

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 2665

Title: Liver transplantation versus liver resection for hepatocellular carcinoma using the Milan criteria after successful downstaging therapy

Reviewer code: 01213124

Science editor: Song, Xiu-Xia

Date sent for review: 2013-03-07 09:13

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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent) | <input type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Y] 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 | <input type="checkbox"/> Existed | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

Dear Authors, This is an interesting paper tackling a very important debate regarding the best management modality for patients with HCC who were successfully down-staged to the Milan's criteria. I have few comments and suggestions: 1. This study included patients with well compensated liver disease (Child's A and B / MELD score around 8), and understandably none of the patients had sever decomposition. I think this should be clearly stated in the paper's Title, Methodology (inclusion and exclusion criteria) and Conclusions. 2. The authors did not explain on which basis patients were selected for either liver resection or liver transplantation; the selection criteria for each modality should be clearly clarified in the Methodology. 3. Almost all of the patients included in this study had HBV-induced chronic liver disease. In such patients, the new antiviral agents can easily control disease progression. It is also well known that controlling viral replication halts disease progression and decreases the risk of tumor recurrence or developing new lesions. That might have significantly contributed to the good outcome after resection in this study group, especially if you compare it to other parts of the world where HCV is the mostly common cause of liver cirrhosis. I think that this argument should be highlighted in the discussion. 4. The authors correctly identified the weakness of this study, which are lack of randomization and small sample size. Therefore, I think the conclusions are overstated. The conclusions should clearly state that "in selected group of patients with compensated liver disease" liver resection "might" offer better or similar outcome over liver transplantation; and that "further randomized studies on a larger number of patients is warranted before drawing any conclusions". 5. In the result, and under Major postoperative complications and mortality, the authors stated that "The patients who



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died in both groups did not have any proof of HCC in the explanted liver, and they were excluded from the recurrence rate calculation". Does that mean the tumor was entirely eradicated by the down staging treatment? Please clarify!! Thanks and regards, Yours Sincerely Hatem Khalaf
Professor of Surgery President-elect, Pan Arab Liver Transplant Society Senior Consultant and head of liver transplant and HPB surgery, Hamad Medical Corporation

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

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Title: Liver transplantation versus liver resection for hepatocellular carcinoma using the Milan criteria after successful downstaging therapy

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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|--|--|-------------------------------------|--|
| <input type="checkbox"/> Grade A (Excellent) | <input type="checkbox"/> Grade A: Priority Publishing | Google Search: | <input type="checkbox"/> Y] 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 | <input type="checkbox"/> Existed | <input type="checkbox"/> Minor revision |
| <input type="checkbox"/> Grade E (Poor) | | <input type="checkbox"/> No records | <input type="checkbox"/> Major revision |

COMMENTS TO AUTHORS

General comments Liver transplantation (LT) and liver resection (LR) offer potential cure for tumors detected at an early stage in well selected patients. It is interesting and important to investigate the advantages and risks of LT and LR in patients with advanced HCC that met the Milan criteria after successful downstaging therapy. I would like to recommend authors to reply to the following comments. Specific comments: a) Major comments: # If two different groups of patients selected for the study in the Methodology will affect the reliability of the result? Please clarify. # The presence of the intrahepatic micrometastases and extrahepatic micrometastases was the very important risk factor affecting recurrence and survival in HCC patients after LT or LR. However, the author did not include such micrometastases in the risk factors for tumor recurrence in the result. I hope that the author should pay attention to it in the result and discussion. # In the discussion, the authors also admitted that "So a larger multicenter study comparing an larger number of patients with HCC after successful downstaging therapies in both groups (LR and LT) would be ideal." Now that there are lack of randomization and small sample size selection in the study, the conclusion drawn in this study should be cautious and narrow. # In the conclusion, the authors stated that "Due to the higher postoperative morbidity and similar survival and tumor recurrence-free rates, the LT should not be considered as the primary treatment for patients with HCC that meets the Milan criteria after successful downstaging therapy." LR is the treatment of choice in noncirrhotic patients and in cirrhotic patients with well-preserved liver function. In patients with advanced cirrhosis and tumor extent within the Milan criteria, liver transplantation is clearly the best option. For advanced-stage HCC patients, successful downstaging does not mean the



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elimination of the pre-neoplastic cirrhotic background. If an underlying chronic liver disease exists, making a decision on which method should be selected is difficult. Treatment decisions must be individualized. I think that these problems should be taken into account in the methodology and conclusion. b) Minor comments: #What does this word "HR" in Introduction mean? Is it a clerical error or a different meaning?