

Format for ANSWERING REVIEWERS



November 2, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5980 review (Answering Reviewers)).

Title: Single HCC \leq 3 cm in Left Lateral Segment: Liver Resection or Radiofrequency Ablation?

Author: Jong Man Kim, Tae Wook Kang, Choon Hyuck David Kwon, Jae-Won Joh, Justin Sangwook Ko, Jae Berm Park, Hyunchul Rhim, Joon Hyeok Lee, Sung Joo Kim, Seung Woon Paik.

Name of Journal: *World Journal of Gastroenterology*

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The manuscript has been improved according to the suggestions of reviewers:

1. The two groups of patients were not comparable in terms of liver function. Even if all patients were Child-Pugh A, a lower liver function was evident in RFA group (higher ICG-R15, lower platelet count, lower albumin). What about portal hypertension in the two groups? What about cirrhosis? It could impact long-term results.

→ We agreed with your opinion about low liver function in RFA group. However, RFA group was treatable with liver resection. Portal hypertension was not examined in all patients. As RFA group did not perform liver biopsy, we did not know the status of fibrosis in RFA group.

2. In order to clarify the effectiveness of RFA, local recurrences have to be considered. It has been reported in the discussion, but no data are available in the results (hepatic recurrences were globally considered).

→ Eleven patients in RFA group developed local tumor progression. The 1-year, 2-year, and 3-year local tumor progression rate in RFA group were 90.9%, 85.1%, and 82.3%, respectively.

3. The conclusions are not supported by the data. Why low PIVKA-II levels should be in favor of RFA?

→ We corrected the conclusion.

4. Theoretically, liver resection can be performed as a salvage treatment after RFA failure. In multifocal or extensive recurrence or liver function deterioration may preclude this option. In the present study only two patients with recurrence after RFA had resection. Please comment.

→ HCC recurred in S6 in one patient and in S8 in the other patient. We resected recurred lesions as patients were Child-Pugh class A .

5. An analysis for HCC lower than 2 cm could be interesting. In such patients the difference between RFA and liver resection could disappear.

→ HCC less than or equal to 3cm can be treated with RFA in our center. In HCC \leq 2cm, the 1-year, 2-year, and 3-year disease-free survival and overall survival rate were 75.8%, 69.7%, 50.3% and 97.0%, 88.2%, 88.2% in LLS group and 78.6%, 60.5%, 35.3% and 97.4%, 94.3%, 80.9% in RFA group, respectively ($P=0.183$ and $P=0.074$, respectively). There were no statistically significant differences in disease-free

survival and overall survival between RFA group and LLS group in patients with HCC ≤ 2 cm.

Minor comments

1. Please comment about the possibility to perform LLS by laparoscopy. It is considered the standard by many authors. Did any patients have laparoscopic resection?

→ Between 2005 and 2010, 24 (35.3%) patients were treated with laparoscopic LLS. However, the follow-up period of patients who received laparoscopic LLS is too short, and we will continue to collect the data about laparoscopic LLS.

2. The number of patients with recurrence and the number of treatments of recurrences are not the same. In the RFA group 35 patients had recurrence, but treatment was RFA in 18, TACE in 21 and resection in 2. In LLS group, 23 patients had recurrence, but treatment was TACE in 13, RFA in 9 and resection in 2. Please verify.

→

LLS group	None	4
	TACE	8
	RFA and	5
	TACE	4
	RFA	2
	Liver resection	
RFA group	None	0
	TACE	15
	RFA and	6
	TACE	12
	RFA	2
	Liver resection	

3. The authors stated: “The 3-year disease-free survival rate was 60.0% in the LLS group, but only 39.6% in the RFA group (P=0.050). The disease-free survival curve was better for the LLS than the RFA group (Figure 1; P=0.012)”; “The 3-year overall survival rate was 93.3% in the LLS group and 74.4% in the RFA group (P=0.018). The overall survival curve was higher for the LLS group than the RFA group (Figure 2; P=0.013).” From a statistical point of view, I think that a single p value should be reported. The direct comparison of 3-year overall survival and 3-year disease-free survival rates is possible only among patients with complete 3-year follow-up. I think this is not the case. I suggest reporting only the p value of log-rank test.

→ We deleted p-values of 3-year disease-free survival rate and 3-year overall survival rate.

Reviewer 2

The paper is relevant to this journal, and in general well written. Below a few minor comments:

-please clarify in abstract/purpose that this is a retrospective study

→ We added retrospective study in the purpose.

-Results: 'recruited' is not appropriate term, since this was a retrospective study

→ We amended as recommended.

-Discussion: 'Many studies reported...' - please provide additional references, currently just one study is

listed

→ We added related references.

-'This study showed that disease free and overall survival...' - revise to 'This study suggests....', since this was not randomized controlled trial and definite conclusions are not possible

→ We corrected the sentence according to your advice.

Reviewer 3

This manuscript is partially interesting. However, several points should be clarified before publication.

1 The authors should re-investigate the results in terms of <2 cm and <3 cm of HCC size.

→ We evaluated the patients with less than 2cm.

2. The authors should describe whether or not liver function was difference between 2 groups.

→ All patients were Child-Pugh A, however RFA group showed lower liver function than LLS group such as higher ICG-R15, lower platelet count, and lower albumin levels. Importantly, All RFA group was capable to LLS.

3. The authors should describe a reason why PIVKA-II is an indicator for RFA treatment.

→ We corrected with conclusion.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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