Clinical paper

Contemporary impacts of a cancer diagnosis on survival following in-hospital cardiac arrest

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Abstract

Aim: The objective of this study was to determine whether survival and post-arrest procedural utilization following in-hospital cardiac arrest (IHCA) differ in patients with and without comorbid cancer.

Methods: We retrospectively reviewed all adult (age $\geq$18 years old) hospital admissions complicated by IHCA from 2003 to 2014 using the National Inpatient Sample (NIS) dataset. Utilizing propensity score matching using age, gender, race, insurance, all hospital level variables, HCUP mortality score, diabetes, hypertension and cardiopulmonary resuscitation use, rates of survival to hospital discharge and post-arrest procedural utilization were compared.

Results: From 2003 to 2014, there were a total of 1,893,768 hospitalizations complicated by IHCA, of which 112,926 occurred in patients with history of cancer. In a propensity matched cohort from 2012 to 2014, those with cancer were less likely to survive the hospitalization (31% vs. 46%, p < 0.0001). Following an IHCA, rates of procedural utilization in patients with cancer were significantly less when compared to those without a concurrent malignancy: coronary angiography (4.0% vs. 13.0%), percutaneous coronary intervention (2.2% and 8.0%), targeted temperature management (0.8% vs. 6.0%); p < 0.0001 for all comparisons. This patient population was less likely to have acute coronary syndrome (12.6% vs. 27.0%) or congestive heart failure (24.5% vs. 38.2%); p < 0.0001 for both comparisons. Survival improved in both groups over the study period (p < 0.0001).

Conclusions: Patients with a history of cancer who sustain IHCA are less likely to receive post-arrest procedures and survive to hospital discharge. Given the expected rise in the rates of cancer survivorship, these findings highlight the need for broader application of potentially life-saving interventions to lower risk cancer patients who have sustained a cardiac arrest.

Keywords: Cancer, Cardiovascular disease, In-hospital cardiac arrest, Cardio-oncology

Introduction

Every year, approximately 200,000 patients suffer an in-hospital cardiac arrest (IHCA) in the U.S. From 2000 to 2014, rates of survival to discharge steadily increased from 14% to 25% coinciding with improvements in the delivery of advanced cardiac life support and the standardized of post-resuscitation care.[1–4] This represents significant progress towards the stated goals of improved IHCA survival by 2020.[5–7]

Concurrently, long-term clinical outcomes among patients with cancer have dramatically improved, with several cancer populations experiencing a median survival well beyond 5 years.[8] However, increasing data have shown that cancer survivors have increased rates of major cardiovascular events, including IHCA, with poorer outcomes.[9] This holds true among this population despite reports of similar rates of CPR use in cancer patients compared to cancer-free subjects.[10] Notably, many of these patients carry diagnoses of highly-treatable or non-advanced cancers (ex. breast or prostate cancers), suggesting that patients with cancer may be under-resuscitated. As such, there has been a focus amongst members of the medical community to address this disparity.

It is reasonable to postulate that cancer patients, particularly those free of advanced disease, should share similar resuscitation rates compared to cancer-free patients. Yet, whether cancer patients share similar improvements in post-IHCA outcomes and post-arrest cardio-resuscitory procedural utilization is unknown.

Methods

Data source

To investigate the aforementioned relationships and temporal trends, we retrospectively reviewed contemporary population data collected via the National Inpatient Sample (NIS) dataset from 2003 to 2014. We specifically selected this interval given the widespread adoption of ICD-9 codes around this time, as well as the publication of sentinel reports from the American Heart Association in 2002–03 describing the state of IHCA within the U.S.[11,12] The NIS is a publicly available database of 7 million admissions per year, representative of all ~35 million inpatient admissions to acute-care, community hospitals in the US and is compiled as part of the Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality. Prior to 2012, the NIS included 100% of discharges from a stratified sample of 20% of eligible hospitals, but in 2012, this database was redesigned to include a stratified sample of 20% of admissions from 100% of eligible hospitals. Medical information contained in the NIS includes the primary diagnosis for hospital admission (labeled "DX1"), secondary diagnoses (labeled "DX2," "DX3," etc.), procedures performed during the admission, and routine demographic information, all recorded using ICD-9 codes.

