Reviewer's report

Title: The preoperative platelet-lymphocyte-ratio is superior to neutrophil lymphocyte ratio as a predictive factor in soft-tissue sarcoma

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Reviewer: Vijaya Bhatt

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The authors provide a single-institution large retrospective analysis of patients with soft-tissue sarcoma who underwent resection from 2000 to 2010. Using a multivariate analysis, the authors demonstrate that elevated preoperative platelet-lymphocyte-ratio but not neutrophil lymphocyte ratio independently predicts survival.

This is a relatively large study. The authors use receiver operating curve (ROC) analysis to calculate the optimal cutoff values for the two ratios. In the multivariate analysis, the authors adjust for important covariates such as tumor grade and size. In my opinion, these are important strengths of the study.

Major Compulsory Revisions

- The results of this study is different than those of the study by Szkandera et al (British Journal of Cancer (2013) 108, 1677–1683). In their study of 260 soft-tissue sarcoma patients, Szkandera et al demonstrated that elevated preoperative neutrophil/lymphocyte ratio was an independent prognostic factor in the multivariate analysis. This is also shown in another study: Biomarkers. 2012 Sep;17(6):539-44. Interestingly, the study by Azab et al (Med Oncol (2013) 30:432), although in breast cancer patients, concluded that "Pretreatment neutrophil/lymphocyte ratio is superior to platelet/lymphocyte ratio as a predictor of long-term mortality." Similarly, Azab et al in colon cancer patients (Cancer Biomark. 2014;14(5):303-12) demonstrated similar findings.

- The authors should thoroughly discuss such prior literature, compare with their study in terms of results and any unique design and provide potential explanations for the discrepancy in their results.

- Two large systematic review and meta-analysis [Cancer Epidemiol Biomarkers Prev. 2014 Jul;23(7):1204-12. and J Natl Cancer Inst. 2014 May 29;106(6)] have analyzed the role of similar markers. These should be referenced and discussed.

- The following study has demonstrated that elevated preoperative systemic inflammatory markers predict poor disease-specific survival in localized soft tissue sarcoma: Ann Surg Oncol. 2014 Mar;21(3):778-85. This study shows that elevation of multiple markers was a more significant prognostic factor than elevation of a single marker. Also, histologic grade was strongly correlated with inflammatory marker values. The study is also important since it utilizes disease-specific survival in a specific subset of soft tissue sarcoma. This study
should be referenced and discussed.

-In the discussion section, the authors should describe the implications of study. In other words, how does PLR compare to other prognostic factors such as tumor grade/size? Can the use of PLR enhance current prognostication?

-The authors should briefly discuss about different cutoff values used in different studies. This is important for clinical practice. What cutoff values does a clinician use to identify whether a ratio for NLR or PLR is elevated?

-It is important to realize that a single test done within 7 days before surgery or other therapy has limitations. Further, these ratios may differ based on age, smoking status, presence of infection or inflammatory conditions etc. A recent study demonstrate that neutrophil lymphocyte ratio may vary by race (Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. PLoS One. 2014 Nov 6;9(11):e112361.) At the least, these limitations should be acknowledged.

-The study population is heterogeneous e.g. the authors have used different types of soft-tissue sarcoma and at different stages. Only some of the patients received radiotherapy. The use of adjuvant or neoadjuvant chemotherapy is not mentioned. Since prognosis may differ because of these factors, this may be another limitation of the study.

-The authors should discuss about the followings: inclusion/exclusion criteria, method of data collection e.g. chart review/use of database, staging evaluation, indication of surgery for stage IV disease and adjuvant radiotherapy in their patient population. The use of adjuvant or neoadjuvant chemotherapy and indication should be mentioned.

-The overall survival also depends on the presence of comorbid conditions. This is very important in potentially curative disease. The unavailability of data regarding comorbid conditions, cause of death or disease specific survival is another limitation. I understand that the authors have included DFS, which is useful. In the same note, what was the source of data regarding vital status (alive or dead) at last follow-up?

-The writing style needs to be improved. Grammar errors should be corrected.

Minor Essential Revisions

-Mean absolute neutrophil count should be mentioned.

Discretionary Revisions

-The author may consider replacing the term "predictive" with "prognostic" in the title.

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

Quality of written English: Not suitable for publication unless extensively edited

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.