Reviewer's report

Title: Clinical and multiple gene expression variables in survival analysis of breast cancer: Analysis with the hypertabastic survival model

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Reviewer: Upender Manne

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The hypertabastic survival model is a good alternative to the Cox regression model for analysis of data having clinical and multiple gene expression variables. This model overcomes main concerns for utilization of multiple gene expression variables, together with standard clinical variables, in finding the best model. In analysis the model treats the important issue of interaction of different gene signatures in the survival analysis.

The authors illustrate the usefulness of the model by modeling breast cancer data. Using statistical measures of goodness of fit the semi-parametric Cox proportional hazards model and the parametric log-logistic and Weibull models are compared. The hypertabastic model does provide better fit among all the models considered. The explicit functions for hazard and survival are analyzed to better understand the time course of progression of hazard and decrease in survival proportion. The authors also analyzed the role of the gene expression variables in determining the time course.

The authors quantified the influence of each gene expression variable on extrema in rates of changes in hazard and survival. Overall, the hypertabastic model is an effective tool in survival analysis for breast cancer patients. In addition, the models offers explicitly defined hazard and survival functions for use as tools for analysis of survival data. The model has improved prognostic capabilities which are of considerable value in breast cancer treatment.

Level of interest: An article of outstanding merit and interest in its field

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