Reviewer’s report

Title: Association between changes in body fat and disease progression after breast cancer surgery is moderated by menopausal status

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Reviewer: Adetunji Toriola

Reviewer's report:

The manuscript evaluated the association between changes in body fat and disease progression after breast cancer surgery. The authors also sought to determine whether this association is modified by menopausal status, which they erroneously referred to as moderation. The sample size is rather small, especially postmenopausal women (N=45) to allow any meaningful conclusions. This is reflected in the very wide confidence intervals. The methods and statistical analyses require a lot of clarification.

Methods

* How could the authors collect data on all-cause mortality from patients? How detailed is the medical chart review? Are there other potential sources of collecting mortality related information not identified by the authors? How was censoring handled?

* What decision drove the factors that were included as confounders? Was this decided a priori or was a formal statistical test done to decide which confounders would be included in the final model? There is no justification to exclude age from the multivariable analyses because menopausal status was included. Treatment-related information should be included in the Cox proportional hazards models. Exercise habit was included in the regression model but no details were provided on how that was collected and how it was classified.

* The set up of the Cox proportional hazards models is odd. Models I and II have different predictors. Model I had body fat as predictor while model II had body fat percentage as predictor. Did these models simultaneously adjust for the other predictor? i.e. did model I adjust for body fat percentage and did model II adjust for body fat.

* What was the time metric in the Cox model? How was the proportional hazards assumption examined? Were the models computed first before the interactions terms were included?
It is very unclear how tests for interaction were performed. Also, using the term moderation to describe interaction is wrong.

Results

The way the results are presented is confusing. For instance, what do the authors mean by "For model I (body fat as the predictor), after adjusting for covariates (i.e., disease severity, ER and PR expression, menopausal status, and exercise habit), the effects of body-fat change and menopausal status had a significant interaction effect on distant metastasis ($\beta=0.3$, $p=0.018$)". First, what is the effect of body fat on distant metastases? Also, did they evaluate the effect of body fat or body fat change?

Why do some of the HRs presented in the text have ranges?

Discussion

The discussion did not take into consideration previous studies on adiposity, changes in adiposity and breast cancer prognosis.

A bit of a stretch making clinical recommendations from findings in observational studies.

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

No

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
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