Reviewer's report

Title: Variations of circulating cardiac biomarkers during and after anthracycline-containing chemotherapy in breast cancer patients

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Reviewer: Michael Fradley

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Overall this is a very interesting study.

We need to develop better ways to identify patients at risk for future cardiotoxicity. Biomarkers are emerging as a possible modality to accomplish this goal.

While much attention has focused on troponin and BNP, we know from the general cardiology literature that other biomarkers including ST2 can be quite helpful in predicting outcomes.

The strength of this study lies in its meticulous evaluation of biomarkers at several different time points and the use of novel markers which have not been extensively studied in the breast cancer/chemotherapy population, particularly ST2 and microRNA sequences. The authors should be congratulated for tackling this topic.

In addition, it is a very well written article.

That being said, the article does have several weaknesses which should be addressed prior to publication in the current journal.

1) There isn't a very good control population. While the baseline (pre-chemo) numbers serve as an internal control and does provide some good information about this issue, it might be helpful to compare these values to population of patients just undergoing definitive treatment with surgery (ie pre surgery/post surgery). This could be accomplished in a triple positive population (prior to endocrine therapy). This could allow the authors to provide more proof that these elevations were specific to the therapy exposures and not just treatment of the cancer itself.

2) We know very little about the patients studied. What were their baseline demographics. Did they have underlying CVD or significant risk factors or were they otherwise healthy.
I think having this information would certainly add strength to the article (elevations in a patient that otherwise was free of CVD has significant implications). I would suggest evaluating and reporting these data in the manuscript.

3) The most significant issue is the lack of outcomes to which the authors admit. While these elevations are observed, we have no idea if they will translate into adverse CV outcomes (ie heart failure, cardiomyopathy, etc). Certainly some of these issues won't be observed immediately but the relevance of these biomarker elevations is not necessarily established in this study. It would be helpful to have some additional information about patient outcomes -- any echocardiographic changes, even mild and not clinically relevant may add support to the biochemical findings observed in the study.

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.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
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