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Comparison of Framingham risk score and chest-CT identified coronary artery calcification in breast cancer patients to predict cardiovascular events

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ABSTRACT

Background: In breast cancer patients, coincidental detection of CAC at chest CT may be important in determining cardiovascular (CV) outcomes and facilitate CV disease primary prevention strategies.
Methods: 408 consecutive breast cancer patients referred to cardiac oncology clinic were included in the study. 256 patients without a prior history of coronary artery disease had undergone a chest CT. CT images were reviewed to detect CAC. Framingham risk score (FRS) was calculated and patient electronic medical records were interrogated to document the incidence of a composite clinical end point of all-cause mortality and cardiac events (coronary revascularization, heart failure hospitalization and de novo atrial fibrillation). Prevalence of statin prescribing was also collected.
Results: Patients were followed for a median of 6.5 years. 112 clinical events occurred. Clinical follow up was 98%. CAC was found in 26% of patients. On multivariable analysis, CAC and advance cancer stage, but not FRS predicted the composite clinical end point (OR for CAC 2.59, $p < 0.01$). CAC but not FRS also predicted the incidence of cardiac events (OR for CAC 4.90, $p < 0.01$). CAC was present in 7.3% of patients with low FRS; none had been prescribed a statin. In patients with CAC and FRS $\geq$ 10%, 45% were not on a statin.
Conclusion: CAC is a common coincidental finding at CT chest in breast cancer patients referred to cardiac oncology. CAC but not FRS was predictive of composite clinical events and cardiac events. Detection of CAC at chest CT could alter the prescribing of primary prevention strategies to help prevent future cardiac events in breast cancer patients.

1. Introduction

Breast cancer patients commonly undergo computed tomography (CT) chest imaging [1]. At CT chest coincidental coronary artery calcification (CAC) may be detected [2]. CAC denotes calcified coronary atherosclerosis and predicts cardiovascular mortality [3]. Cardiovascular disease is an important determinant of long term survival in breast cancer [4]. Coincidental CAC detection at chest CT in breast cancer patients could therefore influence physician and patient attitudes toward cardiovascular risks and cardiovascular primary prevention strategies.

For breast cancer patients, coronary artery disease, heart failure and atrial fibrillation can be important clinical events. In the absence of a clinical risk score to predict all three conditions, clinicians often employ cardiovascular primary prevention scoring systems to help determine a cardiovascular risk. This approach also acknowledges the role of ischemic heart disease in the pathology of heart failure and atrial fibrillation.

As a primary risk stratifier, the Framingham risk score (FRS) is widely used to define cardiovascular disease susceptibility [5]. FRS however may not be reliable in predicting heart failure events or the incidence of atrial fibrillation. Furthermore in some demographic populations FRS may not be accurate at predicting coronary artery disease such as the elderly in whom it over estimates risk; or in patients with cancer in whom it may under estimate risk [5,6]. This reflects the derivation of FRS using a population based approach to predict cardiovascular disease.

Coincidental detection of CAC at chest CT may offer a more personalized assessment of cardiovascular risks in the cancer population. Such personalized data could assist primary prevention strategies. An individualized approach to cardiovascular risk assessment is of particular interest to cancer patients who are often subject to polypharmacy and

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focused care [7]. In addition: CAC, in contrast to FRS, may also be predictive of other important cardiac conditions which contribute to morbidity in cancer patients such as atrial fibrillation and heart failure [8–10]. CAC could therefore provide a potential risk stratification concerning both cardiovascular and cardiac risk assessment in cancer patients.

Assessment of cardiac risk and cardiovascular susceptibility are often undertaken at cardiac-oncology clinics [11]. We therefore sought to establish the prevalence of CAC on CT chest exams from patients with breast cancer attending a cardiac oncology clinic. We hypothesized that CAC would predict cardiovascular and cardiac events in this population and that CAC would be incremental to FRS in risk prediction.

2. Methods

Permission for the study was granted by the Ottawa Hospitals research ethics board.

