Reviewer’s report

Title: Prognostic parameters for recurrence of papillary thyroid microcarcinoma

Version: 3 Date: 8 June 2008

Reviewer: Eric Siegel

Reviewer’s report:

Statistical Review:
Prognostic parameters for recurrence of papillary thyroid microcarcinoma, manuscript submitted to BMC Cancer by Tae Yong Kim, Suck Joon Hong, Jung Min Kim, et al.

Summary: On the one hand, it is possible that the statistical analyses were done correctly. But on the other hand, I see several inconsistencies and deficiencies that make me suspect that the statistical analyses for Table 3 and Table 4 may have been done incorrectly. I cannot tell for sure. Moreover, I found strong indications that the multivariate analysis was done using an incorrect method. My recommendation for the authors is that they find a professional statistician to add as a co-author, and have the statistician re-analyze their data using appropriate methodology, in order to see how much of their analysis results can be confirmed.

Major Inconsistencies and Deficiencies:

• “Definition of Clinical Outcome”: Having a Methods paragraph with this title is a great idea, and more writers should follow the authors’ example. However, for survival analysis, the authors’ current paragraph is incomplete. In addition to the definition of “Recurrence”, we also need the definition of “Time to Recurrence”, namely, the duration of time from when follow-up began to when the patient either had a recurrence or received their last follow-up evaluation (whichever came first). The definition of Time to Recurrence should include whether follow-up began at diagnosis, at treatment, or at some other time. For this paper, Time to Recurrence is (or should be) the true clinical-outcome variable, while Recurrence is (or should be) just the “status indicator” (i.e., the censoring variable) that accompanies Time to Recurrence and helps define it.

• In the Statistical Analysis paragraph of their Methods section, the authors say that “Cox's proportional hazard model and the forward stepwise method were used to analyze the relative importance of various prognostic factors for prediction of clinical recurrence.” But in the Results section of the Abstract, they say that “multivariate logistic regression analysis” was used for this, and in the Multivariate Analyses paragraph of their Results, they say that “multivariate logistic analysis” showed the prognostic value of cervical node metastasis. So already, there is an inconsistency between the Methods and the Results as to
what method was used. Moreover, because their “Definition of Clinical Outcome” paragraph defined Recurrence but not Time to Recurrence, I am almost certain that the authors used multivariate logistic regression with Recurrence as the outcome variable. If so, logistic regression is not the correct multivariate method to use. The authors should have instead used multivariate Cox regression with Time to Recurrence as the outcome variable. The authors’ future statistician co-author will probably want to construct a table of results from the multivariate Cox regression.

• Tables 3 and 4: The footnotes say that “the Kaplan-Meier method with the log-rank test was used to compare recurrence”, and that would be the correct method to use. However, the tables calculate rates of recurrence as the number of recurrences divided by the number of patients; this would be an appropriate summarization for logistic-regression methods or chi-square testing methods, but is not appropriate for survival-analysis methods. What the authors need to do instead is, (1) present for each analysis group the “person-years” of total observation time, then (2) calculate the recurrence rates for each group as number of recurrences divided by number of person-years. The resulting recurrence rates will be “hazard rates”, will have units of proportion (or percent) *per* *year*, and will more accurately reflect the group differences in risk of recurrence than the authors’ current calculation method. The authors’ future statistician co-author will know how to do this effectively and efficiently.

Minor Essential Revisions:

• The Statistical-analysis paragraph in Methods has a couple of deficiencies in addition to the previously noted issue with Cox regression. This paragraph has a sentence that says “values are presented as means ± standard deviations”, but only one quantity (tumor size) is ever presented in this manner. Follow-up time was presented as median and range, and all the other quantities I could find were presented as number and/or percent with a characteristic. The footnote in Table 1 says that baseline characteristics were compared by Fisher’s exact test for two-group analysis variables, and by chi-square test for multi-group analysis variables; this information is missing from the Statistical-analysis paragraph, and needs to be included.

Point of Clarification:

• In the Definition of Clinical Outcome paragraph, Recurrence is defined as “persistence and/or reappearance of disease after initial operation”. How many recurrences were reappearances, and how many were persistent disease? (I haven’t been able to figure this out from the text.) If all recurrences were reappearances, and none were persistent disease, then I don’t see the need to include persistent disease in the definition of Recurrence. On the other hand, if there were cases of persistent disease among the recurrences, then those patients should appear in the Kaplan-Meier curves as recurrences on Day 0, and I don’t see any Day-0 recurrences in the curves. So are the persistent-disease cases inadvertently being excluded from the analysis, or were there none to begin with?
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I have no competing interests.