Reviewer’s report

Title: Coronary Heart Disease and Mortality Following a Breast Cancer Diagnosis

Version: 0 Date: 18 Feb 2020

Reviewer: Na-Jin Park

Reviewer's report:

1. The study addresses the current gap of literature on cardiovascular health in breast cancer survivors: a joint effect (interaction) of pre-treatment cardiovascular health prior to breast cancer (BC) and cardiotoxic BC treatment on post-treatment coronary heart disease (CHD) and all-cause mortality following 10 years of BC diagnosis. That gap is due to, mainly, the lack of available datasets including both pre-treatment/diagnosis cardiovascular risk factors and details of post-BC treatment. The authors used EHR data from a medical center. Limitations of EHR data were briefly addressed but should include deficit of important information, such as physical activity and diet for the complete list of cardiovascular health (CVH) measures. I also wonder why details of BC data on diagnosis and treatment are missing from the EHR, which would be helpful to understand the study sample of BC survivors.

2. While the topic itself is innovative, there are similar publications of cohort observational studies addressing independent effects of existing (post-BC) cardiovascular risk factors and BC treatments (in a separate or combined regimen) on cardiovascular disease (CVD) with mixed findings in variously different characteristics of BC survivors. Unlike other previous studies, this study particularly used machine learning algorithms labeled as "novel" statistical techniques without appropriate justifications and implications relevant to clinical decision-making, which is the main focus of the journal. Therefore, the goal statement here is incomplete without that.

3. From the background, (left-sided) radiation therapy seems the focal exposure among many types of cardiotoxic therapies, which suddenly disappeared in reporting actual data. Total patients who received BC treatments were reported as 17.6% in the study in Table 2. Isn't that odd that in 2006-2007, women with BC diagnosis had treatment so low like that? Only 2% had anthracyclines. There is no radiation therapy reported. Aromatase inhibitors (Ais) are the major hormonal or endocrine therapy, but hormone therapy here appears not to include AIs. Then what include hormone therapy here? I guess tamoxifen? How about Herceptin for HER+ BC? 72% had hormone therapy or aromatase inhibitors, which makes sense in that over 70% of BC cases are hormone receptor-positive in national statistics. It is plausible that those who received any therapies had more advanced BC and poorer prognosis/mortality outcomes given the very low treatment record. My experience additionally tells me that those with advanced BC have poorer CVH compared to early-stage disease. BC-related death statistics (along with CHD/CVD mortality) is missing, which is also important to better understand all-cause mortality in this study sample of BC survivors.

4. CVH metric by the AHA include 7 health factors, including 5 used in the study plus physical activity and diet. However, Table 1 with 5 measures may mislead readers because the clear
description of justification on that decision is missing (I guess the EHR had no reliable data about them). I also want to see specific numbers and percentages for each measure and final categories of poor, intermediate, and ideal health as described. I think that basic information is particularly important with arbitral use of CVH components in this study. I don't understand why CVH scores in Figure 1 (intermediate) had 1 or 2 (ideal) without 0 (poor). I also want the authors to be clear about these categories that were determined by CVH 5 factors. Given that, it may be interesting and better make sense to look at interactions of individual factors and BC treatment on outcomes, which is another major gap in the current literature.

5. Discussion needs more specifics and elaborations relevant to clinical decision-making process in oncology survivorship practice.

6. The whole list of references should be updated to 2020. In last 5 years, there has been an increasing data on BC and cardiovascular disease (CVD) outcomes, including the 2018 AHA publication on Circulation. However, authors provided many 2011 publications despite newly available references. Also, statistics of BC survivors (references 4 & 5) is old.

7. Please consider to revise and reorganize the tables and figures. I consider some figures or information could be better in supplementary materials. Overall, it would be much improved with focused presentation of data and providing specific interpretation for BC survivors and decision-making implications for improved BC care. The revision needs to be more reader-friendly.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

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