2.1. Study sample

408 consecutive breast cancer patients of all stages referred to the cardio-oncology clinic at the Ottawa General Hospital from 2009 to 2017 were included in the study. 269 patients had undergone prior non-ECG gated Chest CT either as part of cancer staging, disease surveillance or to investigate concomitant morbidity (pneumonia or pulmonary embolism). 256 fulfilled the inclusion criteria (a history of breast cancer, prior non-ECG gated CT chest and no documented coronary artery disease, or atrial fibrillation). Patients were excluded from the analysis due to the absence of chest CT or a clinical history of prior atrial fibrillation or coronary artery disease (myocardial infarction or coronary revascularization).

2.2. CT chest derived coronary calcium score

CT scans were performed using multi-detector CTs [12]. Images were non-ECG gated chest CT scans with or without contrast enhancement [1,13,14]. Soft tissue kernel slice-thickness images ranged from 1.0 to 5.0 mm and were acquired using Aquillon 16-, 64-, 320-detector (Toshiba Canada Medical Systems Limited, Markham, Ontario); Lightspeed Plus 16- and Lightspeed 64-detector (General Electric Healthcare, Mississauga, Ontario) and Definition Flash dual source 64 × 2-detector (Siemens Medical Solutions Canada, Oakville, Ontario). CT studies were reviewed to determine the presence of CAC without additional processing using patient archiving and communication system (PACS) software (McKesson Radiology 12.3, McKesson Canada, Mississauga, Ontario).

2.3. Coronary artery calcification (CAC)

CAC was identified using a visual ordinal scoring system [2,15]. Calcium in the left main, left anterior descending artery, left circumflex and right coronary arteries was categorized as absent (0) or present. The degree of calcification (1, 2, or 3) was classified according to the vessel length that was calcified. 1 point was given for involvement of 1/3. 2 if 2/3 and 3 if >2/3 were calcified. The final score was the sum of the individual artery scores from 0 to 12 (see Fig. 3 in Supplementary data). Patients were divided into 4 groups based on their final scores: 0, 1–3, 4–5 and 6–12. These scores correspond to Agatston scores of 0, 1–100, 101–400 and >400 [15].

2.4. Clinical demographics

Patient cardiovascular risk factors, cardiac history and cancer history were obtained from a comprehensive review of the electronic medical records.

2.5. Clinical events

Clinical events were determined from the electronic medical record without knowledge of patients' CAC findings. A composite of all-cause mortality and cardiac events (non-fatal myocardial infarction, coronary revascularization, new atrial fibrillation or heart failure episode requiring hospitalization) was used as a primary end point. Secondary end points comprised the primary end point composite factors. Physician diagnosed cause of death was retrieved from the medical record. Patients with advanced cancer that were referred to a terminal care facility were assumed to have experienced a cancer related death. Evidence of continued event free survival was confirmed through review of oncology and/or cardiology clinic electronic medical records.

Heart failure hospitalization was defined by an admission due to dyspnea necessitating an escalation in diuretic dose. New atrial fibrillation was determined by the clinical reporting of atrial fibrillation in patients not previously known to suffer from atrial fibrillation or atrial flutter. Non-fatal myocardial infarction was determined by the presence of at least two of the following: chest pain, rise and fall in troponin I and ischemic ECG changes [16]. Coronary revascularization was defined by percutaneous coronary intervention or coronary artery by-pass surgery as documented in the electronic medical record.

2.6. Patient follow up

Breast cancer patients included in the study underwent regular (3–12 monthly) follow up in cardiac-oncology and/or oncology as clinically indicated. Follow-up was censored after the first clinical event.

