Reviewer’s report

Title: Colorectal cancer liver metastases - a population-based study on incidence, management and survival

Version: 2 Date: 03 Oct 2017

Reviewer: Feng Gao

Reviewer's report:

This is an excellent written manuscript. The materials are well organized. The study is based on a large population-based data and provides invaluable information regarding incidence and disease management. The strategy for data analysis is clearly outlined and the results are interpreted and summarized properly. The statistical methods are properly used in general, but a few places need some further clarification.

The conventional Cox models assume that all the covariates are measured at baseline (time 0 or CRC diagnosis here). However, the status of metastasis generally becomes available after time 0, except for those "Synchronous metastases". Therefore, when the OS is compared between non-metastasis versus metastasis cases, the status of metastasis should be treated as a time-dependent covariate. On the other hands, when the OS is compared between different subgroups among metastasis cases, the status of metastasis can be either treated as a time-dependent covariate, or the time-0 can be reset as the diagnosis of metastasis. It seems the authors reset the clock in some analysis (Figure 3 and Figure 5), but this is not mentioned anywhere in the section for statistical methods.

Specific comments:

1. Page 6 lines 20-22: the OS for metastasis cases should also be defined here (i.e., reset clock for time-0)

2. Page 9 lines 1: it is unclear how the 51% or 84% were obtained from Figure 1B.

3. Table 5A: the 3 variables for metastasis should be treated as time-dependent variables, unless these 3 variables only represent cases with "Synchronous metastases". This need to be clarified.

4. Table 5B: it is unclear whether this analysis is performed after reset of clock. This should be clarified.
5. Figure 2: it is unclear why the number at risk for metastasis cases are rather small. Is this because only those "Synchronous metastases" are included? Otherwise metastasis should be treated as time-dependent covaroates.

6. Figure 4: the status of metastasis should be treated as time-dependent variable (reference: SM Snapinn, Q Jiang and B Iglewicz. Illustrating the impact of a time-varying covariate with an extended Kaplan-Meier estimator. The American Statistician, 2005; 59, 301-307)

7. Figure 5: it is unclear whether this analysis is performed after reset of clock. The error in the label for time axis should be fixed

A few editorial stuff:

8. Page 9 line 4: p-value does not to be in ()

9. Page 9 line 5: p-value does not need to be in ()

10. Page 9 line 13: incomplete sentence

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.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes
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