Reviewer’s report

Title: Dynamic serum alkaline phosphatase is an indicator of overall survival in pancreatic cancer

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Reviewer: Oliver Strobel

Reviewer’s report:

This is a retrospective study of serum alkaline phosphatase (ALP) and survival in resectable (n=97) and unresectable (n=454) pancreatic cancer. The authors assess "baseline" and "varying" ALP values and show that a stepwise increase of ALP is associated with decreasing survival. While the topic of biomarkers is of interest, I have several concerns with this study.

- Most importantly, it is poorly described which values are really entered into the analysis. While the authors define what baseline values are, they do not describe at which time points "varying" values were assessed and which of these values were entered in which way in the analysis.

Were values from defined time points used or was always the highest value used? What is the variability of the values over time? Etc.

- Patients with progressive disease will at some point (close to death) frequently have elevated ALP due to liver metastases. In these cases no new biomarkers are needed to know that the prognosis is very poor...Therefore, if the survival analysis of varying values rely on the highest ALP value, I do not think that we can learn from ALP as a prognostic biomarker in this situation.

- Similarly, ALP can indicate cholangitis (independent of bilirubin) at least after pancreatic head resection and biliodigestive anastomosis. The authors looked at bilirubine and albumin levels. Can they additionally look at CRP or leucocyte levels?

- Applicability of the results: Only about 40% of resected and unresected patients received chemotherapy. This does not reflect state of the art and severely reduces the applicability of the data in settings where chemotherapyx is applied according to current standards.

I strongly recommend that the paper is additionally reviewed by a statistician.

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.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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