2.7. Statistical analysis

Continuous variables were presented as the mean ± the standard deviation. Categorical data are presented as numbers and percentages. Categorical variables were compared using the Chi squared test: continuous variables were compared using the Mann-Whitney *U* test. The primary analysis was performed using univariable analysis to assess the association of clinical variables and CAC with the primary composite clinical end point. Variables that achieved a significance of $p < 0.2$ were included in the multivariable analysis by binary logistic regression as covariates. A more generous significance value was employed to adjust for the possibility of confounding variables [17,18]. Secondary analyses were performed in patients with cardiac events (cardiac mortality, revascularization, new atrial fibrillation, hospitalization for heart failure) by univariable and multivariable analysis. The association between CAC and the primary composite end point and between CAC and cardiac events was evaluated with adjusted Cox proportional hazard analysis (adjusted for cancer stage and the Framingham risk score which includes hypertension, dyslipidemia, diabetes, smoking and age). Data were analyzed using IBM SPSS 24 statistics for Windows (Armonk, NY: IBM Corp). Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Demographics

256 breast cancer patients were followed for a median of 6.5 years (interquartile range 4.0–10.3 years) after their diagnosis of breast cancer. Detailed demographic characteristics are presented in Table 1. 7 patients (2%) were lost to follow up during the course of the study.

3.2. Coronary artery calcification (CAC)

CT scans were performed within a median of 1 year of the cardiac oncology clinic visit (Interquartile range 0–3 years). CAC was demonstrated in 66 (25.8%) patients on CT chest imaging. Estimated Agatston scores of severe CAC calcification (>400) were seen in 9 patients

Table 1
Patient characteristics.

Demographics	CAC present	CAC absent	p value
Sample	66	190	–
Age (mean/95% CI)	69.2 (66.9–71.6)	54.8 (53.4–56.3)	<0.001
Gender			
Female	64 (97.0%)	188 (98.9%)	0.264
Clinical presentation			
Reduced LVEF (<53%)	29 (43.9%)	109 (57.4%)	0.059
Palpitations	7 (10.6%)	30 (15.8%)	0.302
Chest pain	4 (6.1%)	12 (6.3%)	0.941
Dyspnea	3 (4.6%)	13 (6.8%)	0.507
Other	23 (34.9%)	26 (13.7%)	<0.001
Cardiac risk factors			
Smoking history	31 (47.0%)	70 (36.8%)	0.147
Dyslipidemia	49 (74.2%)	57 (30.0%)	<0.001
Hypertension	42 (63.6%)	51 (26.8%)	<0.001
Diabetes	15 (22.7%)	22 (11.6%)	0.0265
Family history of CAD	16 (24.2%)	16 (8.4%)	<0.001
Framingham risk ≥ 10%	56 (84.8%)	63 (33.2%)	<0.001
Beta blocker therapy	31 (47.0%)	60 (31.6%)	0.036
ARB/ACE inhibitor therapy	40 (60.6%)	78 (41.1%)	0.007
Statin therapy	31 (47.0%)	21 (11.1%)	<0.001
Cancer treatment			
Anthracycline	42 (63.6%)	153 (80.5%)	0.0055
Trastuzumab	38 (57.6%)	130 (68.4%)	0.11
Radiotherapy	41 (62.1%)	124 (65.6%)	0.646
Cancer stage			
Stage I & II	39 (59.1%)	114 (60%)	0.897
Stage III & IV	27 (40.9%)	76 (40%)	0.897

LVEF left ventricular ejection fraction. CAD coronary artery disease. CAC coronary artery calcium.

(3.5%), moderate calcification (101–400) in 16 (6.3%) and mild calcification (1–100) in 41 (16.0%). Patients with CAC were older (69.2 ± 12 years) than those without CAC (54.8 ± 12 years) ($p < 0.0001$). Traditional cardiovascular risk factors were more prevalent in patients with CAC than those without (Table 1). 55.4% of patients with CAC who were statin eligible were prescribed a statin (Supplementary Table A). Estimated Agatston score was found to have a weakly positive correlation with the Framingham risk score ($R = 0.487$, $p < 0.001$).

CAC was found in (10/137) 7.3% of cases with a low FRS (<10%): none of these patients had been prescribed a statin. CAC was prevalent in 56/119 (47.1%) patients considered statin eligible (FRS ≥ 10), 25 (44.6%) of these cases were not prescribed statin medication.