Study population

All patients age ≥18 years old who sustained IHCA during an index admission were analyzed. Cardiac arrests were identified using ICD-9 codes 427.41 or 427.5 (ventricular fibrillation and cardiac arrest, respectively). Since DX1 represents the diagnosis code for the primary reason for hospitalization, only those cases that had

ICD-9 codes of 427.41 or 427.5 ascribed as a secondary diagnosis were included in the analysis. Conversely, if either code appeared as a primary diagnosis, these were considered to be hospitalizations for an out-of-hospital cardiac arrest and were therefore excluded from the analysis.[13–15]

Discharge diagnoses and procedures were recoded using the *Clinical Classification of Diseases Software* ("DXCCS") into broad categories, available as separate variables within NIS. We identified cancer hospitalizations using ICD-9 and DXCCS codes (DXCCS 1–30) or the presence of an indicator of cancer in the comorbid condition files. DXCCS codes indicating cancer are 11–45. The comorbidity file included in the NIS lists 29 comorbidities (also known as Elixhauser's Comorbidity measures) based on ICD-9 CM diagnoses and the diagnosis-related group in effect on the discharge date. These comorbidities are not directly related to the principal diagnosis or the main reason for admission and are likely to have originated before the hospital stay.[16] In 2015, the Healthcare Cost and Utilization Project (HCUP) State Inpatient Database was used to create two indices based on 29 co-morbidity measures designed to predict in-hospital mortality and 30-day readmission.[17] Those indices were calculated for our cohort as well.

For this analysis, all hospitalizations that lacked an ICD-9 or DXCCS code indicating a diagnosis of cancer were considered non-cancer hospitalizations. Admissions with metastatic cancer were excluded due to the metabolic derangements and systemic inflammation associated with advanced malignancy, and the fact that such diagnoses tend to portend limited survival.[18,19]

Data elements utilized from NIS were medical comorbidities, demographic characteristics (age, sex, and race), income quartile, insurance status, hospital level characteristics, and procedures performed. The procedures of interest were cardiopulmonary resuscitation (CPR), coronary angiography and percutaneous coronary intervention (PCI), intra-aortic balloon pump (IABP) placement, defibrillator (ICD) implantation, and targeted temperature management (TTM). Procedural utilization was identified using ICD-9 CM procedures codes, as listed in Supplemental Table 1.

Outcomes

The primary outcome of this study was IHCA survival rates. Secondary outcomes included utilization of aforementioned post-arrest procedures, length of stay, discharge disposition, and adjusted cost of hospitalization. The adjusted cost was obtained by multiplying hospital charges with the cost-to-charge ratios and wage index for each hospital for each year, then adjusting for inflation to 2017 dollars.[19,20] The wage index helps correct for geographic variations in costs among hospitals.

Statistical analysis

We utilized propensity score matching to assess the impact of a cancer diagnosis on our stated primary and secondary endpoints. Three propensity-matched cohorts, using various matching schemes, were employed to study our specific outcomes. We applied the 8 → 1 Digit Match algorithm, which matched a case to a control whose score equaled the 8th decimal point followed by 7th decimal point followed by 6th decimal point and so on using a greedy matching algorithm.[21] This schema afforded 2:1 matching of non-cancer to cancer admissions with IHCA in all three cohorts. Complete details of propensity matching are provided in

Supplemental methods. The consort diagram of the cohorts is detailed in Supplemental Fig. 1.

Sample weight, stratification, cluster and domain information included in the NIS were used to derive national estimates from sample data. Continuous variables were analyzed using Student's *t*-test if they were normally distributed, as determined by the Anderson–Darling test. Non-parametric continuous variables were analyzed using the Kruskal–Wallis test. Categorical variables were analyzed using Chi-Square test. Trends were evaluated using the Cochrane Armitage test and linear regression models for categorical and continuous variables, respectively. Hospitalization cost was logarithmically transformed to yield normally-distributed values for analysis.

