Author's response to reviews

Title: Clinical features and prognostic factors in patients with bone metastases from hepatocellular carcinoma after liver transplantation

Authors:

Jian He (He.jian@zs-hospital.sh.cn)
Zhao-Chong Zeng (zeng.zhaochong@zs-hospital.sh.cn)
Jia Fan (fan.jia@zs-hospital.sh.cn)
Jian Zhou (Zhou.jian@zs-hospital.sh.cn)
Jing Sun (Sun.jing@zs-hospital.sh.cn)
Bing Chen (Chen.bing@zs-hospital.sh.cn)
Ping Yang (Yang.ping@zs-hospital.sh.cn)
Bin-Liang Wang (Wang.binliang@zs-hospital.sh.cn)
Bo-Heng Zhang (Zhang.boheng@zs-hospital.sh.cn)
Jian-ying Zhang (Zhang.jianying@zs-hospital.sh.cn)

Version: 3 Date: 20 September 2011

Author's response to reviews: see over
06 Sep, 2011
Editor
Biomed central
Dear Sir,
Re: Clinical features and prognostic factors in patients with bone metastases from hepatocellular carcinoma after liver transplantation

We herewith resubmit the manuscript of the captioned title for your consideration of publication in Biomed central.

The manuscript has been revised very carefully in response to the suggestions from two reviewers and editors. Every change to the paper is enclosed and listed below point by point.

Reviewer 1:
Abstract
Conclusion: The first sentence needs to be rephrased in order to include what readers need to know and to summarize the main results of the study.
Answer: Yes, we have rephrased this sentence and summarized the main results of the study.

Introduction
Page 4 last paragraph, line 19. “are rarely reported”: a few papers should be quoted, mainly the most significant ones.
Answer: We have quoted the reference 8 in here.

The aim of the study should be included at the end of the introduction section. I suggest: “from HCC after LT in order to identify prognostic factors.”
Answer: That is a good suggestion!
Patients and methods
Was an informed consent needed or obtained?
Answer: Yes. It is necessary to add ethics approve. We added at the page 5.
Page 6: the first paragraph should be amended.
Answer: Yes, we have rephrased this paragraph.
First of all, the tense should be the past instead of the present which is used by the authors from the third sentence to the end of the paragraph!
Answer: Yes. We have changed
Instead of general considerations, the authors should state how the diagnosis of bone metastases was established in their study population: number of CT scans performed, number of MRI examinations performed, number of biopsies?
Answer: The imaging diagnosis of bone metastasis was based on the combination with bone scintigraphy and computed tomography in 14 patients or magnetic resonance imaging in 16 patients. The confirmation of bone metastases by histologic testing was not recommended in this study.
Page 7: last paragraph: please replace “The doctor recorded…” by “.He recorded…”.
Answer: Yes, we have replaced.

The question from Reviewer 2:
The Shanghai criteria should be defined. This manuscript had no original or new data to the literature, especially concerning the risk factors of bone metastases. This major comment leads to the second one, concerning the histological analysis.
Answer: We have added the definition of Shanghai criteria in the page 6 and cited the reference 5.

A major comment is related to the predictors of survival after bone metastases. Histological analysis of the liver tumor is lacking. Some main prognostic factors
have not been studied. However, neither microvascular invasion nor satellites has been depicted and analyzed as a risk factor for bone metastases. These factors are widely accepted to significantly impact the recurrence rate. Moreover, as it has been reported by Fukutomi et al in 2001, HCC bones metastases which were evaluated in 673 patients were mainly related to vascular invasion. These information should be provided and studied in the univariate and multivariate analysis. AFP is discussed in this manuscript while no impact has been found in this series. The authors should raise discuss the role of circulating cells, bone marrow homing etc.. and then the impact of microvascular invasion.

Answer: As this study was a retrospective study, and it was focus on the role of the commonly clinical indexes on the bone metastasis in HCC patients after LT. Considering the clinical utility of the study, we did not include the histological type, vascular invasion, satellite lesion, and circulating tumor cell as prognostic factors in data analysis. In the definition of Milan, UCSF or Shanghai criteria, surgeons and physicians always used clinical indexes to judge liver transplantation for HCC patients. But we will consider the effects on bone metastasis of these factors in our further studies.

Thank you very much for your kind attention and consideration.

Yours Sincerely,

Zhao-Chong Zeng
Corresponding authors:

Zhao-Chong Zeng, MD
Department of Radiation Oncology, Zhongshan Hospital
Shanghai, 200032, China
Phone: 86-21-64041990; Fax: 86-21-64048472
E-mail: zeng.zhaochong@zs-hospital.sh.cn