3.3. Clinical events

The primary composite end point of death, coronary revascularization, heart failure hospitalization or new onset atrial fibrillation occurred in 112 patients (43.8%). 83 patients died during a median of 6.5 years of follow up. The majority of these (81 patients) were non cardiac deaths (Supplementary Table B). Cancer related mortality occurred in 71 cases (87.7%). 10 (10.6%) died of non-cardiac, non-cancer related deaths experiencing pneumonia or pulmonary embolism or intra cranial hemorrhage. No clinical follow up was recorded in 7 patients (2%) who were lost to follow up.

3.4. Cardiac events

Cardiac mortality occurred as a heart failure death and a fatal myocardial infarction, both events occurred in hospital. Coronary revascularization was performed in 7 cases (2.7%) (Supplementary Table B). Three of these cases occurred in the context of a non-fatal myocardial infarction, the remaining cases were performed for chronic stable angina. Heart failure admissions occurred in 19 patients (7.4%). The majority of these (15 cases) were secondary to heart failure with reduced ejection fraction (LVEF < 53%). New onset atrial fibrillation was seen in 3 patients.

3.5. Coronary calcification and clinical events (Table 2)

On univariable analysis the composite end point was more commonly seen in patients with CAC versus those without (35.3% versus 17.9% for patients with and without CAC respectively, $p < 0.001$) (Table 2). Intermediate to high Framingham risk score (FRS) and radiotherapy both trended toward an association with the composite clinical end point but in neither case did this achieve statistical significance ($p = 0.0629$ and $p = 0.07$ respectively). Advanced cancer stage (III–IV) was associated with the composite end point in comparison to early cancer (I–II) ($p = 0.002$) (Table 2). On multivariable analysis CAC and cancer stage were associated with the composite clinical end point (respectively $p = 0.007$ and $p = 0.001$).

Univariable and multivariable analysis were assessed for cardiac events (Table 2). On univariable analysis CAC and FRS were associated with cardiac events ($p < 0.01$ for both), advanced cancer stage and radiotherapy were not ($p = 0.837$ and $p = 0.233$ respectively). Using multivariable analysis of CAC and FRS; CAC but not FRS was predictive of cardiac events ($p = 0.001$ for CAC and $p = 0.154$ for Framingham risk) (Table 2). To determine whether there was a relationship with increasing calcium scores and clinical events, ordinal analysis of CAC was also performed. On multivariate analysis including Framingham risk, increasing CAC severity was associated with cardiac events but not with the composite of cardiac events and mortality (HR 1.214 (95% CI 1.077–1.444, $p = 0.003$), and HR 1.066 (95% CI 0.968–1.174, $p = 0.191$ respectively)).

Table 2
Risk of composite clinical events and risk of cardiac events.

Clinical factor	Cardiac events & mortality (n = 116)	No events (n = 140)	p value
Univariable analysis			
CAC	41 (35.3%)	25 (17.9%)	<0.001
Framingham ≥ 10%	55 (45.5%)	46 (34.1%)	0.0629
Anthracycline	82 (70.7%)	113 (80.7%)	0.327
Trastuzumab	71 (61.2%)	97 (69.3%)	0.507
Radiotherapy	79 (68.1%)	86 (61.4%)	0.073
Advanced cancer	58 (47.9%)	45 (33.3%)	0.002
Multivariable analysis	Odds ratio		
CAC	2.592 (1.300–5.169)		0.007
Framingham ≥ 10%	1.014 (0.982–1.047)		0.403
Advanced Cancer	1.654 (1.214–2.252)		0.001
Radiotherapy	1.675 (0.959–2.925)		0.070

Clinical factor	Cardiac event (n = 31)	No cardiac events (n = 225)	p value
Univariable analysis			
CAC	20 (64.5%)	46 (20.4%)	<0.001
Framingham ≥ 10%	19 (61.3%)	82 (36.4%)	0.008
Anthracycline	23 (74.2%)	172 (76.4%)	0.783
Trastuzumab	17 (54.8%)	151 (67.1%)	0.177
Radiotherapy	17 (54.8%)	148 (65.8%)	0.233
Advanced Cancer	13 (41.9%)	90 (40.0%)	0.837
Multivariable analysis	Odds ratio		
CAC	4.899 (1.952–12.292)		0.001
Framingham	1.033 (0.988–1.081)		0.154
Trastuzumab	0.689 (0.307–1.548)		0.367

