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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

### ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4773

**Title:** Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage 0~A Hepatocellular Carcinoma

**Reviewer code:** 00053820

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:48

**Date reviewed:** 2013-08-06 21:23

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

In this study, a total 129 hepatocellular carcinoma patients with BCLC stage 0 (40 patients) and stage A (89 patients) who all underwent TACE were retrospectively enrolled. Their characteristics, scheduled CT and TACE findings, risk factor for mortality, and survival rates were analyzed and evaluated. The authors concluded that the efficacy of TACE for BCLC stage 0 and stage A HCC might be comparable with that of other curative therapies. It is an interesting and well designed study with novelty, it may be considered to be acceptable for publication.

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4773

**Title:** Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage 0~A Hepatocellular Carcinoma

**Reviewer code:** 00057328

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:48

**Date reviewed:** 2013-08-21 22:27

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

Summary: in this interesting manuscripts, results of TACE in 129 patients with Barcelona Clinic Liver Cancer (BCLC) stage 0 and A hepatocellular carcinoma (HCC) were explored. Results: The mean size of HCC was  $2.4 \pm 1.1$  cm and the mean number of TACE was  $2.5 \pm 2.1$ . The mean overall survival time and 1, 5, and 10-year survival rates were  $80.6 \pm 4.9$  months and 91%, 63%, and 49%, respectively. Child-Pugh score  $> 5$  ( $p = 0.005$ , odds ratio 3.86), presence of arterio-venous shunt ( $p = 0.032$ , odds ratio 4.41), amount of lipiodol used  $> 7$  ml ( $p = 0.013$ , odds ratio 3.51), and female gender ( $p = 0.008$ , odds ratio 3.47) were risk factors of mortality. The authors suggest that efficacy of TACE for BCLC stage 0 and stage A HCC might be comparable with that of other curative therapies. Comments: 1. In general, for small tumours, RFA is considered superior to TACE (especially for tumors  $< 3$  cm). The authors should discuss differences with literature in detail in the Discussion section. 2. Although predictive factors for mortality are identified, potential predictive factors for radiological response (according to modified resist or easl criteria) are not explored. The authors should do this in a revised version. Especially the effect of tumour diameter on response. 3. Time to tumour progression should be given. 4. No data are given on side effects of the TACE procedures. 5. As mentioned in the results section: 18 patients were observed with arterio-venous shunt. Could TACE be performed successfully in these patients or was this considered as contraindication to proceed with the procedure? Were these patients excluded from the analysis? 6. Currently, DEB tace (with drug eluting beads) rather than Tace is generally used.



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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4773

**Title:** Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage 0~A Hepatocellular Carcinoma

**Reviewer code:** 00225249

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:48

**Date reviewed:** 2013-08-25 23:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

In this paper, the authors retrospectively investigate the effect of TACE on early stage HCC survival. As the role of TACE in this Setting is still under debate, the paper is of interest to the Readers of the Journal. The sample size is adequate and the methods are appropriately Chosen. Presentation of results is clear, although text part and figures are somewhat redundant and the text could be simplified here. It is not surprising that amount of lipidiol and numbers/size of Tumors correlates with OS as this is clearly an indicator of disease stage. The authors should provide additional data from their Center comparing the PFS and OS times for patients treated other than TACE in this Setting to Show equality or superiority of their Treatment. Some minor changes (spellings e.g. Frans instead of France) and not to use the word "gender" when speaking of "sex" are recommended.



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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4773

**Title:** Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage 0~A Hepatocellular Carcinoma

**Reviewer code:** 00068364

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:48

**Date reviewed:** 2013-09-02 10:38

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide, and the fastest growing cause of cancer death in the United States. Transarterial chemoembolization (TACE) has been used to treat intermediate-stage patients. Patients with Barcelona Clinic Liver Cancer (BCLC) stage 0 and stage A HCC may be suitable candidates for curative therapies. However, a few studies compared TACE and other curative therapies in patients with early stage HCC, and the results were still controversy. The goal of current study is to evaluate the efficacy of transarterial chemoembolization (TACE) as a first-line therapy for patients with BCLC stage 0 and A HCC. A 10-year retrospective study design was used. If promising results were obtained, the clinical importance is significance. My major concern is that most research contents are discussing the risk factors of mortality and clinical characteristics to influence the survival of HCC with TACE treatment, which is unrelated with the study goal. Therefore, the title is unrelated to the contents; the goal of study need modified if you keep the contents; the results are unrelated with the goal; and finally it is inappropriate to derive the conclusion that "the efficacy of TACE for BCLC stage 0 and stage A HCC might be comparable with that of other curative therapies", if only analyzing HCC underwent TACE, no other therapies involved in comparisons, such as resection, transplantation, or ablation therapy. Overall, the inconsistency in contents and goal make the novelty and innovation of the research significantly reduced. The overall description of the manuscript is clear and understandable. This study has received a priori approval by the institutional review board for human research of hospitals, so no ethical concern. One minor comment on page 11: why the factors of age, gender, and plausible risk factors from univariate analysis with  $p < 0.50$  (not  $p < 0.05$ ) were used in the Cox regression analysis?



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**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 4773

**Title:** Transarterial Chemoembolization in Barcelona Clinic Liver Cancer Stage 0~A Hepatocellular Carcinoma

**Reviewer code:** 00039017

**Science editor:** Wen, Ling-Ling

**Date sent for review:** 2013-07-24 13:48

**Date reviewed:** 2013-08-05 22:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The authors present a retrospective study on 129 patients with BCLC stage 0 and stage A HCC who underwent TACE with Lipiodol, Doxorubicine. They looked for risk factors of mortality after TACE. The authors showed Child-Pugh score, presence of AP shunt, and dosage of lipiodol were independent risk factors after TACE. While this finding is somewhat interesting, some concerns may require the authors' attention.

- The authors conclude that the efficacy of TACE for BCLC stage 0 and stage A might be comparable with that of other curative therapies. However, no studies were performed in this study between TACE and other curative therapies.
- In this study, no information about treatment about recurrent HCCs. I think that overall survival outcome was quite different by recurrent treatment.
- This was not a randomized trial, but the patients were assigned to either a TAI or a TACE group. How were the patients assigned to these treatment group? I think that in this study, dosage of doxorubicin and iodized oil were unclear. In the methods, the authors explain the dosage of doxorubicine/lipiodol ratio was 10mg / 2ml. However, in Table 3, hazard ratio of doxorubicine and lipiodol were different.
- I cannot understand the sentence of 'time to recurrence was defined as time from randomization to recurrence' When randomization was performed in this study?
- There was no studies about recurrence or survival between RECIST, EASL, and mRECIST. Why the authors recommend EASL and mRECIST.
- The authors used Cox-regression analysis for mortality. Odds ratio should describe Hazard ratio.