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Outcomes for Cancer Patients with Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention☆

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ABSTRACT

Background/Purpose: The incidence of cardiovascular disease in cancer patients is rising. The risk of in-hospital complications for cancer patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) is not well defined.
Methods/Materials: A retrospective single-center cohort assessing STEMI patients with a history of cancer ($n = 58$) and without a history of cancer ($n = 551$) who underwent primary PCI between January 1, 2012 and June 30, 2017 was conducted. The primary outcome was a composite of in-hospital complications including reinfarction, cardiogenic shock, new heart failure, stroke, new atrial fibrillation, ventricular tachycardia/fibrillation, cardiac arrest, bleeding, new dialysis requirement, mechanical circulatory support, hospice requirement, and in-hospital mortality.
Results: Overall in-hospital complications occurred in 229 (37.6%) patients. There was no significant difference in overall complications in patients with a history of cancer (39.7%), compared to those without a cancer history (37.4%) (adjusted OR 0.84 [0.46–1.51], $p = 0.58$; unadjusted OR 1.10 [0.61–1.92], $p = 0.73$); there were no differences exhibited in any of the individual complications. Patients with a history of cancer were significantly more likely to be readmitted within 30 days (12.7% vs. 5%; $p = 0.03$) and receive bare metal stents (50% vs. 30.4%; $p = 0.004$) as compared to patients without a history of cancer.
Conclusions: There was no significant difference for in-hospital complications in patients with a history of cancer and those without a history of cancer undergoing primary PCI for STEMI. Patients with a history of cancer were more likely to readmitted within 30 days and receive bare metal stents.
Summary: The risk of in-hospital complications for cancer patients with STEMI undergoing primary PCI is not well defined. In a single-center retrospective cohort, there was no significant difference for in-hospital complications between patients with a history of cancer and those without a history of cancer undergoing primary PCI for STEMI.

1. Introduction

The incidence of cancer in the United States is increasing with 1,700,000 new diagnoses projected in 2018, but with only approximately 600,000 cancer deaths expected [1]. The rate of cancer mortality has decreased from approximately 200 to 160 deaths per 100,000 patient-years from 1982 to 2013 [2]. The increase in cancer diagnoses and decrease in cancer mortality has led to a higher prevalence of long-term cardiovascular diseases, specifically coronary artery disease (CAD), associated with cancer and cancer treatments [3]. The Childhood

Abbreviations: STEMI, ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; CHF, congestive heart failure; CAD, coronary artery disease; AMI, acute myocardial infarction; NCDR, National Cardiovascular Data Registry; CABG, coronary artery bypass graft surgery; MI, myocardial infarction; PAD, peripheral artery disease; CrCl, creatinine clearance.

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Cancer Survivor Study found survivors of childhood cancer had a 15-fold increase in congestive heart failure (CHF), 10-fold increase in CAD, and 9-fold increase in strokes [3]. Patients have the highest incidence of CAD within 6 months of cancer diagnosis, but possess a sustained risk in years thereafter [4]. With this high impact in an ever-growing patient population, understanding risk factors and outcomes for cardiovascular disease in cancer survivors is paramount to guiding proper cardiovascular therapies.

Cancer is a known prognosticator of poor outcomes in patients with CAD. Studies assessing primary PCI patients, both acute myocardial infarction (AMI) and stable CAD, with a history of cancer indicate an increase in all-cause mortality compared to those without a cancer history [5,6]. In fact, one study showed the risk of in-hospital mortality for AMI patients undergoing PCI increased 3-fold when a patient had a history of cancer [7]. Patients presenting with STEMI carry a high risk of morbidity and mortality regardless of cancer history status [7]. Three studies have assessed STEMI patients with and without a cancer history and these studies showed an overall increase in mortality for patients with a history of cancer [8–10]. However, overall in-hospital complications related to primary PCI in cancer history patients presenting with a STEMI are not well defined. A greater understanding of in-hospital complication differences between patients with and without a cancer history undergoing primary PCI for STEMI can lead to potential improvements in patient care.