Univariable and multivariable analyses for composite clinical events (all cause mortality and cardiac events). CAC coronary artery calcium. Framingham risk score (low versus intermediate-high risk). Cancer stage (Stage I–II versus III–IV). Univariable and multivariable analyses for cardiac events (cardiac mortality, coronary revascularization, heart failure hospitalization, new atrial fibrillation). CAC coronary artery calcium. Framingham risk score (low versus intermediate-high risk). Cancer stage (Stage I–II versus III–IV).

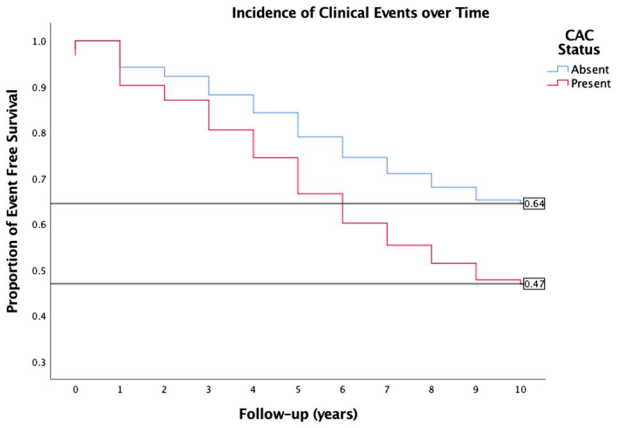
3.6. Coronary calcification and event free survival

Framingham risk score, cancer stage and CAC were used as covariates in a Cox proportional hazards regression. For the composite end point, CAC was associated with reduced event free survival, (hazard ratio 1.73 [95% CI (1.12–2.67), $p = 0.015$]) (Fig. 1). (Advanced cancer stage (III–IV) versus early cancer (I–II) was also associated with reduced composite clinical event free survival (hazard ratio 1.34 (95% CI (1.07–1.63), $p = 0.008$))). Increased Framingham risk score was not associated with reduced composite event free survival, (hazard ratio 1.01 [95% CI (0.98–1.03), $p = 0.584$]).

Using FRS and cancer-stage adjusted, Cox proportional hazard survival analysis, cardiac event free survival was reduced by the presence of CAC (HR 3.84 (95% CI (1.64–8.98) $p = 0.002$)) (Fig. 2). Framingham risk score was not associated with an increased risk of cardiac events (HR 1.03 (95% CI 0.99–1.08), $p = 0.115$).

4. Discussion

Coronary artery calcification (CAC) was detected coincidentally from a chest CT in 25% of 256 breast cancer patients that attended a cardiac oncology clinic. During a median follow up of 6.5 years, CAC was found to be predictive of a composite clinical end point that included all-cause mortality and cardiac events. Secondary analysis demonstrated that CAC was predictive of coronary revascularization and heart failure hospitalization but not all cause mortality or new atrial fibrillation. The relevance of these findings are in enhancing risk stratification of patients in the cardiac oncology setting, reinforcing the importance of cardiac disease in breast cancer patients and emphasizing personal cardiac risk stratification using available patient data. Practical application of the study findings could affect up to 7% of low FRS patients who were not prescribed a statin but demonstrated CAC and



Parameter	Hazard Ratio (95% CI)	P value
CAC	1.727 (1.110-2.685)	0.015
Cancer Stage	1.341 (1.081-1.664)	0.008
Framingham Risk	1.006 (0.984-1.029)	0.584
Radiotherapy	0.946 (0.625-1.432)	0.795

CAC	2 years	4 years	6 years	8 years	10 years
Present (n=66)	58 (87.9%)	48 (72.7%)	34 (51.5%)	22 (33.3%)	12 (18.2%)
Absent (n=190)	179 (94.2%)	164 (86.3%)	118 (62.1%)	84 (44.2%)	62 (32.6%)

Fig. 1. Framingham risk score and cancer stage adjusted Cox proportional regression analysis for the composite clinical event (all cause mortality and cardiac events). The presence of coronary artery calcium (CAC) (red line) was associated with reduced event free survival (47% at ten years) in comparison to patients without CAC (64% at ten years) (blue line) (p = 0.015).

