Reviewer's report

Title: An inflammation-based cumulative prognostic score system in patients with diffuse large B cell lymphoma in rituximab era

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Reviewer: Craig Portell

Reviewer's report:

Sun and colleagues have studied a inflammation based prognostic scoring system for DLBCL and identified that a 4 point system incorporating CRP, albumin, and Lymph:mono ratio. This is an interesting concept. The authors identified 839 patients but included only 564 patients in their analysis. It is unclear why up to 1/3 of the sample was removed, other than selecting for patients receiving only RCHOP, at least as it is currently written. Other exclusion and inclusion criteria are listed but it is unclear if they were utilized to select the 564 patients. This degree of selection may incorporate selection bias which is not discussed at all.

There are further methodology concerns in the construct of the model. First is that the determination of the cut-off values for the inflammatory lab values were based on ROC analysis. this seems appropriate but identified that many of these cut off values are actually within the normal range based on many labs. the normal range at the author's lab is not listed in the manuscript, making these difficult to interpret. If indeed they fall into the normal range, it needs to be explained why a normal albumin, CRP or lymph:mono ratio would be an adverse risk.

The authors very rightfully did a univariate analysis incorporating all the individual IPI risk factors as well as the IPI itself. However, some variables are continuous or quaternary (as in the IPI) but these are evaluated with a two-variable statistical design. This undervalues these variables, particularly the IPI and stage and should be evaluated appropriately.

Next the authors utilized the 3 significant inflammatory markers to identify a scoring system which is not weight based (ie, each of the inflammatory markers will have a different weight than the other, but they all have the same weight in the model). this is fine but needs to be discussed.

Finally, the authors conduct at "advanced multivariate analysis" (page 8, line 28), a term I do not understand, utilizing bi-variate IPI risk factors along with the IPI. this is the wrong analysis to do as it utilizes the IPI factors twice in the multivariate analysis and again under values them. The authors should either include the IPI alone or include all the factors in the IPI, but not both. With this analysis the inflammatory score is the only independent prognostic factor, which is
surprising seeing that many of the univariate factors were highly significant for PFS and survival.

The conclusions/discussion essentially discusses one other inflammatory system and re-iterates the authors methodology. It does not address the potential pitfalls of a study like this (retrospective studies are wrought with error). Finally, the hypothesis presented on page 11, line 34 is very speculative, not supported by this study, and should be removed.

Overall, I am concerned that the conduct of the methodology is the cause for having the significant finding and needs to be addressed prior to publication.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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