

To the Editor

Please find here the revision of the manuscript # 30452 entitled “Competing risk analysis on outcome after hepatic resection of hepatocellular carcinoma in cirrhotic patients” to be considered for publication in WJG. The manuscript was modified in accordance with Reviewer’s and Editor’s requests. A certificate language was provided and the grammar entirely checked for correctness. The audio core-tip was also provided.

Reviewer # 00051373

A very interesting observation study provided a first competing risk analysis of causes of death after hepatic resection of hepatocellular carcinoma particular on the patients with Child’ A functional class. This manuscript is well written and analyzing. It should benefit to kind in mild that those patients having a risk of dying from cancer resection that significantly overcome the risk of dying from liver failure. The current manuscript should be accepting without alter.

Re: We thank the present Reviewer for his/her comments.

Reviewer # 02445541

By retrospective competing risk analysis of prospectively collected data of 864 Child-Pugh class A cirrhosis patients, the authors define features to distinguish optimal from non-optimal surgical candidates. Their distinction is based on the assumed risks of dying from liver failure and risk of dying from tumor recurrence as given in Fig 2. I have several questions about this Fig 2. 1. It is said that in the horizontal column % risk (5.1, 7.9 and 12.2) of dying from tumor recurrence in T1, T2 and T3-T4a patients is derived from the calculation of the area under the cumulative incidence curve obtained from competing-risk regression, divided by time.

- 1) I miss on how many patients per group this is based (in any case less than numbers of UNOS stage given in Table 1)?

Re: Figure 2 derives from solving the equation of competing-risk of the Fine and Gray method applied here (it is identical to solve a Cox-regression formula based on beta values and baseline cumulative hazard over time). Consequently, the competing-risk model is based on proportion of UNOS T stages reported in Table 1 but percentages reported in the Figure 2 are not directly observed but predicted by the model as was already reported in the Figure 2 legend: *“Comparison between the predicted average risk of dying for liver failure (rows) and for tumor recurrence (columns) within the first 5 years after surgery”*. For further clarification we now modified the legend of the figure as follows: *“Comparison between the predicted average risk of dying for liver failure (rows) and for tumor recurrence (columns) within the first 5 years after surgery resulting from the competing-risk prediction model”*

- 2) In Table 2 it is shown that death for tumor recurrence for T3-T4a in 5 yr period amounts to 34.6 % . I wonder how valid it is to use a percentage of 12.2% in Fig 2 for T3-T4a patients? I miss some foundation for this reasoning.

Re: In Table 2 a 5yr predicted cumulative incidence of death for tumor recurrence 34.6% is reported for T3-T4a, thus, this percentage is specific for the 5-year time-point (and not consider covariates handled by multivariate reported in Table 3) As was already stated in the method section: “the area under the curve was then calculated using trapezoidal rule and expressed as average risk within the first 5 years from surgery” meaning that for each time interval considered, the corresponding CIF was considered and the area under the CIF curve calculated using the trapezoidal rule [<http://www.intmath.com/integration/5-trapezoidal-rule.php>]. Thus, the 12.2% is the average during 5 years after surgery that includes both low CIF values (i.e. 3.2% at 6 months) and high CIF values (i.e. 34.6% at 5 years). We now modified methods at Page 8, results at page 10, legends of Table 3 and of Figure 2 to made our methodological approach clearer.

- 3) I have the same question for the percentages of risk of dying from liver failure (Fig 2 fourth column): what is there validation? Are they based on a statistically sufficient number of patients per group?

Re: As stated in points #1 and #2, Figure 2 reports results from a competing-risk prediction model based on the number of patients per group reported in Table 1 (which we believe can be adequate, since we did not find any inconsistency in the competing-risk model, with acceptable 95% confidence intervals – Table 3) and percentages are the results of the AUC calculation of the CIF distribution over time. We modified Figure 2 and Table 3 legends to make these aspects clearer. Methods and Results section were also modified (page 8 and 10). We thank the Reviewer for his/her observations.