Reviewer's report

Title: Preoperative serum levels of lipocalin-2 and matrix metalloproteinase-9 (MMP-9) are associated with prognosis of breast cancer.

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Reviewer: Jeremy M Taylor

Reviewer's report:

In this paper the authors investigate the association between two serum biomarkers and disease free survival in a set of 303 breast cancer patients.

The authors find marginally significant associations in adjusted analyses. They also found some speculative interactions, which they appropriately label as speculative, and I would be not confident they would be reproduced in the next dataset.

The concern I have with the finding is that the magnitude of the effect is not that big (as shown in table 3). They are smaller than those of known prognostic factors, ER, stage, size. Hazard ratios of around 2 are not going to be big enough to impact clinical practice, even though the results of an independent association may be valid. The lack of a monotonic trend in hazard ratios across the three tertiles is not very reassuring.

The authors need to include in their discussion the fact that hazard ratios of 2 are not big enough to expect much impact on clinical practice.

The paper does lack an independent validation dataset, on which the model developed on the 303 patients could be tested on the new data. If the results did replicate this would strengthen confidence in the finding of an association. The authors may be able to develop a cross-validation approach to mimic this.

There may be better ways to combine the two biomarkers, such as linear combinations, rather than the simplistic adding tertiles, this would likely lead to a hazard ratio.

What is the median follow-up of the 303 patients?

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

Quality of written English: Acceptable

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

Declaration of competing interests:

'I declare that I have no competing interests