Dec 22, 2020

Dear Editor, World Journal of Clinical Cases

Thank you very much for your constructive and insightful comments on the manuscript entitled "**Short-Term Outcomes of Radiofrequency Ablation for Hepatocellular Carcinoma Using Cone-Beam CT for Planning and Image Guidance**".

We have made the revision based on the comments from the reviewers. The responses have been given in the "Reply to Reviewers' Comments" separately point-by-point for their concerns.

Thank you for the opportunity of revising the manuscript, and we are looking forwards to hearing from your favorable decision.

Sincerely Yours,

Reply to Reviewers' Comments

For Reviewer #1:

Comments：The manuscript submitted by the authors is relevant as it reports the results of a study to assess the treatment response to RFA for HCC using cone-beam computed tomography. Materials and methods are consistent with the aims of the study and meet a high scientific level. The manuscript is well structured with well-prepared tables and illustrations. The high proportion of patients with post-RFA disease progression, which could be caused by the predominance of larger tumors (≥3 cm in 62.5% patients), does not affect the effectiveness of the method. The authors' conclusions/recommendations on well-targeted needle insertion with an adequate ablation technique, precise planning using CBCT and pre-operative diagnostic CT / MR in conjunction with real-time image guidance, and an immediate CBCT assessment following treatment for better management of patients are of high clinical importance. The manuscript can be published.

Reply：Thank you for your comments.

For Reviewer #2:

Comments: The author summarized the potential usefulness of CBCT for the RFA for HCC. However, the essential problem of the study is the unclear superiority of CBCT compared to US with no irradiation. In addition, the recent advancement of the US and navigation systems combining the CT and MR images with US allowed the detailed assessment of therapeutic efficacy and planning. Based on these concerns, the study will not provide the novel findings to the reader of this journal and therefore, it is difficult to be further considered.

Reply: Thank you for your comment and suggestion. It was our study's limits that we don't compare with US. We would do more research in this field in furture.

For Reviewer #3:

Comments: The manuscript entitled "Short-Term Outcomes of Radiofrequency Ablation for Hepatocellular Carcinoma Using Cone-Beam CT for Planning and Image Guidance", by Xuesong Yao et al, is an interesting report of short term results of radiofrequency ablation (RFA) under Cone-Beam CT (CBCT) for treatment of hepatocellular carcinoma. The article is well written in English, as certified by the editing certificate of the AJE, and provides good overall results for this modified treatment modality. Anyway, on my opinion, it should be better specified which criteria have been used to choose this technique instead of surgical resection, and better detailed the adjunctive treatment modalities used for patients with partial response. If corrected accordingly, on my opinion the paper deserves publication.

Reply: Thanks for your comment and suggestion. The criteria used to choose RFA instead of surgical resection is based on patients willing. In patients with BCLC B, the major criteria was patients' willing, most patients refused to surgical resection.

The treatment used for patients with partial response include transarterial chemoembolization, hepatoprotection and symptomatic treatment.

Comments: Yao et al. reported a retrospective study showing short-term outcomes after RFA for HCC using cone-beam computed tomography (CBCT). They satisfied the clinical outcome of their strategy, which did not compare to the other strategy. The major concerns are the lack of clinical data that made it difficult to understand. Etiology of the HCC, physical data, nutritional conditions, functional indicators, platelet counts, fibrotic indicators, and oncological markers should include the analysis. Also, the indication of this strategy should be presented. I also cannot entirely agree with the conclusion, which was good results. The study's response rate was only 35%, which indicated the strategy was not acceptable to manage the HCC.

Reply: Thanks for your comment and suggestion. We added the base line information in our Result part, including liver function and BCLC stage. The indication of this strategy is based on patients' willing. The patients in our study were refused to surgical resection. Turn to tumor response, The post-RFA initial clinical assessment using contract-enhanced CT or MRI showed 38 cases of CR (79.2%), 10 of PR (20.8%), 0 of SD and 0 of PD. Response rate were 100% after RFA. At end of follow up (median period of 25.6 months, range from 13.5 to 35.2months), final mRECIST assessments indicated 16 cases of CR (33.3%), 1 of PR (2.1%), 0 of SD and 31 of PD (64.6%). It had been relatively long time from RFA procedure to last follow up. We think it was acceptable.

For Reviewer #5:

Comments: This is an interesting manuscript about short-term outcomes of radiofrequency ablation (RFA) for hepatocellular carcinoma using cone-beam computed tomography (CBCT). The authors have compared the planning estimation using CBCT with RFA treatment outcomes. In addition, the authors have examined predictors of overall survival (OS) and progression free survival (PFS). Forty-eight patients were followed up for 25.6 months. Treatment response was categorized as complete response (CR), partial response (PR), stable disease (SD) or progressive disease (PD). The data have demonstrated that the post-RFA initial clinical assessment is strongly correlated with the planning estimation before treatment. Female sex and tumor size <2cm were atatistically significant factors for OS on univariate Cox regression analysis. Age and post-RFA mRECIST were independent predictors of PFS. This manuscript is nicely structured and well written. I have no question about this manuscript.

Reply：Thanks for your comment.