The aim of this study was to better define in-hospital complications associated with primary PCI in patients presenting with a STEMI with and without a history of cancer.

2. Material and methods

A retrospective single-center cohort study was conducted which included subjects admitted to an academic tertiary care medical center for STEMI and underwent primary PCI between January 1, 2012 and June 30, 2017. The academic medical center is a primary PCI center and a leading comprehensive cancer center. Subjects were included if age was between 18 and 89 years and were identified using the electronic medical record and a pre-existing cardiac database, the ACTION Registry®-GWTG™ from the National Cardiovascular Data Registry (NCDR®). Patients were excluded upon chart review if PCI was not pursued or did not carry a final diagnosis of STEMI. Patients were divided into those with a history of cancer and those without a history of cancer. All types of cancer were included in the cancer history with the exception of non-melanoma skin tumors due to their limited systemic effect. Data collected upon retrospective chart review included patient demographics, baseline characteristics, medications prior to, during, and following admission, interventions, laboratory values, imaging, complications/mortality, 30-day outcomes, and disposition. The research protocol was reviewed and approved by the Institutional Review Board and the Clinical Scientific Review Committee.

The primary outcome was a composite of in-hospital complications, which included reinfarction, cardiogenic shock, new heart failure, stroke, new atrial fibrillation, ventricular tachycardia/fibrillation, cardiac arrest, bleeding, new dialysis requirement, mechanical circulatory support, hospice requirement, and in-hospital mortality. Secondary outcomes included the individual components of the primary outcome as well as 30-day mortality and readmission, patient disposition, treatment modalities, and procedural and discharge medications. Endpoints were adjudicated based on the pre-defined criteria for data collection in the ACTION Registry®-GWTG™. Due to limited data on STEMI patients not undergoing primary PCI, a pre-planned subgroup descriptive analysis was intended for patients excluded from the primary analysis lacking primary PCI.

Characteristics of patients with a history of cancer were compared to those without a history of cancer. Student's *t*-tests, with the mean ± SD, or Wilcoxon rank-sum tests, with the median and interquartile range, were used for continuous variables, and chi-square tests or Fisher's exact tests were used for categorical variables, as appropriate.

Multivariable logistic regression was used to assess the association between cancer history and complication occurrence in STEMI patients. Multiple imputation was performed to account for missing covariate values, generating 10 imputed datasets. The method for model selection from multiple imputed data was described by method W1 from Wood et al. [11], where the 10 imputed datasets were combined into one, and the observations were weighted as 1/10 to correct the standard errors. Backward selection was used, sequentially removing variables that caused the lowest percentage change in the regression coefficient for cancer history from the model, until all variables remaining would result in a change of the coefficient by >10% if removed. The variables in this final model were then applied to the imputed datasets separately, and the results were combined using the MIANALZE procedure to produce a final odds ratio and 95% confidence interval for cancer history and complication rate while controlling for confounders. As a sensitivity analysis, the primary outcome was analyzed using inverse probability of treatment weighting using propensity scores. All analyses were performed using SAS version 9.4 (SAS Institute, Inc. Cary, North Carolina).

3. Results

A total of 609 subjects were identified as STEMI patients undergoing primary PCI via the ACTION Registry®-GWTG™ between January 1, 2012 and June 30, 2017. There were 58 (9.5%) patients with a history of cancer and 551 (90.5%) patients without a history of cancer. Baseline characteristics are described in Table 1. The average age of the population was 60 years with 75% of patients being male. Patients with a history of cancer tended to be older (63.6 years vs. 59.4 years; $p = 0.01$), female (43.1% vs. 23.2%; $p < 0.001$), with a lower creatinine clearance (78.6 mL/min vs. 91.6 mL/min; $p = 0.013$), lower BMI (28.1 kg/m^2 vs. 30.0 kg/m^2; $p = 0.031$), and higher incidence of prior stroke (15.5% vs. 5.6%; $p = 0.009$) and coronary artery bypass graft surgery (CABG) (12.1% vs. 3.6%; $p = 0.01$) compared to those without a history of cancer.