Moreover, in order to better understand if procedure utilization differed based on general prognosis, a sensitivity analysis was performed on a subgroup of subjects with cancers that portended a relatively favorable survival. This was defined as a 5-year survival >90% and included subjects with non-advanced thyroid, breast, prostate, and testicular cancers, or non-Hodgkin lymphomas.[22] Another sensitivity analysis was undertaken to classify a sicker group of patients in the ICU. However, since NIS does not have a dedicated ICU field, a sub-cohort of patients was created with the All Patient Refined Diagnosis Related Groups (APR-DRGs) severity variable.[23] APR-DRG severity is classified based on the severity of illness and the risk of mortality into 4 subclasses, namely, minor (1), moderate (2), major (3) and extreme (4). APRDRG of 3 and 4 was used to create a group of these possible ICU patients.

Given the discrepancy in survival of IHCA patients with and without cancer, a non-parsimonious multivariable regression analysis was performed using a multivariable regression model described by Secemsky et al.[24] The model is detailed in the supplemental methods.

Subgroup analysis was performed to explore differences in procedural utilization within the matched cohort. Subgroups included hospitalizations with a primary presentation of acute myocardial infarction (AMI) and congestive heart failure (CHF). Among subjects with a primary diagnosis of AMI, we compared utilization of CPR, angiography, PCI, and TTM. In subjects with a primary diagnosis of CHF, we compared the use of CPR, IABP, angiography, PCI, percutaneous ventricular assist devices (PVAD) and left ventricular assist devices (LVAD). All analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA). In all analyses, two-tailed α was set at 0.05.

Data availability

The dataset used in this analysis is publicly available through AHRQ, and all inquiries for the data should be directed to AHRQ. The authors cannot directly share this data, according to the HCUP data use agreement.

Results

Population characteristics

Overall, 1,893,768 admissions complicated by IHCA from 2003 to 2014 were identified, of which 112,926 occurred in those with non-metastatic cancer. This represented 0.5% and 0.2% of all US admissions in those without and with co-diagnosis of non-metastatic cancer, respectively. The annual rate of IHCA increased in both groups over the study periods, p < 0.0001 (Fig. 1A).

Incidence of IHCA by cancer status

Among admissions which had IHCA with and without cancer, respectively, the average age was 71 vs. 68 years old; 37.9% vs. 43.2% were female; 15.4% vs. 28.4% were admitted with a co-diagnosis of acute coronary syndrome; 25.7% vs. 36.7% had CHF (p < 0.0001 for all comparisons). Further demographics, hospital-level variables and comorbidities are listed in Table 1.

Over the full twelve years considered, survival to hospital discharge improved in both risk-matched groups (22.6%–30.2% in cancer vs. 40.2%–45.1% in non-cancer; p-trend and $p_{cancer\ vs.\ non-cancer}$ = <0.0001), but was significantly higher in the group without cancer (p < 0.0001), as demonstrated in Fig. 1B. In a higher APR-DRG severity group, the survival to hospital discharge was lower, but improved in both cancer and non-cancer (22.0%–31.7% in cancer vs. 36.4%–46.4% in non-cancer; p-trend and $p_{cancer\ vs.\ non-cancer}$ = <0.0001, supplemental Fig. 2)

In an exploratory multivariable regression model, we found that the 32 of the 39 variables were associated with mortality after IHCA. A concurrent cancer diagnosis had the strongest association associated with mortality after IHCA (OR = 3.36 [3.25–3.47]; p = <0.0001). All the multivariate odds ratios are presented in Supplemental Table 2.

Post-IHCA procedural utilization

Among risk-matched groups, CPR was utilized at a significantly higher rate in hospitalizations with cancer (35.2%) than without cancer (29.5%) (p < 0.0001), with rate increasing over time in both groups (p-trend < 0.0001) (Fig. 2). Differences in procedural utilization persisted after matching hospitalizations based on propensity score (Fig. 3A, p < 0.001 for all comparisons). Angiography (6.4% vs. 21.7%), PCI (2.3% vs. 12.3%) and TTM (0.9% vs. 2.6%) were utilized less in those with cancer compared to those without cancer (p < 0.0001 for all comparisons).

