Author's response to reviews

Title: The invasive lobular carcinoma as a prototype luminal A breast cancer: a retrospective cohort study

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Author's response to reviews: see over
Dear Editor,

We revised the following article as you and reviewers recommended.
“The invasive lobular carcinoma as a prototype luminal A breast cancer: a retrospective cohort study”

Reviewer #1:
This is a very well written manuscript that is succinct and addresses the study question. There is some new information regarding the luminal A subtype in ILC, although most of the study confirms what has already been reported. However, this particular patient population has not been well described, and I congratulate the authors on their work.

1. The grade of ILC was shown to be less than IDC, but this is not discussed or commented on further, and is not included in the univariate analysis in Table 2.

As your recommendations, we reanalyzed the prognosis of histologic grade and added in Table 2. Additionally, we discussed for the difference of the grade between ILC and IDC (Discussion, Page 12, 2nd paragraph).

Added sentences:
We reported that ILC had lower histologic grade than IDC. Previously, Li et al. analyzed Surveillance, Epidemiology, and End Results Program data and demonstrated that ILC showed lower tumor grade than IDC specifically in 30-49 years old patient group. Although Rakha et al. reported that histologic grade of ILC provided a strong predictor of outcome in breast cancer patients and should be provided routinely in pathology reports, we did not find such correlation. (Discussion, Page 12, 2nd paragraph)

Reviewer #2
Overall the manuscript is relatively well written and easy to understand. The methods are appropriate, and the data are sound and well presented. I have a few comments and the authors need to address these either in the Result section and/or Discussion section.

1. Were all the ILC cases in this cohort classic subtype, or were there any other variants such as
pleomorphic ILC? How were the morphologic variants correlated with ER/PR/HER2 status (or molecular subtypes as defined by immunohistochemistry)? About 9% of the ILC cases in this study are not luminal A and based on the literature, those are likely to be non-classic ILC.

We reviewed those 9 mentioned cases which showed classic type except for one case of pleomorphic lobular carcinoma (triple negative by IHC). Although intrinsic classification is easily translated by IHC, and the subtype by IHC itself has proven an independent prognostic factor (PL Nguyen et al. JCO 26; 14, 2008: 2373-2378), the subtypes do not exactly overlap the gene expression profiling.

Added sentence:
All ILC cases were classic subtype except for one case which was pleomorphic type. This particular case was triple negative by IHC. (Materials and methods, Page 5, 1st paragraph).

2. The authors concluded that “ILC is a prototype of luminal A breast cancer”. It may be more appropriate to state that “most ILC are luminal A breast cancer”. The authors should address, in the Discussion Section, the work by Weigelt et al (Refinement of breast cancer classification by molecular characterization of histological special types. J Pathol 2008;216:141-50) which showed that while most ILC fall into luminal A molecular subtype, some ILC cluster with either HER2 subtype or apocrine subtype.

I agree with you that not all ILC appears luminal A by IHC, but most ILC are luminal A breast cancer. But if you allow me, I would like to keep a word “prototype” in the new sentence as below, knowing the limit of IHC method replicating gene expression profiling.

We corrected the sentence in the conclusion (Conclusions, Page 14, last sentence) and addressed the work by Weigelt et al (Discussion, Page 13, 1st paragraph).

Corrected sentence:
This study shows that the prognosis of ILC as a prototype luminal A breast cancer, is similar to that of LA-IDC, and both are better than the other subtypes.

Added sentences:
Weigelt et al. also showed that most ILC fall into luminal A molecular subtype, although some ILC had clusters with either HER2 subtype or apocrine subtype. (Discussion, Page 13, 1st paragraph).
3. Wrong references were cited for ref 10 and 11 in the 3rd paragraph of the Introduction Section, with the luminal A subtype showing the best prognosis.

As your recommendations, we corrected the ref 10 and 11 to 13, 14. (Introduction, Page 3, last paragraph).

Added references:

We sincerely hope that the revised manuscript could be reviewed as acceptable for publication in BMC cancer.

Best regards,
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