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RESEARCH LETTER

Suboptimal Use of Cardioprotective Medications in Patients With a History of Cancer

Modern cancer therapies have led to improved survival rates for many cancers. Rates of cardiovascular diseases (CVD) and risk factors are increased in cancer patients and survivors compared with the general population, and CVD has emerged as a leading cause of long-term morbidity and mortality in this population (1). Cardioprotective medications, including statins, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, and antiplatelet therapies remain cornerstones of primary and secondary CVD prevention. However, data regarding the use of cardioprotective medications among cancer patients and survivors have been inconsistent.

To examine the use of cardioprotective medications in a high-CVD risk population with or without a history of cancer (CaHx), we conducted a cross-sectional observational study of 333 patients admitted to the cardiology unit at John Hunter Hospital between July 2018 and January 2019. Cardioprotective medication prescription was assessed preadmission; patients who did not have an indication for cardioprotective medications were excluded (n = 13). Data were collected directly from patients and medical records. Patients were divided into 2 groups: those with CaHx and those without CaHx. This study was approved by the Hunter New England Human Research Ethics Committee. All patients provided written informed consent.

Patient characteristics were summarized as mean ± SD or number (percentage). Between-group differences were compared using Student *t* tests for means and the chi-square analyses for percentages. Logistic regression analyses were used to estimate the adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for CaHx as an independent predictor of cardioprotective medication use and prescription at the time of admission, with each cardiovascular therapy modeled separately. All models were adjusted for age, sex, body mass index (BMI), smoking status, hypertension, dyslipidemia, diabetes mellitus, and CVD. All analyses were performed using the SPSS 25 System for Windows (IBM Corp., Armonk, New York). Statistical significance was defined as a 2-tailed $p < 0.05$.

Table 1 summarizes patient characteristics for the entire cohort (N = 320) and stratified by CaHx (n = 69). Only 11 patients were receiving active cancer treatment, as the cancer diagnosis on average predated the index admission by 11 ± 12.9 years. Predominant cancer types were colorectal (20.3%), breast (13.0%), and melanoma (11.6%). In this cross-sectional analysis, of the 69 patients with cancer, 25 (36.0%) had established CVD prior to their cancer diagnosis, while 44 (64.0%) developed CVD after their cancer diagnosis. Cardiovascular risk factors were similar in CaHx patients compared with those without CaHx. There were no significant differences in age, BMI, sex, hypertension, diabetes, dyslipidemia, or atrial fibrillation between these 2 groups. However, CaHx patients had lower utilization rates of antiplatelet therapies (p = 0.007) and statins (p = 0.010), compared with those without CaHx. There were also lower rates of ACE inhibitor or ARB and beta-blocker use, although these were not significant (p = 0.405 and p = 0.243, respectively). Notably, CaHx patients were more likely to have heart failure as the reason for admission.

In multivariable analysis, adjusted for age, sex, BMI, hypertension, dyslipidemia, smoking status, diabetes mellitus, and CVD, patients with CaHx were less likely to be on a statin or antiplatelet therapies (OR: 0.41; 95% CI: 0.22 to 0.77; p = 0.006; and OR: 0.53; 95% CI: 0.29 to 1.00; p = 0.049, respectively). ACE inhibitor or ARB and β-blocker use were not statistically significantly different between the 2 groups (OR: 0.62; 95% CI: 0.34 to 1.12; p = 0.109; and

OR: 0.63; 95% CI: 0.35 to 1.14; p = 0.132, respectively), although point estimates were <1. We also evaluated prescription of cardioprotective medications at the time of admission. In multivariable models (adjusted for the same confounders as detailed previously), prescriptions of antiplatelet agents and statins were similarly lower in patients with CaHx (OR: 0.43; 95% CI: 0.25 to 0.77; p = 0.004; and OR: 0.38; 95% CI: 0.20 to 0.70; p = 0.002 respectively).