In the sensitivity analysis investigating procedural utilization in subjects with a generally favorable 5-year survival, significant differences in utilization of CPR, angiography, PCI and ICD implantation persisted, but TTM, IABP were used at similar rates (Fig. 3B).

Restricting the analysis to those admitted with AMI and IHCA, angiography was utilized more frequently in hospitalizations with co-diagnosis of cancer than those without cancer (62.6% vs. 53.9%, p = 0.001), as was PCI (48.7% vs. 41.8%, p = 0.008) (Fig. 3C). In the cohort of hospitalizations admitted with CHF, overall procedural utilization was similar in both groups (Supplemental Table 3), with the exception TTM (0.3% in cancer vs. 3.4% in non-cancer, p = 0.03).

Economic and disposition outcomes

There was no economically meaningful difference in the cost of admission or median length of stay based on cancer status. Among all IHCA admissions from 2003 to 2014, the cost of care among those with cancer was higher than those without ($28,150 vs. $27,817, respectively; p < 0.0001). However, there is no difference in cost of care in the contemporary propensity matched years of 2014–15 ($33,044 vs. $31,234, respectively; p = 0.71). Similarly, there was no
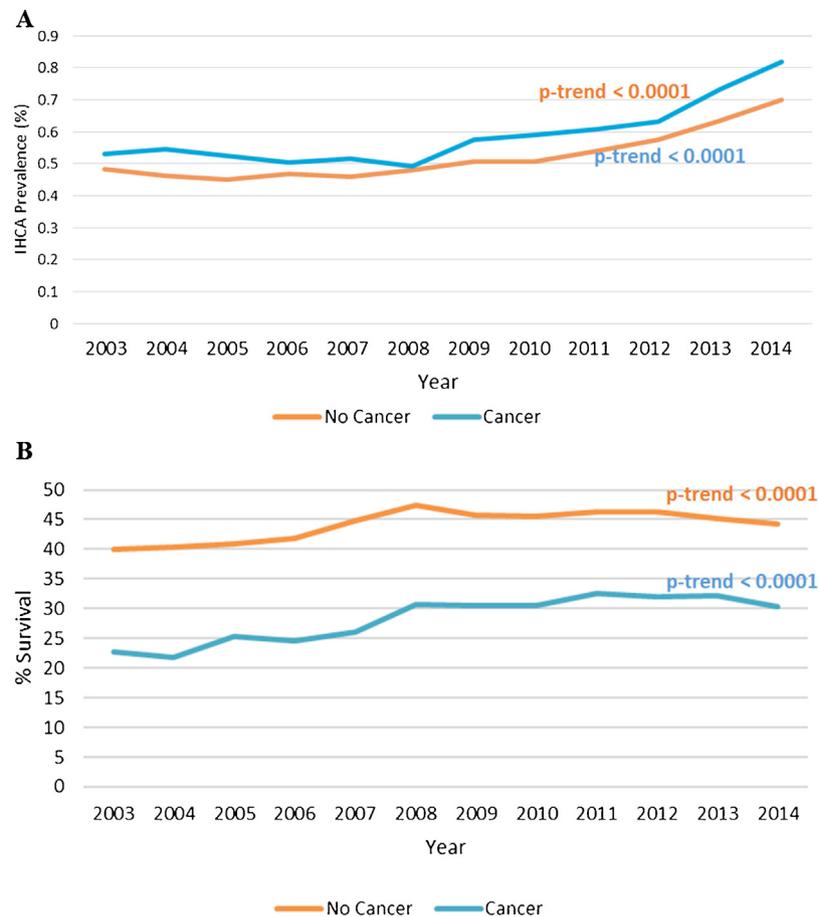
A

B

Fig. 1 – (A) Annual rate of IHCA among hospitalizations with and without co-diagnosis of cancer. (B) Propensity matched survival trends of IHCA among hospitalizations with and without cancer. [Hospital admissions from 2003 to 2014 were divided into individual year cohorts, after which cancer admissions with documented in-hospital cardiac arrest (IHCA) were propensity matched to non-cancer admissions using age, gender, race, insurance, hospital level variables, diabetes, hypertension, cardiopulmonary resuscitation (CPR) use, and Healthcare Cost and Utilization Project (HCUP) mortality score].

difference in the median length of stay in cancer vs. non-cancer cohorts in the contemporary years of 2014–15 (median LOS 3 vs. 3 days, respectively; 0.16).

