



Revision and addendum to the manuscript titled “Propensity score matching study of 325 patients with spontaneous rupture of hepatocellular carcinoma”

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Response to: He T, Zou J. Is transarterial embolization plus two-stage hepatectomy the optimal strategy for the treatment of spontaneous rupture of hepatocellular carcinoma? *HepatoBiliary Surg Nutr* 2023. doi: 10.21037/hbsn-23-113.

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We gratefully receive the comment entitled “*Is transarterial embolization plus two-stage hepatectomy the optimal strategy for the treatment of spontaneous rupture of hepatocellular carcinoma?*” (1). We apologize for the two typing errors in the paper: mortality rate of rupture of hepatocellular carcinoma (RHCC) patients was “0.8%” in the abstract should be changed as “0.9%”; “TNM stage” in the discussion should be replaced by “tumor diameter”. Thanks for the careful reading.

To reply the comment, the addendum of the manuscript title with “*Propensity score matching study of 325 patients with spontaneous rupture of hepatocellular carcinoma*” (2) is present as following:

- (I) We agree with Prof. Chen XP’s opinion (3) absolutely: “open surgical method is the main treatment to stop bleeding” in early period; and later, “TAE/TACE has been increasingly used as an effective, less invasive treatment for achieving immediate hemostasis”.

Since the timespan of data harvested in our study is longer than that of Prof. Chen’s [18 years (2002–

2020) (2) vs. 10 years (2010–2020) (3)], the rate of one stage hepatectomy for ruptured HCC was higher in our study (53% vs. 23%). It may present that the careful selection of patient is the base of the better outcome. The same view has been shown in our previous study: “good outcome of one-stage hepatectomy may be the result of selection of low-risk patients” (4). So, in Prof. Chen’s study, there was no statistical difference of overall survival (OS) between one stage hepatectomy and transarterial embolization (TAE)+ two stage one, which based on their careful selection of patients.

Although we have noticed that the selection conditions for patients is changed over time, due to the limited number of cases (30 ones) who had undergo TAE+ two stage hepatectomy in our study, which is the minimum number defined by a large sample in statistics (5), we have adopted the propensity score matching (PSM) statistical method to reduce the data bias in retrospective analysis, to instead of a subgrouping study.

Statistically, if the sample size is ≥ 30 and the hazard ratio (HR) confidence interval width is reasonable, it means that the data variability is small, and reliable finite inference can be made based on the P value (5); based on this, our analysis results should belong to a reliable inference.

Meanwhile, the higher rate of TAE/transarterial chemoembolization (TACE)+ two stage hepatectomy in Prof. Chen's study (9.5% from Prof. Chen *vs.* 9.2% from our) may display that the two-stage operation is gradually being accepted by more and more surgeons.

- (II) In our study, the time interval from diagnosis to one-stage hepatectomy is about 12–14 days, which is also the interval time from emergency TAE to two-stage hepatectomy. In Prof. Chen's study, it was 4 and 18 days, respectively. Adequate supportive treatment can improve the patient's overall condition and reduce the double damage on patient's liver function (tumor rupture/bleeding and ischemia reperfusion injury during resection).
- (III) Because of the differences in patient selection, number of cases, and treatment intervals between the two hospitals, the treatment results from Prof. Chen's and ours cannot be compared statistically.
- (IV) Based on the limited experience, we propose that radiofrequency ablation may be a remedy for failed hemostasis by TAE. However, due to the limited number of cases with ruptured HCC, a large sample of prospective randomized controlled trials is difficult to be carried out. This is the main reason that there is no evidence currently based medical evidence for surgical indications and radiofrequency ablation treatment so far.
- (V) There are two statistical meanings of the number "0" in *Tab. 4*: (i) the number is zero; (ii) cutoff value, statistical analysis cannot be conducted because of insufficient data.
- (VI) Refer to Prof. Chen's results and our study, for tumor ruptured patients with surgical conditions, we may conclude as following:
 - (i) the selecting of lower-risk patient could improve the outcome of one stage hepatectomy;
 - (ii) TAE+ second stage hepatectomy might be a better option for other patients.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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