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Short Communication

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Baseline Electrocardiographic Abnormalities in Pre-Treatment Cancer Compared With Non-Cancer Patients: A Propensity Score Analysis

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Abstract

Background: Most studies have compared post-treatment electrocardiogram (ECG) abnormalities in cancer patients to the general population. To assess baseline cardiovascular (CV) risk, we compared pre-treatment ECG abnormalities in cancer patients with a non-cancer surgical population.

Methods: We conducted a combined prospective (n = 30) and retrospective (n = 229) cohort study of patients aged 18 - 80 years with diagnosis of hematologic or solid malignancy, compared with 267 pre-surgical, non-cancer, age- and sex-matched controls. Computerized ECG interpretations were obtained, and one-third of the ECGs underwent blinded interpretation by a board-certified cardiologist (agreement r = 0.94). We performed contingency table analyses using likelihood ratio Chi-square statistics, with calculated odds ratios. Data were analyzed after propensity score matching.

Results: The mean age of cases was 60.97 ± 13.86; and 59.44 ± 11.83 years for controls. Pre-treatment cancer patients had higher likelihood of abnormal ECG (odds ratio (OR): 1.55; 95% confidence interval (CI): 1.05 to 2.30), and more ECG abnormalities (χ^2 = 4.0502; P = 0.04) compared with non-cancer patients. ECG abnormalities were higher in black compared to non-black patients (P = 0.001). In addition, baseline ECGs among cancer patients prior to cancer therapy demonstrated less QT prolongation and intra-ventricular conduction defect (P = 0.04); but showed more arrhythmias (P < 0.01) and atrial fibrillation (AF) (P = 0.01) compared with the general patient population.

Conclusions: Based on these findings, we recommend that all cancer patients receive an ECG, a low-cost and widely available tool, as part of their CV baseline screening, prior to cancer treatment.

Keywords: Arrhythmia; Electrocardiography; Guidelines; Screening; Cancer patients

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Introduction

The cardiotoxic effects of cancer treatments contribute to approximately 5 million emergency visits annually in the United States. As such, much attention needs to be paid to pre-existing cardiovascular disease (CVD), which may be undiagnosed prior to cancer therapy. In most trials, limited cardiac screening before cancer therapy makes it difficult to assess pre-existing, undiagnosed CVD; as a result, subsequent CVD manifestations are sometimes improperly attributed to cancer therapy. In this cohort with a diverse racial makeup, we aimed to explore pre-treatment electrocardiogram (ECG) abnormalities as a marker of baseline CVD among patients prior to cancer treatment compared with non-cancer patients.

Materials and Methods

We performed a prospective (n = 30) and retrospective (n = 229) cohort study on patients aged 18 - 80 years old, with hematologic or solid malignancy. The control group comprised 267 pre-surgical, non-cancer, age- and sex-matched controls. Prospective data were obtained from a randomized selection of patients planned to receive their cancer treatment at Rush University Medical Center (RUMC) while retrospective data were obtained from 2013 - 2018 archives of RUMC Cancer Registry and a pool of pre-surgical, non-cancer patients. This study was approved by the RUMC Institutional Review Boards committee; and all prospective patients provided informed consent. This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Each ECG, recorded at 25 mm/s speed and 10 mm/mV amplification, was interpreted by the integrated software, and confirmed by an experienced cardiologist per standard prac-

Table 1. Baseline Characteristics and Electrocardiogram Comparisons Between Cases and Controls

Characteristics	Controls n = 267, (%)	Cases n = 228, (%)	P value	OR[a] (95% CI)
Demographic				
Age (years ± SD)	59.44 ± 11.83	60.97 ± 13.86		
White	133 (49.8)	110 (48.2)		
Hispanic and Latino	57 (21.3)	23 (10.1)		
Black/African American	84 (31.1)	86 (37.7)		
Native American/American Indian	1 (0.4)	2 (0.9)		
Asian/Pacific Islander	4 (1.5)	8 (3.5)		
South Asian	1 (0.4)	0 (0.0)		
ECG parameter				
ECG abnormal[b]	103 (39)	108 (48)	0.02	1.55 (1.05 - 2.30)
ST/T abnormalities	61 (22.8)	46 (20.2)	0.64	0.87 (0.54 - 1.41)
Bundle branch block	24 (9.0)	18 (7.9)	0.86	0.89 (0.43 - 1.83)
Arrhythmias[c]	7 (2.6)	52 (22.8)	< 0.01	10.88 (4.53 - 31.75)
Premature beats	17 (6)	22 (10)	0.04	2.16 (0.97 - 5.06)
QT prolongation	21 (7.9)	8 (3.5)	0.04	0.40 (0.15 - 0.98)
Low voltage QRS	8 (3.0)	4 (1.8)	0.54	0.56 (0.12 - 2.26)
Heart block	10 (3.7)	7 (3.1)	0.80	0.77 (0.24 - 2.37)
LVH	14 (5.2)	13 (5.7)	1.00	1.00 (0.42 - 2.40)
RBBB	17 (6.4)	13 (5.7)	0.70	0.80 (0.34 - 1.82)
LBBB	12 (4.5)	7 (3.1)	0.80	0.77 (0.24 - 2.37)
Intraventricular conduction defect	18 (6.7)	5 (2.2)	0.04	0.31 (0.09 - 0.94)
Atrial fibrillation	1 (0.4)	10 (4.4)	0.01	10.37 (1.45 - 452.90)
Left atrial abnormality	18 (6.7)	7 (3.1)	0.08	0.42 (0.14 - 1.11)
Left axis deviation	14 (5.2)	12 (5.3)	1.00	1.09 (0.43 - 2.80)
Right axis deviation	3 (1.1)	2 (0.9)	1.00	0.66 (0.05 - 5.85)