Among the propensity-matched cohort, the two groups had significantly different discharge dispositions as demonstrated in Fig. 4, those without a history of cancer were more likely to be discharged home (34.1% vs. 29.0%, p < 0.0001) while those with a co-diagnosis of cancer were more likely to be discharged to a skilled nursing facility or home with home health care.

Discussion

In this analysis spanning over a decade, cancer-related hospitalizations were associated with similar rates of IHCA, but lower overall post-resuscitation procedure utilization, poorer survival rates, and worse discharge dispositions than those without comorbid cancer. This relationship persisted even after accounting for comorbidities, and general cancer prognosis. Although the rates of PCI may have been expected to be lower among cancer hospitalizations, the

implementation of more general post-resuscitation interventions such as TTM also remained significantly lower among cancer hospitalizations. When considering an acute life-threatening primary diagnosis like AMI, all procedure utilization was higher in the cohort of hospitalizations with co-diagnosis of cancer.

From a public health perspective, these findings are important given increasing rates of cancer survivorship coinciding with the high prevalence of cardiovascular disease. To our knowledge this is the first report evaluating contemporary usage patterns of routine post-IHCA care among those with cancer. Given goals set by the American Heart Association[5] and European Society of Cardiology[7] targeting improved IHCA survival, increased focus on the application of potentially lifesaving post-IHCA measures among the growing number of patients with a current or prior cancer diagnosis, particularly when the likelihood of long-term survival is high, will prove critical.

Our findings are consistent with previous reports detailing CPR utilization rates in patients with cancer.[10,25] Reported IHCA survival among patients with cancer has lagged behind that of non-cancer patients. However, many of these prior studies are smaller in scope, stem from analyses conducted prior to widespread use of standard post-IHCA

Table 1 – Hospitalization characteristics of all subjects.

Characteristic	No cancer		Hx cancer		p-value
	n = 1,780,842		n = 112,926		
Age (years old, median, IQR[a])	68	(56.0–79.0)	71	(61.0–79.0)	<0.0001
Female (n, %)	768,304	(43.15)	42,814	(37.91)	<0.0001
Race (n, %)					<0.0001
White	1,049,562	(69.66)	68,634	(70.19)	
Black	236,955	(15.73)	15,874	(16.23)	
Hispanic	128,131	(8.50)	7238	(7.40)	
Asian or Pacific Islander	38,167	(2.53)	2899	(2.97)	
Native American	9004	(0.60)	384	(0.39)	
Other	44,828	(2.98)	2755	(2.82)	
Comorbidities (n, %)					
ACS[a]	505,341	(28.38)	17,338	(15.35)	<0.0001
Atrial fibrillation	443,780	(24.92)	27,225	(24.11)	0.0056
CAD[a]	681,024	(38.24)	28,489	(25.23)	<0.0001
CHF[a]	653,829	(36.71)	29,057	(25.73)	<0.0001
Valvular heart disease	82,986	(4.66)	5490	(4.86)	0.1646
Hyperlipidemia	463,637	(26.03)	23,148	(20.50)	<0.0001
Hypertension	974,669	(54.73)	54,774	(48.50)	<0.0001
Diabetes	521,801	(29.30)	26,344	(23.33)	<0.0001
CKD[a]	355,313	(19.95)	18,209	(16.12)	<0.0001
PAD[a]	50,141	(2.82)	1892	(1.68)	<0.0001
Obese	160,736	(9.03)	5784	(5.12)	<0.0001
Alcoholism	87,386	(4.91)	3621	(3.21)	<.0001
Smoking	200,971	(11.29)	9823	(8.7)	<.0001
Non-traditional					
Weight loss	119,022	(6.68)	10,859	(9.62)	<0.0001
Anemia	321,396	(18.05)	25,463	(22.55)	<0.0001
Arthritis and collagen vascular disease	37,463	(2.1)	2056	(1.82)	0.0034
Chronic liver disease	54,286	(3.05)	4431	(3.92)	<0.0001
Chronic lung disease	385,951	(21.67)	27,570	(24.41)	<0.0001
Hypothyroidism	153,493	(8.62)	9351	(8.28)	0.0703
Psychiatric	56,310	(3.16)	3045	(2.7)	<0.0001
Fluid/electrolyte disorder	669,434	(37.59)	45,557	(40.34)	<0.0001
Coagulation disorder	168,482	(9.46)	15,185	(13.45)	<0.0001
Substance abuse	56,783	(3.19)	2044	(1.81)	<0.0001
Total Elixhauser's comorbidities ≥ 3	641,942	(36.05)	49,539	(43.87)	<0.0001
Elixhauser's readmission score (mean ± SE)	7 (15–27)		29 (18–39)		<0.0001
Elixhauser's mortality score (mean ± SE)	8 (0–15)		16 (9–25)		<0.0001
Hospital size					0.30
Small	178,106	(10.04)	11,651	(10.35)	
Medium	433,422	(24.44)	27,479	(24.42)	
Large	1,161,902	(65.52)	73,392	(65.22)	
Hospital region					<0.0001
Northeast	289,474	(16.25)	19,818	(17.55)	
Midwest	392,566	(22.04)	24,033	(21.28)	
South	738,248	(41.45)	45,966	(40.70)	
West	360,555	(20.25)	23,109	(20.46)	
Hospital ownership					<0.0001
Government, non-federal	61,310	(11.65)	7915	(13.30)	
Private, not-profit	382,025	(72.56)	43,315	(72.77)	
Private, invest-own	83,135	(15.79)	8290	(13.93)	
Primary payer					<0.0001
Medicare	129180	(62.01)	1,190,916	(61.62)	
Medicaid	19967	(9.58)	185,611	(9.60)	
Private insurance	47703	(22.90)	397,577	(20.57)	
Self-pay	5567	(2.67)	96,121	(4.97)	
No charge	625	(0.30)	8248	(0.43)	
Other	4910	(2.36)	50,912	(2.63)	

