Reviewer's report

Title: Prognostic factors for breast cancer patients with axillary lymph node dissection (pathological stage I-III) and the reversal of survival rate between estrogen receptor positive and negative breast cancer patients after long term survival

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Reviewer: Emad Rakha

Reviewer's report:

This is a good written paper that addresses an important issue. However, there are major points that need to be addressed.

This study covers a long period of time (1980 -2005). During this period, dramatic changes and advancement in the management of breast cancer have taken place including introduction of systemic therapies.....etc. Therefore, combining old cases with recent cases in the same analysis is expected to give biased results on the outcome of these patients even with using models that include types of surgery in the multivariate analysis. For examples, oestrogen positive cases before 1990’s may have not received hormonal therapy while cases after that have received. From the reviewer’s point of view, the best way to assess the effect of any individual variable on the outcome of breast cancer patients is to divide this patients cohort into different (but homogeneous) subgroups based on the time-points at which significant changes have taken place e.g., time of introduction of hormonal treatment, chemotherapy and Herceptin or significant changes in the local treatment protocols.

In the survival analysis (Page 5), death from any cause should be censored in overall and disease free survival analysis and not as events. Also, the best measure of outcome of breast cancer is breast cancer specific survival rather than overall survival.

Inclusion of the unknown subgroup in the analysis of oestrogen groups is not correct may bias the results as those cases could be positive or negative and therefore, should be excluded (please review the tables as it appears that both ER positive and ER negative cases have been compared to the unknown group).

The authors did not include histologic grade in the analysis which is expected to produce the same pattern of survival (low grade cancers are usually ER positive, have better outcome and indolent behaviour while high grade cancers tend to be ER negative and have aggressive course and likely to cure from the disease). In fact, the observed effect of ER could be grade dependent.

The authors concluded that ‘the overall survival and disease-free survival between ER positive and negative patients were reversed after 20 and 10 years
after surgery, respectively'. However, this observation was not supported by their analysis. Their figures may show that the survival curves for both ER positive and negative converge but did not prove reversal of survival. From these figures, it appears that the number of events after these time periods is very limited to make such a comment on outcome.

**What next?:** Reject because scientifically unsound

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.