[a]After propensity score matching for CAD, hypertension, and Hispanic or Latino ethnicity. [b]Based on summed ECG score with each abnormality tallied as 1 point. [c]Includes tachycardic, bradycardic and irregular rhythm. CI: confidence interval; ECG: electrocardiogram; LBBB: left bundle branch

tice. One-third of ECGs underwent blinded interpretation by another board-certified cardiologist (agreement r = 0.94). ECG abnormalities were compared between cancer and non-cancer patients, and a summed ECG score was calculated with each abnormality tallied as 1 point (Table 1). Statistical analysis was performed using R statistical software version 3.4.3. Package Matchit was used for propensity score matching. Nearest neighborhood method was used for matching. Results were reported as odds ratio (OR) with 95% confidence interval (CI). P value < 0.05 was considered significant.

Results

A total of 228 cases and 267 controls were included in the final analysis. The mean age for the cases cohort was 60.97 ± 13.86 years, and 59.44 ± 11.83 years for the control cohort; 243 (49%) white and 170 (34%) black. The study included 300 (61%) females; and a sum of 211 patients had abnormal ECGs: 35.2% diabetes, 72.5% hypertension, 18% CAD, 3.8% coronary artery bypass graft, 10.9% atrial fibrillation (AF), and 9% valvular issues. Nearest neighborhood propensity score matching was performed for CAD, hypertension, and Hispanic or Latino ethnicity based on parameters that were significantly different between groups; 228 cases were matched with 228 controls, mean age 57.12 ± 10.91 and 60.97 ± 13.86, respectively. More abnormal ECGs were noted among the pre-treatment cancer group than the control group (OR: 1.55, 95%, CI: 1.05 - 2.30; P = 0.02) (Table 1). ECG abnormalities were higher in black compared to non-black patients (P = 0.001). In addition, baseline ECGs among cancer patients prior to cancer therapy demonstrated less QT prolongation and intra-ventricular conduction defect (P = 0.04); but showed more arrhythmias (P < 0.01) and AF (P = 0.01) compared with the general patient population.

Discussion

We found that cancer patients referred to our cancer center had an overall 55% higher chance of ECG abnormalities, based on

a summed ECG parameter score, when compared with the non-cancer population. These ECG abnormalities were two times higher among black compared with non-black patients. To our knowledge, this is the first study that has compared baseline ECG characteristics of cancer patients with non-cancer patients before chemotherapy; and with racial/ethnic implications. In a general population of patients, Movahed et al found that African Americans had 2.5 times higher baseline ECG abnormalities independent of echocardiographic abnormalities or demographics [1]; our study demonstrated similar findings.

Although cancer patients are known to have a high prevalence of arrhythmias during and post-chemotherapy, our study found that they also have higher likelihood of arrhythmias (including AF) in the pre-treatment phase. These arrhythmias can be attributed to electrolyte abnormalities, paraneoplastic syndrome, overlapping risk factors for cancer and cardiac disease, and metastasis of cardiac and autonomic nervous system in cancer patients [2, 3]. At least one electrolyte or acid-base abnormality has been demonstrated in nearly 58% of cancer patients, with hypocalcemia being most common [4].

Our study was limited by a small sample size. Even after propensity score matching, there were significant differences in certain baseline variables between cases and controls that could affect ECG outcomes in our study participants. Furthermore, not all study participants were prospectively enrolled, and this study was not a randomized controlled trial; thus, residual confounding was not accounted for at this time.

In conclusion, we found that cancer patients had more baseline ECG abnormalities, particularly arrhythmias and AF, compared with non-cancer patients. These findings of ECG abnormalities were higher among blacks in our study and could possibly be a marker of higher baseline cardiovascular risk in this population going into cancer therapy. In line with the new cardio-oncology guidelines [5], we recommend that all cancer patients receive an ECG, a low-cost and widely available tool, as part of their cardiovascular baseline screening, prior to cancer treatment. Baseline cardiac screening with ECG may help with overall cardiac outcomes, by detecting early pre-existing conditions that can result in alternative chemotherapeutic treatments and closer cardiac monitoring during cancer treatment. The peri-treatment cardiovascular prognostic implications of higher baseline ECG abnormalities among black cancer patients require further exploration. Further research could also evaluate how our study findings translate into future prediction of cardiovascular events.

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Financial Disclosure

None to declare.

Conflict of Interest

All authors have nothing to disclose.

Informed Consent

Informed consent was obtained from the patients who participated in the prospective portion of the study. Patient information was deidentified.

Author Contributions

Lolita Golemi and Alexandra Sarau were involved in data collection and drafting and revising the manuscript. Akash Sharma assisted with analysis and data interpretation. Rajiv Varandani was involved in data collection and conception and design of the project. Christopher W. Seder gave final approval of the manuscript submitted. Tochi M. Okwuosa designed the study and was also involved in data interpretation, revision of the manuscript and final approval of the submitted manuscript.

Data Availability

The data that support the findings of this study are available from the corresponding author (TO), upon request.

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