Reviewer’s report

Title: Validation of a frailty index in older cancer patients with solid tumours

Version: 0 Date: 04 Mar 2018

Reviewer: Thomas P. McCoy

Reviewer's report:

Thank you for your important work and submitting to BMC Cancer. Below are comments which are hoped can help increase enthusiasm for the submission.

Major comments:

The range of ages for frailty studies has a topic of keen research interest to revisit as of late. Given such, it would be good to define what this study considers as "older adult" early and explicitly (say, in Abstract) as it is not until Page 6 Line 14 when this is described.

The flexibility of the FI-CGA to include 'whatever a researcher wants' is also what makes it controversial to non-advocates of the accumulating deficits approach. This ad hoc way of measuring frailty hinders reproducibility if every investigator is creating an index on their own, as that is prohibitive to cumulative validity and reliability evidence.

The authors boast of the FI-CGA's measurement level as continuous - but it's really a count of the number of achieved deficits with a constant offset of the number of total potential deficits. So technically it is taking dichotomous data and tallying them up in a discrete summary (i.e., not all possible fractions between 0 and 1 are possible for any given FI).

Line 31-36 on Page 7: Why weren't types of chemotherapy regimens taken into account in analyses?
Line 1 Page 8: Why was survival only followed for 3.5 years? This precludes studying 5 year "cure" rates for some cancers.

Line 49, page 9: Why was the FI categorized to get ORs? The pseudo-continuous index could have been used (or multiplied by 100 to scale an increase from 0.01 to 0.02, etc., rather than 0 to 1). Categorizing results in loss of statistical power to detect relationships.

Line 18 page 10: Why weren't cancer diagnosis (or cancer stage) accounted for in analyses? The expected survival for advanced lung cancer is different for non-advanced breast cancer, for example.

Line 24 page 10: The authors state the FI could be calculated for all patients. So, every patient had non-missing data on all 42 FI deficit components (is that correct)?

FI dichotomized for 0.25 or less was not statistically significantly associated with increased survival (but close to with p = 0.055). Was leaving FI as pseudo-continuous statistically significantly associated with survival?

A major pitfall of the survival analyses is that they do not account for major influences of survival experience such as age, cancer diagnosis type, or severity of cancer. This leaves the reader to critically question if these bivariate results can be accurately interpreted as potential effects of FI on survival. Adjusting for such influences using parametric survival regression models, Cox proportional hazards regression, or extended Cox regression modeling can investigate.

The authors are to be commended for potentially considering making the datasets used/analyzed available under a reasonable request.

Minor comments:

Line 55 page 4: When mentioning the Fried Phenotype, provide a citation.
Setting and participants: The explicit time-frame over which the consecutive patient series was pulled from the electronic medical record needs to be detailed.

Line 18 page 9: Report the median follow-up time for patients here and range.

Lines 54-57 page 10: Consider re-writing as (0.24 [0.19-0.29], Mann-Whitney U=679.5, Z=-8.86, p<0.001, r=-0.67) and eliminate sentence Mann-…

Line 60 page 10: Define what the r effect size being reported is in the Data Analysis section by citing a reference such as by Cohen or writing r = Z/sqrt(N) if that is indeed the measure being reported.

Table 4 Last Column: The last column is titled "Test Statistic" but is r or OR. Consider re-titling this as "Effect size".

Table 4 Treatment plan: Only 1 OR is presented. Does this mean FI was the independent variable and treatment plan was considered an ordinal dependent variable where not planned was the lowest level, terminated the middle level, and completed the highest level? Make clear.

Table 4. Add a column for P-value and give the values of the p-values rather than dichotomously stating in the footnotes.

Line 14 page 12: It does not feel appropriate to report a % died (i.e., the 62%) because this is relative to at what time-point over follow-up you are talking about and instead a Kaplan-Meier estimate which also takes into account censoring should be used for. Recommend to just report a number of events. Reporting the one year estimate (if 44.24%) from Kaplan-Meier is OK, though (if this is the 1 year K-M estimate).

Table 3 : Change "population" to "sample".
Figure 1. Change Y-axis increment to be 0.1 instead of 0.2 (e.g., 0.0 to 0.1 to 0.2). This will allow reader to see median survival at 0.5 easier. Change X-axis increment from 1.0 years to 0.5 years. Add Log-rank p-value in added text box, say, in top-left corner.

Again thank you for your important work.

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

**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.
No

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