Of the 58 cancer patients, 50 (86.2%) had a solid tumor diagnosis, with most having breast cancer (Fig. 1). Some subjects had multiple types of cancer leading to a total of 64 cancers identified. Patients diagnosed within 6 months comprised 17.2% of cancer patients and stage IV cancer was found in 13.8% of the cancer population. Cancer treatments included cytotoxic chemotherapy (41.4%), radiation therapy (34.5%), immunotherapy/targeted therapy (13.8%), and surgery (67.2%).

The composite primary endpoint occurred in 229 (37.6%) patients, with 23 (39.7%) in the cancer history group and 206 (37.4%) in the group without a history of cancer (unadjusted OR 1.10 [0.61–1.92], $p = 0.73$). This association remained insignificant after adjustment for the following confounders: sex, creatinine clearance, PCI access site, and initial hemoglobin (adjusted OR 0.84 [0.46–1.51], $p = 0.58$). A sensitivity analysis using inverse probability of treatment methodology with propensity scores yielded consistent results, showing no significant association between cancer history and in-hospital complications (OR 1.05 [0.53–2.08]; $p = 0.89$).

No significant differences existed between groups for individual complications within the composite outcome as seen in Table 2. Overall 30-day mortality was 6.4% with no difference between groups ($p = 0.78$). Patients with a history of cancer were more likely to be readmitted within 30 days (12.7% vs. 5%); $p = 0.03$). This excluded the 36 patients who died prior to discharge.

Secondary endpoints assessed treatment modalities as well as procedural and discharge medications. Cancer patients were significantly more likely to receive bare metal stents (50% vs. 30.4%; $p = 0.004$) versus drug eluting stents when compared to patients without a cancer history; however, no significant differences were noted in the number of diseased vessels between groups. There was no significant difference in femoral artery access site between those with a history of cancer

Table 1
Baseline characteristics. Data are presented as mean ± SD (range), median (IQR), or n (%). BMI = body mass index; MI = myocardial infarction; PCI = percutaneous coronary intervention; CHF = congestive heart failure; PAD = peripheral artery disease; CABG = coronary artery bypass graft; CrCl = creatinine clearance.

	Cancer history ($n = 58$)	No cancer history ($n = 551$)	p-value
Age (years)	63.6 ± 11.7	59.4 ± 11.5	0.01
Male	33 (56.9)	423 (76.8)	<0.001
Caucasian	56 (96.6)	505 (91.7)	0.59
BMI (kg/m^2)	28.1 ± 6.3	30.0 ± 6.6	0.031
Current smoker	24 (41.4)	240 (43.6)	0.75
Hypertension	40 (69.0)	338 (61.3)	0.26
Hyperlipidemia	33 (56.9)	286 (51.9)	0.47
Diabetes	20 (34.5)	143 (26.0)	0.47
Prior MI	10 (17.2)	89 (16.2)	0.83
Prior PCI	14 (24.1)	108 (19.6)	0.41
Prior CHF	1 (1.7)	33 (6.0)	0.24
Prior atrial fibrillation	3 (5.2)	20 (3.6)	0.47
Prior stroke	9 (15.5)	31 (5.6)	0.009
Prior PAD	6 (10.3)	27 (4.9)	0.12
Prior CABG	7 (12.1)	20 (3.6)	0.01
Current dialysis	1 (1.7)	7 (1.3)	0.55
CrCl (mL/min)	78.6 ± 34.8	91.6 ± 37.7	0.013
Hemoglobin (g/dL)	13.7 (11.7–15.2)	14.5 (13.3–15.6)	0.004
Platelet count (k/μL)	221 (197–283)	223 (182–262)	0.37
Diseased vessels	1 (1–2)	1 (1–2)	0.52

and those without a history of cancer (48.3% vs. 37.4%; $p = 0.1$). There was no significant difference in the number of patients between groups who underwent CABG, with 19 (3.1%) total patients undergoing further CABG. Nor was there a significant difference in the number of patients who received thrombolytics, with 30 (4.9%) total patients receiving thrombolytics prior to PCI.

Procedural medications were not significantly different between groups, with an overall utilization rate of 99.5% for heparin, 53.5% for bivalirudin, and 48.4% for glycoprotein IIb/IIIa inhibitors. Some patients received multiple procedural medications. Discharge medications (Table 3) showed no significant differences between groups. Although not significantly different, patients with a history of cancer were discharged on ticagrelor less often than those without a history of cancer (3.7% vs. 10.9%; $p = 0.1$).

Possible disposition locations were discharge to home, a facility (skilled nursing facility, rehabilitation center, or long term acute care hospital), or hospice/mortality. Overall, 87.4% of patients were discharged to home. No significant differences were evident between cancer history versus no cancer history with respect to discharge location ($p = 0.34$): home (82.8% vs. 87.8%), facility (10.3% vs. 5.9%), and hospice/mortality (6.9% vs. 6.4%).

4. Discussion

This study showed no difference in the incidence of in-hospital complications between patients with a history of cancer and patients without a history of cancer undergoing primary PCI for STEMI. Additionally, we reported a lower rate of drug eluting stents in patients with a history of cancer compared to those without a history of cancer.

To our knowledge, only one previous study has assessed multiple in-hospital complications in STEMI patients with a history of cancer undergoing primary PCI [9]. In this retrospective single-center study, Wang et al. found 11.1% of STEMI patients undergoing PCI had a history of cancer [9]. In addition, the authors reported an increase in in-hospital mortality (4.9% vs 7.7%; $p = 0.07$) and 5-year all-cause mortality (16.8% vs 34.2%; $p < 0.001$) largely due to cancer related deaths. Furthermore, they found an increase in select in-hospital complications, such as blood transfusions (15.7% vs 7.9%; $p < 0.001$) and acute kidney injury (7.3% vs 2.9%; $p < 0.001$) with no difference in CHF or shock. Another study assessing the effect of cancer history on STEMI patients by Velders et al., showed significantly higher utilization of intra-aortic balloon pumps in patients with a history of cancer compared to those without a history of cancer (6.7% vs. 3.9%; $p = 0.041$) [8]. For our study, similar results were found regarding incidence of cancer in STEMI patients undergoing PCI (9.5%) and overall in-hospital mortality (5.9%). However, our study showed no significant differences in overall or individual in-hospital complications. These differences in complication rates between studies may be due to differing definitions of complications, variations in institutional practices and patient populations, and changes in overall practice from the years of 2006–2009 for Velders et al., 2000–2010 for Wang et al., and 2012–2017 for our study.

While no differences were noted in in-hospital complications, key differences in treatment modalities were highlighted within our results. Patients with a history of cancer were less likely to receive drug eluting stents compared to bare metal stents. This finding is consistent with two previous studies assessing cancer history in STEMI patients [8,9]. During our study period, guideline recommendations shifted toward use of the more potent $P2Y_{12}$ inhibitors, ticagrelor and prasugrel [12]. Differences in discharge rates for the potent $P2Y_{12}$ inhibitors were not statistically significant, but included 5 (9.3%) patients with a history of cancer and 84 (16.3%) patients without a history of cancer receiving ticagrelor or prasugrel upon discharge. The lower rate of potent $P2Y_{12}$ inhibitors upon discharge and preferential use of bare metal stents, ultimately requiring shorter durations of dual antiplatelet therapy, may indicate a

