Reviewer's report

Title: Resectable adenocarcinomas in the pancreatic head: The retroperitoneal resection margin is an independent prognostic factor

Version: 6 Date: 18 September 2007

Reviewer: Roger Davis

Reviewer's report:

General

This paper uses Cox proportional hazards regression to model survival in surgically-treated pancreatic cancer with macroscopically tumor-free margins and to determine the prognostic value of microscopically clean margins in these patients. The study includes 114 consecutive patients from a single hospital in Norway who met these criteria.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Statistical analysis section, second paragraph states that “the group with the best prognosis" was used as the reference group. This does not appear to accurately describe the methods that were used, and is probably not the best approach. A better approach is to use the largest group as the referent, which appears to be the method that was actually used for origin of tumor.

2. The statistical analysis section indicates that, “Hazard ratios were proportional for all covariates." I assume you mean that hazards were proportional. You need to indicate (in the methods section) how proportionality was evaluated and present the results of the evaluation in the results section.

3. The methods indicate that the models were constructed using a stepwise approach. If that method was used, it is not clear why base model 1 includes covariates that are not statistically significant.

4. It is probably not appropriate to exclude the seven patients with multiple margin tumor involvement (top of page 8 and top of page 10).

5. The presentation of the association of resection status by tumor origin (page 9 and figure 5) is not very convincing. The discussion of the results of your current analysis (bottom of page 12) seem a bit strong, given that the sample size within each origin site is small, so the difference seen is probably not statistically significant. The appropriate way to evaluate this question is to fit a model with origin and resection status and a model with origin, resection status and the interaction of origin and resection status. A likelihood ratio test comparing those models will evaluate whether there is significant effect modification of resection status by origin.
6. Table 1 should be expanded to include a more complete description of the study population, including, at a minimum, the covariates in base model 1.

7. Base model 2 (table 2) includes distal bile duct margin as a covariate. From Table 1, it appears that this variable defines a group with only 2 patients. It does not make sense to model such a small group.

8. My interpretation of the results of base model 2 is quite different than the authors. I don’t think the results argue for evaluating retroperitoneal margins as a separate entity. The hazard ratio for involvement of the pancreatic neck is virtually identical to that for retroperitoneal and distal bile duct also has HR greater than one (although as noted above, it is based on too small a sample to mean anything). I would conclude that the type of margin is not important, i.e., that microscopic involvement of the margin increases mortality rates. I would not single out retroperitoneal margins.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

9. Throughout the paper, the use of the term multivariate is not appropriate. Multivariate refers to methods for dealing with multiple dependent variables simultaneously. Multivariable is an appropriate term for multiple independent variables. I would recommend using ‘unadjusted’ and ‘adjusted’ rather than ‘univariate’ and ‘multivariate’.

10. Beginning of statistical analysis section, ‘Survival data was’ should be ‘Survival data were’

11. In the next sentence, “Fischer’s exact test” should be , “Fisher’s exact test”

12. In Table 2, please explain the p-value (0.056) associated with the reference group for origin site.

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests