

Nikolaos Pyrsopoulos, MD, PhD, MBA, FACP, AGAF
Division Director, Gastroenterology and Hepatology
Medical Director of Liver Transplantation

July 3, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format: *Lisa Waller HCC review revisions_v2.docx*

Title: Hepatocellular carcinoma: a comprehensive review

Author: Lisa P Waller, MD, Nikolaos Pyrsopoulos, MD, PhD, MBA

Name of Journal: *World Journal of Hepatology*

ESPS Manuscript NO: 18004

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

- (1) **Reviewed by 02943023:** Reviewers comments: "This manuscript thoroughly reviewed a complete aspect of the hepatocellular carcinoma, especially focusing on liver transplantation with updates of recent data. However, there is still need to be revised in several points.

We appreciate the reviewer's comments and opinions. We have edited the manuscript in certain areas as suggested, thank you.

(2) **Reviewed by 02861333:** Reviewers comments: "This study comprehensively reviewed recent progressions of diagnosis and treatment for HCC.

1. There are several mistakes in the manuscript, such as in the TUMOR MARKERS AS CRITERIA FOR HCC section, "80.3%, respectively, for patients with an AFP level > 1000 ng/mL".

2. References need to be matched correctly. for example, Ref 41 is not a study from United States, but from Japan. There are several other studies of NLR, such as " A scoring model based on neutrophil to lymphocyte ratio predicts recurrence of HBV-associated hepatocellular carcinoma after liver transplantation." or " A novel prognostic nomogram accurately predicts hepatocellular carcinoma recurrence after liver transplantation: analysis of 865 consecutive liver transplant recipients."

We appreciate the reviewer's comments and have corrected these mistakes.

(3) *Reviewed by 02861363*: Reviewers comments: “Although, this review article is well written about transplantation for HCC and Milan criteria, the paragraph for “Etiology” or “Pathophysiology” or other part is poor. I recommend that rather authors concentrate more on transplantation for HCC not discussing about the other topics. Otherwise, authors should describe more deeply about the other significant topics, e.g. NASH for etiology and pathophysiology or Gadolinium contrast MRI for diagnosis.

Also it is important to describe “Recurrence” not only after transplantation but also after conventional resection.”

We appreciate the reviewer’s comments. We agree that these sections are short and focused, which is one of the reasons we have included Table 1, which lists all etiologies, including NASH. As this is a review, our primary aim is to provide a brief overview of all topics related to HCC while stressing a few certain topics of interest, such as expansion of the Milan criteria, increasing living donor transplant for HCC, as well as changes in post transplant management of HCC to increase overall survival for these patients.

In regards to recurrence after resection, we have discussed salvage liver transplantation under the section “Resection”, and have added, as per reviewer’s suggestion, some additional information regarding recurrence after resection in this section as well.

(4) *Reviewed by 00058444*: Reviewers Comments: “Hepatocellular carcinoma (HCC) is one of the most common tumors and a major cause of mortality worldwide. In this manuscript, the authors reviewed and discussed the epidemiology, pathophysiology, diagnosis, staging, and current management of hepatocellular carcinoma. This is a comprehensive review on hepatocellular carcinoma. The manuscript was well prepared. The authors discuss the recent advances on the diagnosis and management of HCC in detail. Thus, this review article provides useful information to the clinicians in managing hepatocellular carcinoma.”

We appreciate the reviewer’s positive comments, thank you.

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

Sincerely yours,

Lisa P Waller, MD

Nikolaos Pyrsopoulos, MD, PhD, MBA, FACP, AGAF
Division Director, Gastroenterology and Hepatology Medical Director of Liver
Transplantation New Jersey Medical School MSB H538 185 South Orange Avenue
Newark, NJ 07103
P: 973-972-5252 F: 973-972-3144
pyrsopni@njms.rutgers.edu