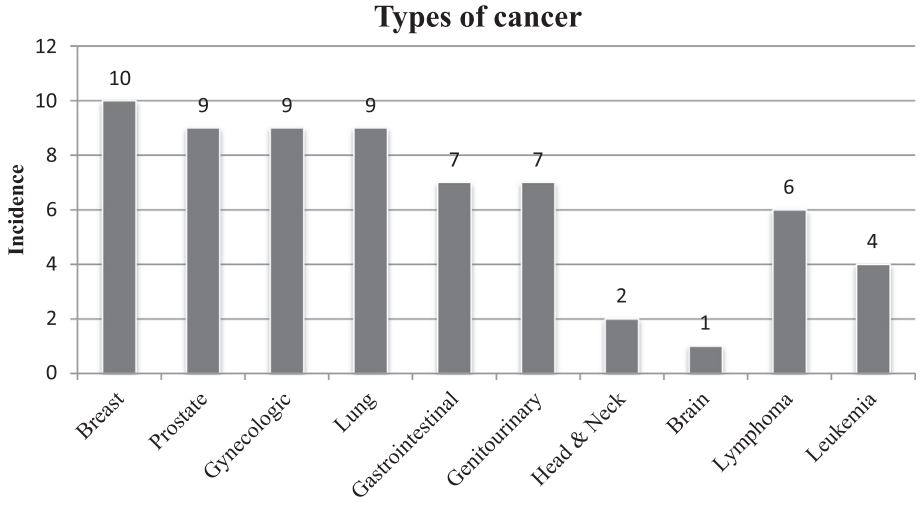

Fig. 1. A total of 58 subjects had a history of cancer. Some subjects had multiple types of cancer leading to a total of 64 cancers identified.

Table 2
In-hospital complications. Data are presented as n (%).

	Cancer history (n = 58)	No cancer history (n = 551)	Odds ratio (95% confidence interval)	p-value
Composite primary endpoint	23 (39.7)	206 (37.4)	1.10 (0.61–1.92)	0.73
In-hospital mortality	3 (5.2)	33 (6.0)	0.86 (0.25–2.88)	0.85
Cardiogenic shock	6 (10.3)	59 (10.7)	0.96 (0.40–2.34)	0.93
Heart failure	2 (3.5)	45 (8.2)	0.40 (0.10–1.70)	0.22
Mechanical circulatory support requirement	4 (6.9)	46 (8.4)	0.81 (0.28–2.35)	0.70
Ventricular arrhythmia	11 (19.0)	104 (18.9)	1.01 (0.50–2.01)	0.99
Atrial fibrillation	5 (8.6)	27 (4.9)	1.83 (0.68–4.95)	0.23
Cardiac arrest	5 (8.6)	47 (8.5)	1.01 (0.39–2.65)	0.98
Stroke	1 (1.7)	8 (1.5)	1.19 (0.15–9.69)	0.87
Bleeding	6 (10.3)	55 (10.0)	1.04 (0.43–2.53)	0.93
New dialysis requirement	0	8 (1.5)	–	–
Re-infarction	1 (1.7)	7 (1.3)	1.36 (0.17–11.3)	0.77

trend in practice surrounding the idea that cancer patients are at a higher bleeding risk. This may be due to the perceived risk of thrombocytopenia and anemia from cancer therapy or the need to discontinue dual antiplatelet therapies for impending surgeries. The optimal type of stent, antiplatelet regimen, and duration of therapy for the cancer population is not well defined, particularly the strategies to best balance the bleeding and hypercoagulable risk associated with cancer.

The unique cancer population is strength of our study. There was a high incidence of breast, prostate, genitourinary, gynecologic, and lung cancers as compared with previous studies that focused only on certain cancers or had a lower rate of genitourinary cancer patients [8–10]. The utilization of cytotoxic chemotherapy (41.3%) noted in our patient population was markedly higher than what was seen in previous studies with 22.2% by Wang et al. and 23.2% Velders et al. This may be due to the large comprehensive cancer center associated with our institution, which, as a tertiary care academic referral center, may have a more advanced and variable patient population. While many types of chemotherapy are likely to cause anemia and thrombocytopenia, no clinically significant differences between baseline hemoglobin and platelets were noted. This is likely due to the low proportion of patients who were actively undergoing chemotherapy during the time of STEMI diagnosis.