[a] Abbreviations: ACS, acute coronary syndromes; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; IQR, interquartile range; PAD, peripheral artery disease.
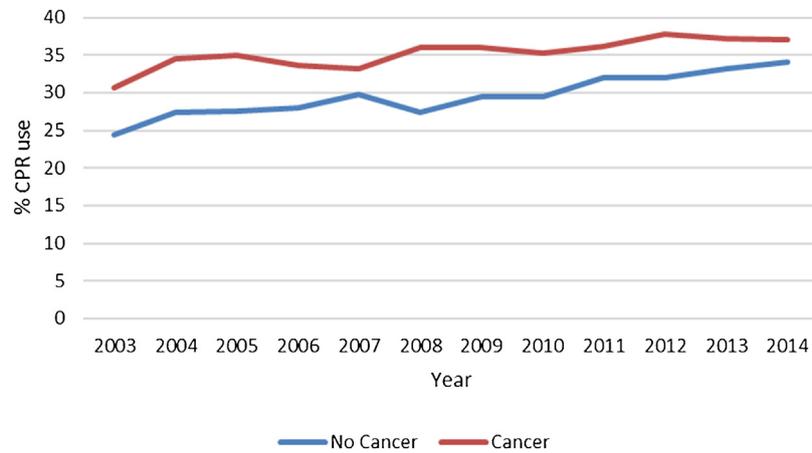
Fig. 2 – Cardiopulmonary resuscitation utilization rates, by cancer status in a propensity matched cohort.
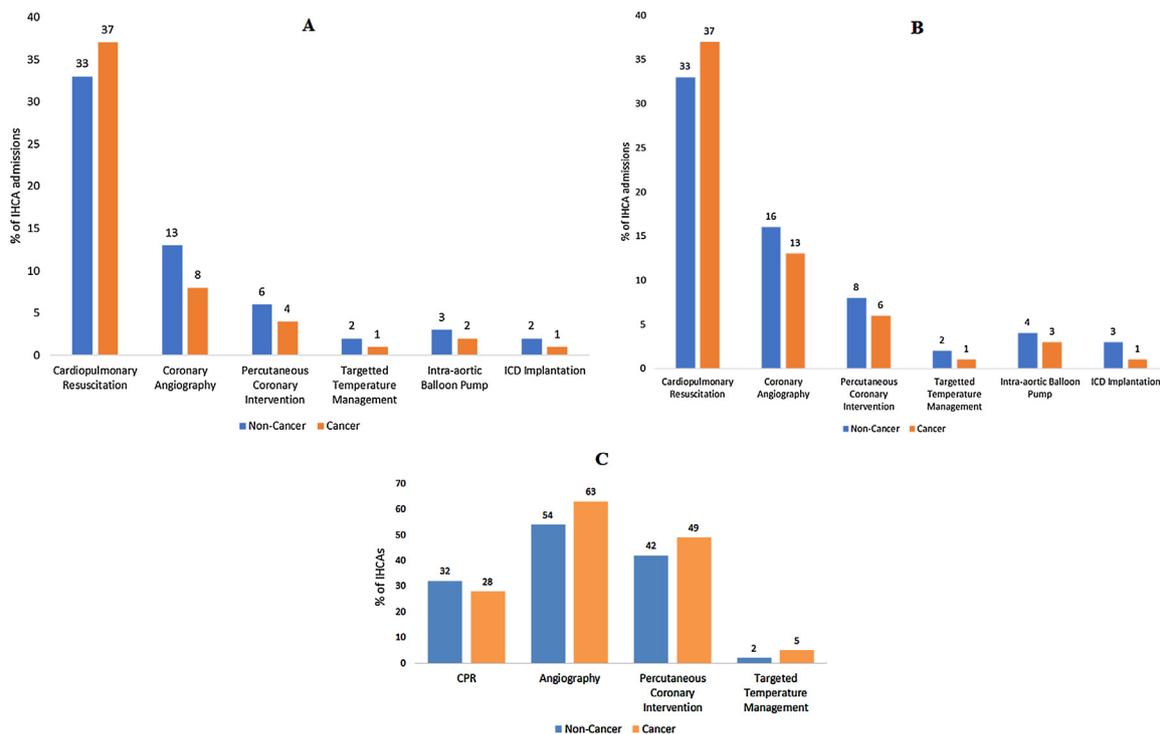