These results suggest that management of modifiable cardiovascular risk factors in patients with cancer is suboptimal compared with those without a

TABLE 1 Patient Characteristics

	All Patients (N = 320)	Patients Without History of Cancer (n = 251)	Patients With History of Cancer (n = 69)	p Value*
Age, yrs	65.3 ± 13.3	64.5 ± 13.4	68.2 ± 12.5	0.039
Male	207 (62.3)	163 (64.9)	38 (55.1)	0.160
BMI, kg/m^2	29.4 ± 6.9	29.3 ± 6.4	30.0 ± 8.5	0.444
Primary reason for admission				
ACS/CHD	218 (68.1)	178 (70.9)	40 (58.0)	0.057
Heart failure	61 (19.1)	40 (15.9)	21 (30.4)	0.009
Atrial fibrillation	9 (2.8)	6 (2.4)	3 (4.3)	0.411
Other	32 (10.0)	27 (10.8)	5 (7.2)	0.500
Past medical history				
Ischemic heart disease	287 (89.7)	227 (90.4)	61 (88.4)	0.396
Hypertension	148 (46.3)	112 (44.6)	36 (52.2)	0.278
Dyslipidemia	94 (29.4)	74 (29.5)	20 (29.0)	1.000
Diabetes	82 (25.6)	64 (25.5)	18 (26.1)	0.676
Heart failure	72 (22.5)	71 (28.3)	24 (34.8)	0.049
Atrial fibrillation	58 (18.1)	39 (15.5)	19 (27.5)	0.033
Stroke	31 (9.7)	23 (9.2)	9 (13.0)	0.611
Cardiovascular medication use				
Statins	244 (76.3)	200 (79.7)	44 (63.8)	0.010
ACE inhibitor/ARB	192 (60.0)	154 (61.4)	38 (55.1)	0.405
β-blockers	219 (68.4)	176 (70.1)	43 (62.3)	0.243
Antiplatelets	229 (71.6)	189 (75.3)	40 (58.0)	0.007
DOAC	47 (14.7)	36 (14.3)	11 (15.9)	0.705
Cancer type/site				
Brain		N/A	3 (4.3)	
Breast		N/A	9 (13)	
Colorectal		N/A	14 (20.3)	
Lung		N/A	3 (4.3)	
Lymphoma		N/A	4 (5.8)	
Melanoma		N/A	8 (11.6)	
Ovarian		N/A	4 (5.8)	
Prostate		N/A	6 (8.7)	
Renal		N/A	3 (4.3)	
Upper GI		N/A	3 (4.3)	
Other		N/A	12 (17.4)	
Any active cancer therapy		N/A	11 (15.9)	
Anthracycline-containing		N/A	3 (4.3)	
Immunological/biological therapy		N/A	6 (8.7)	
Nonanthracycline chemotherapy		N/A	2 (2.9)	

Values are mean ± SD or n (%). *Statistical comparison between the groups without vs. with history of cancer.

ACE = angiotensin-converting enzyme; ACS = acute coronary syndrome; ARB = angiotensin receptor blocker; BMI = body mass index; CHD = coronary heart disease; DOAC = direct oral anticoagulant; GI = gastrointestinal; N/A = not applicable.

history of cancer. Cancer survivors have up to a 15-fold higher risk of developing CVD (1), and CVD is recognized as a leading cause of long-term morbidity and mortality. While a major focus of cardio-oncology research has been on cancer therapy–induced cardiotoxicity, optimization of cardiac care in patients with CaHx has not been widely addressed. In patients with CVD and a high burden of cardiovascular risk factors, we observed that use of cardioprotective therapies was significantly lower in patients with previous cancer compared to those without, despite similar cardiovascular risk profiles. Moreover, given that CaHx is associated with an increased CVD risk (2), we believe that this issue is of substantial public health importance.

Some prior studies have also suggested that there may be a greater use of guideline-directed therapy but less use of coronary artery bypass surgery in cancer patients (3), whereas data from a large registry of patients who suffered from a myocardial infarction suggest underutilization of statins and $P2Y_{12}$ blockers in this population (4). Our study supports the latter finding and expands it to other CVD groups, as cancer patients or survivors with comparable CVD and risk factors were less likely to receive guideline-recommended therapies compared with those without prior cancer.

In terms of study limitations, although there is left truncation of our data, we expect that immortal time bias would result in the creation of a healthier survivor cohort. Although this was a single-center study from a large tertiary regional hospital, this may also not be reflective of other health centers. However, utilization of cardioprotective therapies in patients without CaHx is consistent with clinical guidelines and other health centers. Although we accounted for a number of covariates, there is also a risk for uncontrolled confounding, and the exact indications for medication prescription were not identified in each individual patient. We also lacked data on cancer treatments; however, our study was not designed to look at effects of cancer treatments on cardiovascular sequelae, but rather to look at utilization of cardioprotective therapies.

In conclusion, our study identified that cardioprotective therapies, especially statins and antiplatelet agents, are underutilized in patients with CaHx compared with patients without cancer and comparable cardiovascular risk factors. This highlights practice and policy gaps and the need to develop strategies to improve guideline-directed cardioprotective therapies in cancer patients and survivors.

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