Due to the increased incidence of cardiovascular disease in cancer patients, it is imperative to ensure patients are treated appropriately. Therefore, our study assessed differences in discharge medications following a STEMI. The data are encouraging and contradict what is described in previous studies that have shown cancer patients as less likely to be discharged on appropriate guideline recommended therapies [13,14] including aspirin, $P2Y_{12}$ inhibitors, statins, and beta blockers [15]. Our results illustrated nearly all cancer patients being discharged on guideline recommended therapies with 100% of cancer patients receiving aspirin, 94.4% receiving a $P2Y_{12}$ inhibitor, 98.2% receiving a statin, and 100% receiving beta blockers.

There is a paucity of data describing characteristics of cancer patients without PCI for STEMI. An exploratory analysis of the 44 patients excluded for not undergoing PCI included 7 (15.9%) patients and 37 (84.1%) patients with and without a cancer history, respectively. Treatment modalities for non-PCI subjects included isolated CABG, thrombolytics without further PCI, and medical management. Of note, medical management was utilized in 5 cancer patients (71.4%) and 19 non-cancer patients (51.4%). The composite endpoint occurred in 5 (71.4%) patients with a history of cancer versus 25 (67.6%) patients without a history. Although complication rates were similar between the groups, the overall complication rate of 68.1% was much higher in those who did not pursue PCI than the 37.6% complication rate of patients in the PCI cohort, potentially pointing to an overall higher risk patient population. This is consistent with the results of a nationwide registry study in which cancer patients were less likely to receive PCI and had a higher incidence of mortality if PCI was deferred [10].

Table 3
Discharge medications. Data are presented as n (%). Excludes patients whose final disposition was mortality or discharge to hospice. ACE = angiotensin converting enzyme.

	Cancer history (n = 54)	No cancer history (n = 516)	p-value
Aspirin	54 (100)	516 (100)	–
Clopidogrel	48 (88.9)	429 (83.1)	0.28
Prasugrel	3 (5.6)	28 (5.4)	1.0
Ticagrelor	2 (3.7)	56 (10.9)	0.1
Statin	53 (98.2)	508 (98.5)	0.59
Beta blocker	54 (100)	504 (97.7)	0.62
ACE inhibitor	40 (74.1)	349 (67.6)	0.33
Angiotensin II receptor blocker	2 (3.7)	39 (7.6)	0.41
Aldosterone antagonist	4 (7.4)	16 (3.1)	0.11

A few limitations existed within our study. First, the study had a limited sample size and was single-centered. Additionally, as with any registry study, the definitions for data collection were pre-defined within the registry, but the data were subject to error on data abstraction, recording, or availability within retrospective chart review. To minimize errors in data abstraction, endpoints previously collected in the registry were validated upon individual chart review. The study was limited to in-hospital and 30-day outcomes, and long-term outcomes were not defined. Furthermore, differences in the use of bare metal stents versus drug eluting stents are unlikely to impact in-hospital complications and mortality, but rather are more likely to impact long-term outcomes, which cannot be determined from this study. This may start to be evident with the higher rate of 30-day readmission in patients with a history of cancer. Also, the heterogeneous cancer population relays a real-life example of the wide variety of cancer patients who can undergo a STEMI. This data categorizes all patients with a history of cancer into one group regardless of the differing cancer characteristics. Each patient has a unique type of cancer, treatment, and staging/time since diagnosis, which makes guiding appropriate therapy difficult. Further research into select cancers, treatments, and staging/time since diagnosis is needed to guide clinical care on an individual basis. Lastly, three key patient populations that need to be elucidated in further studies are those actively undergoing cancer treatment, stage IV cancer patients, and those not undergoing PCI. With a limited sample size in the current study, the results cannot be fully applied to those sub-groups of patients. Ultimately, the proper management, both in-hospital and at discharge, for STEMI patients undergoing PCI with cancer is still relatively unknown. Due to the unlikelihood of randomized controlled trials to be published on this patient population, further guidance from registry studies are needed to help determine proper care for these patients.

5. Conclusions

In conclusion, this single-center retrospective registry study found no significant difference for in-hospital complications in patients with

a history of cancer as compared to patients without a history of cancer undergoing primary PCI for STEMI.

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