Fig. 3 – (A) Procedural utilization among cancer hospitalizations within the propensity-matched 2012–2015 cohort. P values (all comparisons saw P-values < 0.001). (B) Procedural utilization in the high-survival cancer matched cohort. For this analysis, subjects with a history of cancer with a favorable five-year survival (thyroid, breast, prostate and testicular cancers or non-Hodgkin lymphoma) were matched to two controls without a history of cancer. Utilization of some procedures differed by co-diagnosis of cancer: P = 0.0498 for CPR use, P = 0.0337 for angiography use, P = 0.0151 for PCI use, P = 0.0804 for TTM use, P = 0.0543 for IABP use and P = 0.0080 for ICD implantation. (C) Procedural utilization among subjects with and without a cancer with presenting diagnosis of MI. *All comparisons were significant, expect for CPR use.

measures, and predate the emergence of more novel cancer therapeutics associated with improved cancer survival rates.[26] The rise in post-IHCA survival has largely correlated with standardized implementation of post-resuscitation measures. Critical to this has been the increased use of TTM, coronary angiography, and PCI. However, we note the rate of use of these measures in the presence of a cancer history has remained low, despite improving cancer survival overall.

Previously, restricted use of PCI was advised on the basis of elevated bleeding risk, potential for provocation of coronary thrombosis and futility of intervention in those with underlying cancers. However, recent data does not appear to support these concerns. In this study it is demonstrated that AMI was diagnosed less in cancer patients but once diagnosed, these patients received adequate care in terms of angiography and PCI. There is a likelihood that cancer
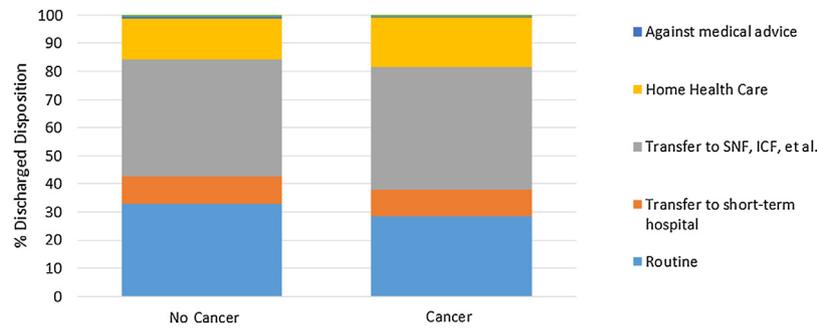
Fig. 4 – Discharge disposition of hospitalizations following IHCA (p < 0.0001 for each pairwise comparison).

