Reviewer's report

Title: CLINICAL AND PATHOLOGICAL FACTORS INFLUENCING SURVIVAL IN A LARGE COHORT OF TRIPLE-NEGATIVE BREAST CANCER PATIENTS

Version: 1 Date: 16 Oct 2017

Reviewer: Michael O"Rorke

Reviewer's report:

The authors have conducted a retrospective cohort study spanning 21 years using clinical records and clinical pathological data from four major oncology centres in Sardinia. Just over 840 patients with triple negative breast cancer (TNBC) were included in the study and the authors report that lymph node ratio (in node positive tumours) and ki-67 may be relevant predictors of overall survival and recurrence in TNBC. The surgical specimens from these women were independently reviewed by 3 pathologists, which lessens the possibility of TNBC misclassification. Overall the study is well written, and the statistical analysis is appropriate, however I have several recommendations for the papers improvement and documentation.

Specific comments:

1. Do the author's feel that a mean follow-up of 4.3 years is long enough for outcomes of recurrence or overall survival? If so, can they reference relevant literature to support this? i.e.: paper on patterns of recurrence in TNBC such as Dent et al. Clin Cancer Res. 2007 1;13(15 Pt 1):4429-34.

2. I've noticed that the authors are inconsistent with regards their reporting of 95% CIs i.e.: page 10 lines 34 and 41. Personally I'd prefer to read the 95% CIs around the effect estimates, as invariably in this study numbers in the analysis fluctuate depending on the clinical pathological factors being examined.

3. Results, page 9, line 7 - the authors report excluding approx. 27% of patients with no vital status. To assess the potential of selection bias in the remaining cohort, could the authors put a table in supplementary data of these patients' characteristics? I imagine that these patients may also include a proportion of women with higher stage disease at diagnosis, given that they seem grossly under-represented in Table 2 (i.e.: only 10 patients with stage IV disease?)
4. Why not merge Tables 1 and 2 together, why are they separate? Also could the proportion (%) of missing data be presented in italics for ease of reading. Please also correct the titles of the tables to reflect the survival analysis under study - i.e.: Tables 3 and 4 state 'mortality' and 'death' are these OS or DFS? Also the second N(%) columns presumably reflects the number and proportion of events (can this be labelled accordingly?). Also Tables 4 and supplementary Table 2 - what's the difference in these tables? Both refer to mortality, but have different numbers of cases - is this reporting on DFS or OS? Please specify.

5. Results page 10 lines 50-60, this is a very long sentence with lots of results, consider revising.

6. Results page 11, lines 14-15 seem contradictory to the conclusions being drawn in the abstract and conclusion sections. Ki-67 seems to be predictive of OS presumably in Table 3, but unrelated to recurrence outcomes (available for under 40% of the cohort) in supplementary Table 1. Also on page 11, line 43, the authors refer to '26.7% for stage I' - I think this is a typo and should read stage IV?

7. In relation to statistical analysis - How were the variables for fully adjusted analysis selected? I've noticed that baseline characteristics such as lifestyle/family history and, more importantly co-morbidities, are absent from the adjusted models? Were these not statistically significant? what level of significance/threshold was used to enter covariates in the adjusted models?

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
Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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