Reviewers report

Title: Outcomes and factors influencing the survival in cases with spontaneous rupture of hepatocellular carcinoma: a multicenter study

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Reviewer: Jeong Won W. Jang

Reviewers report:

Dear the editor,

Kirikoshi et al. conducted a study of the prognosis and outcome in cases of spontaneous rupture of hepatocellular carcinoma (HCC). From the analysis, the authors stated that transarterial embolization (TAE) appears to be a very useful treatment strategy associated with a longer survival for patients with spontaneous rupture of HCC, and the size of the tumor is an important survival factor in HCC patients in whom TAE was accomplished successfully. The manuscript is easy to read. However, the data analyses and descriptions are basically limited by the small number of the case series. Moreover, no conclusions can be drawn by the lack of randomization and retrospective nature in this manuscript, which could skew the results.

<Major criticisms>

1. Method: The authors stated that the decision to perform TAE was taken according to the patients’ will. This appears to make no sense; more patients in the conservative group had worsened liver function, in terms of high bilirubin, AST levels, and Child-Pugh scores, more cases of ascites in the conservative group. Given that all of these are found to be associated with early 30-day mortality (even though they are not significant in the multivariate analysis), the discrepancies between patient characteristics in the two groups are a challenging issue for the data interpretation. This could introduce an unintentional bias and perhaps may not strengthen the conclusions from these data.

2. Table 1: The data suggest that some proportion of patients had very decreased hepatic function at baseline. This implies that those were intrinsically not eligible for TAE. It is highly likely that such patients with decompensated liver function could have contributed to confounding factors in the analyses. To substantiate the role of TAE, it is relevant to include only patients with reasonable hepatic function who are eligible for TAE.

3. There have been many reports concerning natural course, prognostic factors, and treatment strategy for ruptured HCC. Thus, the overall findings are not new in this field.

<Minor criticisms>

1. Some previous publications including review articles have indicated that
surgical resection (including delayed resection following TAE) for ruptured HCC, if resectable, is a reasonable approach and offers a better, long-term survival. Are there any surgical cases in this study?

2. Results, Page 10: TAE was identified as the only independent predictor of the 30-day survival. These data could be provided by Table.

3. Page 6, background: The sentence, “– increasing prevalence of hepatitis B.. infections”, appears to be inappropriate. With the introduction of HBV vaccination, the prevalence of HBV infection is now decreasing in many countries.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.