Reviewer’s report

Title: Physician workload associated with do-not-resuscitate decision-making in intensive care units: an observational study using Cox proportional hazards analysis

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Reviewer: Tomohiro Shinozaki

Reviewer's report:

I carefully reviewed a statistical aspect of the manuscript Dr. Lin et al. and have some suggestions to improve the validity of the study's results.

They examined the association between physicians' workload (measured by the numbers of patients in charge per day) and time from surgical ICU admission to decision-making of do-not-resuscitate for each patient. Here, the study inherently had a multilevel data structure: outcome (patient's level) was nested within a primary exposure variable (physician's level). I strongly recommend the authors to employ statistical methods that can account for multilevel data, such as random-effect Cox modeling or a robust variance estimator of confidence intervals, as explained below.

1) As main variables is physician-level workload, physician-level summary of these variables would be helpful for readers. Namely, I want the authors to show the rates of do-not-resuscitate decision (per patient-day, patient-month, or patient-year) for each physician; this can be calculated by usual person-time method (ie, the number of do-not-resuscitate decision is divided by patient-day in Fig 2 for each physician). Moreover, it may be informative to provide the physician-level correlation between the rates and the number of patients in charge per day by, eg, a scatter plot and correlation coefficient. This "ecological study" analysis seems insufficient by themselves, but it is a good starting point to summarize multilevel data. They will also show between-physician variability of the data.

2) The authors included multiple variables into their analyses to reduce variability in outcome. However, most of them were patient-level variables and there seems to be only one physician-level variable: physician's age. If physician-level variables other than physician's age affect the outcome (and it is likely as described in Introduction) and if their values are different from physician to physician, such variables would confound the association between the physician-level exposure and the patient-level outcome. So, I request further adjustment for more physician-level factors (eg, those presented in pp. 6-7) to account for physician-level variability of do-not-resuscitate decision-making.

3) Given the above 2 points are addressed, I think that patient-level analysis including the Cox model will be appropriately performed and interpreted. However, it should account for multilevel structure of the data. Two commonly used techniques for survival analysis are (a) the frailty Cox model including random effects for between-physician difference and (b) the
marginal Cox model that does not adjust for between-physician difference by fixed/random effects but using robust (sandwich) variance estimator treating each physician as a cluster (like generalized estimating equations or GEE analysis for uncensored outcome). I think the either is okay in this manuscript, but please consult local biostatisticians or statisticians if the authors cannot run the model fitting.

(Side note: The Cox model parameterizes and estimates hazard ratio, rather than odds ratio, so please rephrase them appropriately throughout the text.)

Log-rank test also neglects the outcome dependence within the physicians; it should be replaced with appropriate one, if presented after revision.

**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.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
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No

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