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ANSWER REVIEWERS

REVIEWER 1:

1. New interventional options especially for patients with HCC and BCLC scores B and C give rise to disputes about the optimal therapeutic management. CT-guided brachytherapy complements established interventional techniques like RFA and TACE since it may also be used successfully in tumors much greater than 5 cm in diameter. The manuscript is well-written and may bring some new light in the treatment of HCC. However, the table are quite difficult to read and the statistical analysis with .999 is not understable. I would suggest reviewing again the statistics with a senior statistician. The discussion is very informative, although in one sentence should be paid attention to the combined HCC-cholangiocelular carcinoma.

Response: Thank you for your valuable comments. After discussing with the statistician, the p value of 0.999 has been modified to 1.000 in table 1,2 and 4.

As per your suggestion, we have mentioned about combined HCC-cholangiocelular carcinoma in discussion part on page no 21 and line no 6.



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REVIEWER 2:

Zhang et al. reported a preliminary clinical result of endovascular brachytherapy combined with TACE and sorafenib for advanced HCC patients. The results are interesting, but allocation criteria and the factors for propensity matching should be presented clearly. In Fig 4, how do you calculate disease free-survival under which the tumor had never removed? In P4, one sentence is duplicated.

Response: Thank you for your valuable comments. As per our exclusion criteria mentioned in the methods section, the patients who had undergone previous surgery were excluded from the study. The duplicated sentence has been deleted on page no 4.



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REVIEWER 3:

The manuscript is interesting one dealing with hard and very tedious cases of HCC and PVT but there are many comments 1- It is not accepted to use abbreviations in the title. 2- the structure of the abstract is deficient as the introduction was missed, use of many abbreviations without key. 3- The term of (portal vein tumor thrombus) not accepted, better to be changed to (Malignant portal vein thrombosis) 4- The Number of the groups in the abstract is 2 groups (A& B) While in the patients and methods is 3 groups(A,B &C),but in the tables it is only 2 groups.????? 5- The presentation of the data in the tables is not clear and confusing not show the main idea of the study. 6- The discussion is badly written.

Response: Thank you for your valuable comments.

1. The title has been changed to “Combined Endovascular Brachytherapy, Sorafenib and Transarterial Chemobolization therapy for Hepatocellular Carcinoma patients with Portal Vein Tumor Thrombus”.
2. Background has been added to the abstract in page no 3. The abbreviation key is inserted in abstract on page no 3.
3. As the term portal vein tumor thrombus is most commonly used in PubMed/ Medline we have retained in our manuscript.
4. There was a type error in mentioning the number of groups. It is two groups as



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mentioned in abstract and tables.

5. "Table 1" was the baseline characteristics of patients before propensity score matching. To reduce the biases of patients' selection, propensity score matching was used. "Table 2" was the baseline characteristics of patients after propensity score matching. "Table 3" was about Log-rank test and Cox regression analysis of factors potentially related to overall survival. According to the results of "Table 3", treatment regimen was an independent factor related to overall survival. And the EVBT-stent-TACE-sorafenib therapy provided better OS. "Table 4" was about adverse events related to sorafenib administration and TACE in the 2 groups. There was no significant difference of adverse events related to sorafenib. But the occurrence rates of new ascites, liver dysfunction, gastrointestinal hemorrhage were higher in Group B. This result could be attributed to the restore of main portal vein. The patent blood flow of main portal vein provided better liver function.
6. The discussion has been modified.



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REVIEWER 4:

We are glad to review the article entitled "Combined endovascular bradytherapy, sorafenib, and TACE therapy for HCC with PVTT". The authors described that EBVT with stent placement, TACE and sorafenib showed better OS and TTP in patients HCC (+MPVTT), compared to TACE and sorafenib. Further, treatment related adverse effects were less in this combination therapy. This is well-written and this new therapy gives a chance for patients with HCC (+PVTT), whose prognosis is currently very poor. We consider this article is worth-publishing, but we have several questions and suggestions. 1, The author has published several publications regarding the same topic in the past. What is new in this study, comparison to the paper published in Hepatology International? 2. We wonder if they should include extrahepatic metastasis patients, because their focus is on the primary tumor with PVTT. 3. Can author clarify how many TACE they have performed in both groups? 4. Some articles are describing efficacy of proton beam therapy for HCC with PVTT. Can they mention about this therapy? 5. They should refine English.

Response: Thank you for your valuable comments.

1. In our previous study, published in Hepatology International, we considered EVBT with TACE. However, in the current study, we evaluated the safety and efficacy of EVBT along with TACE and sorafenib.
2. As patients with advanced HCC were considered, hence extrahepatic metastasis was considered.
3. During the course of the study, 163 and 90 times of TACE procedures were performed in Groups A and B, respectively.
4. The language has been refined.



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