patients either have delay or lack of effort in diagnosing this life-threatening condition due to bias. A recent publication by Potts et al.[27] showed that there has been increase in overall use of PCI for various primary diagnoses which supports this current finding. Furthermore, there are no definite contraindications to their use, outside of expected survival of less than 6 months in persons with cancer.[28] Even in the presence of thrombocytopenia, coronary angiography and PCI can generally be safely performed in cancer patients.[29] In a review of more than 15,000 real-world patients referred for PCI during a 15-year period, cancer was not associated with worse cardiovascular outcomes or intervention failure following PCI.[30] Finally, among patients presenting with out-of-hospital cardiac arrest, the use of a more aggressive post-arrest management strategies, including PCI, was associated with improved outcomes in the setting of cancer.[31] Given the preponderance of data showing cardiac catheterization followed by an intervention appears to be associated with improved outcomes in those with both ACS and cardiac arrest, greater efforts at diagnosing AMI and increasing post-resuscitation measures in non-AMI IHCA patients is warranted. Prospective studies and cardio-oncology registries are needed to more completely study this phenomenon in the future.

Several limitations must be acknowledged. First, the NIS database relies on clinician coding for accurate diagnoses based on available ICD-9 codes. It is possible some patients may have had cancers that were omitted from the NIS because they were either not reported or were diagnosed remotely from the clinical presentation. Procedure utilization similarly depends on accurate clinician coding. Specific to this point, the study group acknowledges that CPR use might have been under-coded. Additionally, end-of-life discussion cannot be ruled out given the administrative nature of this database. However, given the consistent use of ICD-9 codes for more than a decade, general reflectance of recent or contemporary clinical practice and possibly equal amount of missing data in both cancer and non-cancer cohorts use of these measures may still allow for crucial insights into more broad clinical practice. The NIS dataset also does not allow for accurate staging of cancer, beyond the presence of advanced or metastatic disease, nor is there a provision for timing or type of anticancer therapy (ex. targeted vs. traditional), nor notification of code status. Unavailability of this information can possibly explain overall less utilization of procedures in cancer patients. However, sensitivity analysis of high survival cancers shows procedural use discrepancy which shows disparity beyond these unavailable fields. Moreover, although the use of ICD codes may identify likely causes underlying cardiac arrest, this does not provide linked information regarding exact causes of arrest. Similarly, the nature of our retrospective review provides insight on associations, but not causation. Finally, even though statistically necessary, risk matching using propensity score may have masked true and relevant associations. Despite the performance of extensive analyses and the overall comprehensive nature of the NIS dataset employed, the precise factors underlying IHCA and survival to discharge, including cancer disease status, discordance in physician and patient perception of cancer severity and prognosis, patient-physician discussion of goals of care, and use of active or recent treatments could not be determined. Finally, even though we attempted to define a group of patients in the ICU setting, APR-DRG is only an administrative marker of severity and not a true marker of clinical sickness. Further elucidation of these interactions will require prospective studies, or retrospective analyses with greater clinical granularity.

Conclusions

Despite similar rates of in-hospital cardiac arrest and CPR use, cancer patients have lower survival to discharge than patients without cancer. This difference persists even after controlling for general prognosis and comorbidity status and appears to be associated with less aggressive use of post-resuscitation procedures, such as TTM, PCI and mechanical support. Additional research is needed to clarify the role of patient-physician perceptions of cancer prognosis and selective applications of post-resuscitation care.

Conflict of interest

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2019.07.005.

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