Reviewer's report

Title: Age-related differences in the clinical management of women with metastatic breast cancer

Version: 2 Date: 9 April 2006

Reviewer: Manoj Pandey

Reviewer's report:

General
As authors have agreed that inclusion of performance status is a short coming in retrospective analysis, they have now included the data on co-morbidity as a surrogate and have included the reference of Kimmick and Muss. With this information now available the manuscript looks much better than before but also becomes interesting as 12/20 (60%) of patients above the age of 70 had cardiovascular diseases which could have prevented use of anthracyclin based chemotherapy in these patients and hence the treatment differences are not true differences due to age but are surrogate to poor medical condition which prevented active treatment in these patients. Based on this information the authors should now conclude that their data is not robust enough to say for sure that the differences in the treatment observed are true differences due to age (as high prevalence of comorbid conditions are confounders and small sample size for patients above 70 is limitation). The author can further provide a cross tab of treatment received and co-morbid conditions in following format to clear the picture:

<table>
<thead>
<tr>
<th>Comorbid conditions</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Hormone therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-49</td>
<td>50-69</td>
<td>&gt;70</td>
<td>20-49</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No comorbid condition</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Other specific comments are:
1. From table 1 it dies appear that mean number of subsequent metastasis is higher in older patients but this too is a surrogate for less aggressive treatment and poor survival in this group of patients compared to young adults. I feel that this should be added in the discussion. A significant higher proportion of bone as first metastasis in young women also could have contributed to present results.

2. Table 1 tumor size: there are number of cells having value of 0 or 1, what statistical tests were applied and how accurate are these when 6/15 cells have a value of 0 or 1. Would not it be better to club T3, T4 and Tx to form a relatively bigger group before applying statistical tests.

3. Table 1 : Primary systemic therapy 70+ age group the % should be 70

4. Table 1: What statistical tests have been applied to calculate individual p value for site of metastasis (until death). If chi square or Fishers exact what were the numbers used in other group?

5. 148 patients assumed not to have died of breast cancer? On what basis the assumption was made? Were these patients disease free prior to their death? It should be noted that this number is higher than the number of patients reported in the present manuscript.

6. Page 6 statistical analysis it is not mentioned what statistical tests were applied. This need be added.
7. Page 6 results: no significant difference…. At the time of diagnosis see earlier comments on statistical tests
8. Page 7 Management
   a. Diagnostic procedure and imaging: Isn’t that related to higher survival and or more metastasis rather than age? Shouldn’t it be so discussed
   b. The same is true for visits to medical oncologists which are directly proportional to number of patients receiving chemotherapy and number of cycle each women would receive and complications therein
   c. Same argument for hospital admissions
   d. Last para- choice of chemotherapy related to age vs. related to performance status and co morbid conditions. Authors themselves have quoted on page 9 Christman et al(15) on this issue. I feel that this point need to be discussed that what meet the eye is not true and there are no true age related differences in management of breast cancer, on the other hand age is a surrogate for poor performance status and comorbid conditions that prevent an oncologist to go for aggressive treatment. What will happen if authors take 60+ as the last group this will lead to more number of patients in this group and probably will reduce co-morbid conditions. Will the differences still persist?
   e. Page 8 hormone treatment: proportion does not differ probably because hormone treatment depends on receptor positivity and this does not differ significantly between age groups! Would authors like to comment on receptor positivity and choice of hormone treatment? Were 70+ women who were receptor negative were still given hormone treatment?
9. In all data from the present study does not show convincingly that there are age related differences in the management of patients but as there are only 20 patients >70 and 60% of them have cardiovascular disease it is not possible to conclude that there are true age related differences. I feel that authors should conclude that age is a surrogate for other factors that influence choice of treatment in these patients. The word age related should also be deleted from the title.
10. The manuscript can be accepted after suitable modifications
11. The manuscript will need statistical evaluation

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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

Statistical review: Yes

Declaration of competing interests:
‘I declare that I have no competing interests'