic cancer are indeed at increased cardiovascular risk and to determine the mechanistic reasons why that may be. This will be critically important for providers who continue to treat cancer patients in order to prevent future cardiovascular morbidity and mortality.

5. Conclusion

Cancer patients are more vulnerable to cardiac death than the general population. Minority patients and those with prior metastatic disease were at an even higher risk of cardiac death. Risk also varied based on cancer type, with patients with prior pancreatic, lung, and colorectal cancer at the greatest risk for cardiac death. Further studies are required to investigate why the cardiac death rate is higher in these subgroups and to better understand the stressors that a cancer diagnosis can place on the cardiovascular system. Health care providers should be aware of cardiac morbidity and mortality risk in cancer patients and should pay special attention to patients of specific malignancies associated with higher long-term cardiovascular disease risk.

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