Author's response to reviews

Title: A retrospective analysis of survival and prognostic factors of male breast cancer from a single center

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Version: 4 Date: 25 February 2014

Author's response to reviews: see over
Subject: Re-Submission after major correction

“A retrospective analysis of survival and prognostic factors of male breast cancer from a single center”.

Dear Ms. Patricia Ratin,

I express my gratitude on behalf of the authors for considering our manuscript for publication in your journal, and hereby would like to re-submit a modified version of the manuscript that was changed according to reviewers indications.

I would also like to thank the reviewers for the effort and the time they invested reading, commenting on and discussing the submitted text. In response to their mandate, after informing and getting approval of all authors, I changed the text, responded to their comments and discussed their discretionary reviews. You will find below my response to the reviewers’ comments point by point. Changes in the text are typed in a different color and underlined.

Thank you once more for considering our work.

On behalf of the authors
With best regards

Dr. Amr A Soliman

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Reviewer's report

Title: A retrospective analysis of survival and prognostic factors of male breast cancer from a single center

Version: 3 Date: 1 February 2014

Reviewer: Tiffany Berry

Reviewer's report:

Dear Editor,

The above article discussing male breast cancer is acceptable in my opinion for publication pending the following changes:

Major Compulsory Changes-
- There are several occasions where Tumor "Stage" should more accurately be stated as tumor "size" (p2 line 18, p7, line 8, page 9 line 8). This is accordingly changed in text.
- Need to explain why all patients received an axillary dissection rather than sentinel node as sentinel node is standard of care in the years the data was collected (at least in the US and Europe) as noted on page 5, line 23. Unfortunately sentinel lymph node is not standard of care in Egypt, not even as an experimental procedure. This is elaborated in the corresponding part in text.
- Need to explain why so many patients received radiation and chemotherapy as above 90% is high as an overall rate (page 7, line 12).

The local consensus in our institution is somehow generous as regards adjuvant radiation and chemotherapy due to lack of national recommendations or guidelines, lack of Her2 status testing and subsequently treatment, lack of a national follow-up program for cancer patients and above all very poor patient compliance to treatment and to the limited follow-up services available. Moreover the tumor characteristics of the patients in this cohort are somehow aggressive with more than 75% presented with lymph node involvement, and around 78% had tumor grades G2 or G3. This part is optimized and elaborated accordingly in the text as indicated by the reviewer.
- The highlights of the tables should be explicitly stated in the Results section on page 7. For example, the p values should be listed for the statistically significant factors of lymph node positivity and tumor grade. Tumor grade is not even referenced at all in the Results section except that it is contained in a table. Lymph node status is referenced, but still needs the p value for ease of author reading. Also any factors that were not statistically significant, but unexpected should also be contained in the Results section including p value. For example,
Stage is explored as is tumor size and ER status in the Discussion. The data/p value for each of these should be reflected in the Results even if in just a single sentence.

The text is accordingly changed and we tried to elaborate the findings in a better way in the Results section as indicated by the reviewer.

-The authors initially concludes that their results are not influenced by their country's stage of development (page 8, lines 15-18), but then they state on page 9 in lines 23-26) that country stage of development may have influenced treatment and outcome. Perhaps this is how I am interpreting the statements, but further explanation for better clarity may be more reader friendly.

The first paragraph in page 8 is optimized. In the first submission we mistyped India instead of Turkey, which is now corrected. This part was meant to discuss a possible ethnic role affecting survival, as Iran, Turkey and Egypt all belong to middle eastern ethnicity. The paragraph on page 9 was not changed. We hope after correcting the mistake it is now more reader friendly.

-I am confused as Table 1 on page 16 and Table 2 on page 17 seem to be contradictory. In Table 1, there were 64 of 69 patients noted to have distant metastasis. However, Table 2 lists that 91.4 percent (n=64) of patients were M0.

There was a mistake in Table 1 that is corrected.

Minor Essential Revisions-

-page 9, line 8 should read "In regard to the tumor...."

The text is corrected.

-page 9, line 15 should have a period to separate the two sentences with one ending in a citation [10-14] and the next sentence beginning, "Hormone receptor status..."

The text is accordingly corrected.

Discretionary Revisions-

-Hormone status did not statistically affect survival. Do the authors believe this is due to the fact that Her2 was not captured and treated with directed therapy? In other words, was the difference in survival related to hormone status overshadowed by the lack of Her2 directed therapy?

This is a valid argument that throws light on the meaning of the results we are presenting. Although we believe lack of Her2 testing and directed therapy could have masked the impact of hormone status on survival, we were not very confident mentioning it in the first version due to lack of published data regards Her2 over-expression rates in the Egyptian population.
The text is now modified as inspired by the reviewer's comment.

-on page 8, line 14 concludes that the differences in survival in this study compared to the others quoted may be due to a higher stage at presentation of patients in this study. While this may be true in regard to overall survival, the author could more accurately compare "apples to apples". In other words, the author could compare survival for patients with a specific Stage in this study to the same Stage in the other cited studies. It is a big jump to make the statement that the survival is different overall simply because of the higher stage at presentation without a mention as to the composition of the patients in the other studies.