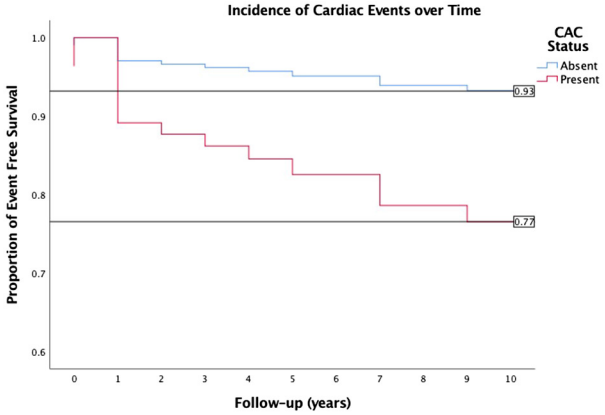
up to 45% of intermediate or high FRS patients who similarly were not prescribed a statin but had CAC.

4.1. Chest CT detection of CAC

We have previously noted that the reporting of CAC on chest CT is only clinically recorded in approximately 40% of studies [1]. The rates of CAC reporting are likely to increase in view of 2016 guidelines that recommended that CAC be clinically reported if detected at chest CT [2]. In the current study on multivariable analysis CAC was associated with an increased risk for cardiac events of (OR 4.90 (95% CI, 1.95–12.29 p = 0.001)). FRS however was not associated with cardiac events in this breast cancer population (OR 1.03 (95% CI, 0.99–1.08) p = 0.154). Thus, whilst the impact of guideline directed reporting is adopted, there will be an onus for clinicians to determine whether CAC is present on chest CT. This is particularly relevant in cardiac oncology where long term cardiac event free survival goals are being sought.

4.2. Framingham risk or CAC which is preferred?

In the absence of a universal clinical risk tool that predicts heart failure, atrial fibrillation/arrhythmias and atherosclerosis, risk stratifiers like the FRS will continue to be used to determine cardiac risk in clinical settings including cardiac oncology. Clinical risk systems such as FRS are the guideline preferred method of stratifying patients for atherosclerotic disease rather than using a cardiac CT derived CAC score [5,20,21]. According to primary prevention guidelines there are however certain restricted circumstances when CAC assessment could be considered and these are defined by the initial clinical risk assessment [5,20,21]. Thus to be concordant with current primary prevention guidelines, CAC assessment can be used in conjunction with FRS (or alternative clinical stratification system) but not as a replacement [5]. Co-incidental CAC assessment at CT chest probably should be considered in the same manner. In the presence of a high clinical risk score absence of CAC does not normalize cardiovascular risk and primary prevention should be continued. Coincidental detection of CAC in low risk or intermediate cardiovascular risk patients might however prompt statin therapy depending on the extent of CAC [2,5]. Our sample size did not allow calculation of a net reclassification index to evaluate the impact of CAC detection on statin eligibility. Nevertheless 7% of low FRS patients and 45% of intermediate to high FRS patients were found to have CAC and were not on a statin which based on the results of our study might be considered.



Parameter	Hazard Ratio (95% CI)	P value
CAC	3.837 (1.639-8.984)	0.002
Framingham Risk	1.033 (0.992-1.075)	0.115
Trastuzumab	0.903 (0.438-1.859)	0.781

Fig. 2. Framingham risk score and cancer stage adjusted Cox proportional regression analysis for cardiac events (cardiac mortality, coronary revascularization, heart failure hospitalization, new atrial fibrillation). The presence of coronary artery calcium (CAC) red line was associated with reduced event free survival (77% at ten years) in comparison to patients without CAC (blue line) (93% at ten years) (p = 002).

The majority of the cardiac events in the current study were coronary revascularization and heart failure events (there were very few episodes of new atrial fibrillation). The utility of FRS to predict heart failure events in breast cancer patients may be limited [22]. Furthermore it is possible that FRS may underestimate coronary atherosclerosis in breast cancer patients due to confounding influences such as the impact of cancer therapy or due to the influence of cancer on atherosclerosis. In the initial Framingham cohort cancer diagnoses were present in 0.6% of subjects before study entry and the inadvertent under subscription of cancer patients may have limited the utility of FRS in this population [23]. More recently Gernaat et al. demonstrated in 1103 breast cancer patients that FRS underestimates cardiovascular events in comparison to age and gender matched controls [6]. In view of these potential limitations of FRS, our data do not argue for an abandonment of traditional clinical risk scoring systems, rather that CAC detection on chest CT could be used alongside clinical risk scores to augment cardiac risk prediction.

4.3. Impact of CAC on survival analysis

Cardiac event free survival at 10 years was 93% in patients with no CAC versus 77% in those with CAC (Fig. 2). Coronary revascularization and heart failure hospitalizations accounted for the majority of cardiac events. There were only 2 cases of cardiac mortality, both cases occurred in patients with CAC.

Non-cardiac death occurred in 83 patients (32.4%) during follow up. CAC was not associated with non-cardiac death which, for the majority of cases, was due to a cancer related cause (86%). Advanced cancer stage (Stage III–IV versus I–II) was associated with the composite end point that included all-cause mortality. Inclusion of all-cause mortality in the survival analysis reduced the event free survival time for both patients with CAC and no CAC (47% versus 64% respectively at 10 years) (Fig. 1). Despite the reduced event free survival with inclusion of all-cause mortality, CAC was predictive of survival whereas FRS was not. CAC therefore remains a significant risk factor to predict event free survival even in the context of a diagnosis of breast cancer. This is consistent with prior data demonstrating the importance of cardiovascular disease to determine prognosis in breast cancer patients [4].

4.4. Limitations

This was a single center, retrospective study of consecutive breast cancer patients attending a cardiac oncology clinic and the applicability of the findings to an unselected breast cancer population may be limited. To detect coronary calcification we utilized reconstructed sections from varying widths as per clinical protocols. In original descriptions, CAC scoring was performed using 3 mm section widths, section widths greater than this may be less sensitive, but specificity is maintained at 90% across the section widths used in this study [15].

It was assumed that patients were not prescribed statins due to focus of care on cancer therapy rather than for statin intolerance or contra–indications. It is possible that some intermediate or high FRS patients had previously taken statins but their prescriptions had been discontinued at the time of cancer diagnosis.

It is presumed that any cardiac events or hospitalization that did not occur at the Ottawa Hospitals would have been self-reported and therefore recorded in the electronic medical record. It is however possible that patients attended other health care facilities during this period and these events were not recorded. There is the potential that differences in event rates in patients with or without CAC might be as a result of differences in cancer therapy, however the continued separation of the survivals curves suggest this is unlikely but cannot be completed ruled out. The role of cardiovascular medications to influence the study findings was considered (Table 1). On univariable analysis there was no association between these medications and a reduction in the composite clinical end point. The low prevalence of prescriptions for these medications within the study cohort however may have limited any observation of potential benefit such medications may offer to reduce cancer therapy related cardiotoxicity [24–26].

5. Conclusions

In breast cancer patients CAC detected co-incidentally on CT chest predicted cardiac events. The findings of the study highlight that despite a life changing cancer diagnosis, attention to cardiovascular risk factors is important, for although cancer is a significant co-morbidity, coronary atherosclerosis remains a long-term determinant of cardiac clinical events. Prospective clinical studies with larger patient numbers would be useful to further clarify the utility of prediction tools such as FRS and CAC to assess cardiac risk prediction in cancer patients.

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Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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