Reviewer's report

Title: Prognostic scores in brain metastases from breast cancer

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Reviewer: Lucyna Kepka

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Major Compulsory Revisions

The validation of prognostic scores for a general population of patients as well as for specific subgroups of patients is often subject of published works. The authors are going in the same direction performing multiple statistical comparisons for a small size group.

The authors conclude that the published prognostic models reflect the prognosis of patients with brain metastases from breast cancer “to a more or less satisfactory degree”. And, the reason for “the less satisfactory degree” is related to the fact, that all published models are derived from the whole population of patients with brain metastases, whilst brain metastases from breast cancer have the unique biology and time course of the disease. So, they propose their own prognostic model derived from the survival of 68 patients (this was a number of patients from the overall 83 who were retrospectively analyzed for a prognostic value of published scores), for whom the information on all parameters was available. Dr Nieder and colleagues believe that their findings need validation in large studies and will be base for broad clinical application.

I completely agree that patients with brain metastases from breast cancer may differ from overall population of patients with brain metastases. However, this is not true, that the problem of applicability of such a basic prognostic score as RPA RTOG classes was not subject of previous analyses. It was, and the conclusion was that this score is also applicable for prognosis for this population. And there are also references for this in the work of Dr Nieder and colleagues. Additionally, the prognostic value of this basic score was also confirmed by the present work. The authors, however, are not completely pleased with this confirmation. Apparently, they are looking for ideal prognostic model, which will allow for predicting the future of the patient treated in 100%. This is seen in the expressed permanent concern of Authors about the tails in the respective survival curves. In my opinion we cannot get rid of these tails, because we will always have patients from the RPA class 1, who will die one day after our diagnosis or from acute complications of treatment as well as we will have some Class 3 patients who will survive unexpectedly long for various reasons. So, curves without tails are the scientific fiction. And after all, the tails do not matter; the median survivals are important and statistically predictable. And the main value of RPA RTOG prognostic score is its simplicity, which makes its use easy for all comparisons and analyses.
The study of SIR prognostic score should not be performed for this population of patients managed exclusively with WBRT, because SIR is applicable for patients managed with radiosurgery. And this was not a treatment used in this population. And the GPA? The authors did not acknowledge the very limited size of patients (and the small subgroups) for a validation of this 4-tiered score.

I agree with authors, that the biology and the course of the disease are unique in breast cancer. However, the authors did not provide us with any information which may influence treatment outcome in breast cancer as hormonal receptor status, HER-2 receptor status, treatment of extracranial disease, leptomeningeal disease. The authors state that the breast cancer patient is not the same as lung cancer patient. This is true, especially for extracranial metastases, as for the latter there are less therapeutic option for the treatment of extracranial extension that for the former. So, the existence of potential therapeutic options of extracranial disease has the obvious impact on survival and decision making. But, for showing the prognostic significance of this factor we would need much more patients, than the authors had. So, for now we should use our good sense when making therapeutic decisions about management of brain metastases in lung and breast cancer patients with brain metastases. The authors did not discuss this.

However, when looking at another (the most important) component of the RTOG RPA prognostic score – the performance status, we probably cannot find a difference between lung and breast cancer patients. The poor performance status leads both to exactly the same hopeless prognosis preventing from any efficacious aggressive treatment.

In this context, the proposition of new prognostic score of the authors basing on four factors derived from 68 patients and giving two points to the low KPS and one point each for presence of extracranial metastases, presence of more than one brain metastasis and interval <38 months appears very surprising. According to this score, the prognosis would be equal for patient with presence of two metastases, the interval from diagnosis of 37 months and good KPS as for patient with poor KPS. Such a model is derived from multiple statistical analyses on a small number of patients, and in my opinion has a very limited clinical value. I would not imagine that this may be taken very seriously into account in clinics.

• Problem of multiple comparisons and a small size of group should be discussed and acknowledged.
• Type of treatment offered to patients studied should be briefly provided, as well as fact that there were treated in two institution over a long period of time.
• The abstract should be rewritten, the small size of group should be clearly stated, and a proposition of a new score also should be clarified. In this form is too general, and looks much more promising than the content of the work.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal
Quality of written English: Acceptable

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' below.