The text is changed according to the reviewers indications in the corresponding part, elaborating the results of other studies regards tumor size in terms of rate and survival and this is compared to the data in this cohort.

Overall, the article contributes to the scientific body and I recommend the paper for inclusion in your journal.

Tiffany Berry, MD

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I am a speaker for Lifecell Corporation and receive honoraria for speaking engagements, but I declare that I have no competing interests that influence my
Reviewer's report

Title: A retrospective analysis of survival and prognostic factors of male breast cancer from a single center

Version: 3 Date: 4 February 2014

Reviewer: lydia choi

Reviewer's report:

Major compulsory revisions

1. Abstract: (methods): this is not a cross sectional study - it is a cohort study. You also can't link causation from a cross sectional study, so predicting prognosis related to TNM stage or lymph node involvement would not be possible from a cross sectional study.

   This is accordingly changed in the text.

2. General comment: Abstract and Background specifically refer to male breast CA patients doing worse than female, but this paper does not include any comparison to prognosis in female breast CA patients at the same hospital. It would be interesting to see the 5 year survival rates for women at the same hospital.

   Thank you so much for this nice comment. We plan to start soon a project concerning analyzing the survival of female breast cancer in our institution.

Minor essential revisions

1. Abstract: (methods): should read "Demographic data, age, height, weight and body mass index (BMI) were registered." (capitalization and punctuation)

   The text is accordingly optimized.

2. Abstract: (results): The collective 5-year survival in this cohort (was) 46.4%.

   The text is accordingly corrected.

3. Methods: "we checked the records" should read "we surveyed medical records"

   The text is corrected as indicated by the reviewer.

4. Methods: "Demographic data, age, height, weight and body mass index (BMI) were registered." (capitalization and punctuation)

   The text is accordingly optimized.

5. Methods: "routinely examined in breast cancer patient(s)"

   The text is corrected.

6. Methods: "Each of the patients, who met the inclusions criteria" - should be "inclusion criteria"

   The text is corrected.
7. Methods: run-on sentence - "Obtaining data concerning disease free intervals was extremely difficult in the social and medical services context in a developing society like Egypt, that is why - should read "society like Egypt. That is why"
The text is corrected.
8. Methods: "standard operative therapy..." - modified radical mastectomy includes axillary dissection - no need to say MRM with axillary dissection
The text is changed.
9. Methods should include whether when death information was obtained through phone calls, breast cancer specific death was specified.
The text is accordingly optimized.
10. Results: (paragraph 2) "lymph node affection" should be "lymph node involvement"
The text is changed.
11. Discussion: (paragraph 1) "the files of" should read "the medical records of"
The text is corrected.
12. Discussion: (paragraph 1) "Giordano...found out" should read "Giordano...found"
The text is corrected.
13. Discussion: (paragraph 1) typographical error - "possible causes that ...may by" to "may be"
The text is corrected.
14. Discussion: (paragraph 1) - please explain what you mean by quality of care, since almost all patients received adjuvant radiation and chemotherapy it's hard to say patients received poor quality care - would also be good to include what national recommendations for breast cancer care are in Egypt, if any.
Unfortunately there are no national recommendations or guidelines for breast cancer care or any other malignancy in Egypt. This is in itself a deficit in the quality of care. By the term 'quality of care' (page 9 line 14) we meant the accuracy of calculating the dose and the application of chemotherapeutic agents, the stereotactic planning and application of radiotherapy doses, Her2 testing and treatment, and general supportive care to cancer patients. All these aspects have many deficits putting them way below the optimum standard but we unfortunately do not have solid published data to refer to as it concerns this point. The text is modified according to reviewer's indications to give the reader more details about what we meant by poor quality of care.
15. general comment - please keep consistent the punctuation for percentages - for example, sometimes you write 46,4% and other times 46.4%
The percentages and the numbers were revised and changed accordingly in the text sticking to one consistent format.

Discretionary revisions

15. Hormone receptor negative breast CA has a lower survival than hormone receptor positive. Wouldn't that alone explain the lower survival in your group? The statistics may not show significance because of your small sample size. May be nice to include hormone receptor rates from other studies and compare survival.

Of course it is true that hormone receptor negative breast cancer has worse prognosis than hormone receptor positive, but in our case it needs a bigger sample size and more sophisticated statistical analysis in order to incriminate the high negative hormone receptor expression rate as the sole culprit for the lower-than-reported overall survival in the cohort. According to published data including large numbers of patients based on national patient registries hormone receptor status did not affect survival (Giordano et al., reference 2), so we felt uncomfortable to give a solid statement about such a controversial issue in the first submitted version. However, the text is changed in the corresponding part to elaborate the rates from other studies and compare it to the rates and the survival in our cohort, so that the reader can get a clearer perspective of the issue being presented.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

All the corrections indicated by the reviewer are accordingly changed in the text.

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests.