Reviewer’s report

Title: Long-Term Outcomes After Surgical Dissection of Inguinal Lymph Node Metastasis from Rectal or Anal Canal Adenocarcinoma

Version: 0 Date: 14 May 2019

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?
Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?
Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?
No - there are major issues

STATISTICS - Is the use of statistics in the manuscript appropriate?
No - there are issues with the statistics in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?
Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?
Maybe - with major revisions

PEER REVIEWER COMMENTS:

GENERAL COMMENTS: Overall its a well written study. However there are numerous ways in which it can be improved if authors really want to target a high impact journal

REQUESTED REVISIONS:
The authors deal with somewhat sparse data...Meaning low number of patients with even lower number of patients who do not develop a recurrence following inguinal lymph node dissection. There are some
basic statistical considerations which must be respected while reporting results

1) Mean survival is only reported if every patient in the cohort experiences an outcome (meaning death if we are talking about os or recurrence if we are talking about dfs).....If 100% patients do not experience an outcome under consideration then median survival should be reported instead of mean.....So for example authors report mean relapse free survival when only 25/31 experienced a relapse.....This is incorrect.

2) Sparse data needs its own set of statistical tests. So a common approach is to use univariate analysis and then select variables significant in univariate analysis for multivariate analysis. However detecting significance in sparse data situation can be problematic due to sparse data bias. So authors should use firth's penalised survival analysis for survival analysis. This can be done using coxphf package in r program. Now univariate analysis will give authors exaggerated effect size which needs further penalisation. So if more than one variable is found significant in univariate analysis then inverse probability treatment weights can be used for multivariate analysis. This will give much restricted and unbiased effect size. Another approach can be to use elastic net regression to straightaway perform multivariate analysis and then perform stratified analysis using firths penalised survival method if two variables turn out finally significant. Please see this paper to read more about sparse data and how it should be handled.


3) Lastly survival analysis should be performed using time dependent covariate method where time is split at the junction of performance of lymphadenectomy. ....This would take away the bias of late performance of lymphadenectomy leading to inferior outcome....And also account for synchronous and metachronous lymph nodal positivity.

Just consult a trained statistician and he should be able to easily sort this out using r or sas

ADDITIONAL REQUESTS/SUGGESTIONS:
The paper is excellent. There are similar papers in the literature. if authors can perform a more rigorous statistical analysis then this paper shall have more impact.

Note: This reviewer report can be downloaded - see attached pdf file.

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.

No
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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 am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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