

December 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6725-edited.doc).



**Title:** Non-invasive diagnosis of cirrhosis: a review of different imaging modalities

**Author:** Riccardo De Robertis, Mirko D'Onofrio, Emanuele Demozzi, Stefano Crosara, Stefano Canestrini, Roberto Pozzi Mucelli

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

**ESPS Manuscript NO:** 6725

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

- 1- we performed an additional language editing;
- 2- we provided a short running title, author contributions, abstract, key words and core tip;
- 3- we have included some sentences regarding the specific role of non-invasive diagnostic methods for cirrhosis in the setting of NAFLD, as requested by the reviewer n° 01136482. In particular:
  - section "*Transient elastography - TE - Clinical applications, normal and pathological values*": "Liver biopsy is often not recommended in the NAFLD patients, because of its cost, the potential risk of complications and the absence of consensus regarding the histopathological criteria that firmly differentiate between the NAFLD entities; due to the remarkable increase in the prevalence of NAFLD, which represents the most common chronic liver disease in the general population and is expected to increase in future as a result of an ageing population, and the concomitant efforts in developing novel therapies, a non-invasive, simple and reproducible technique as TE is needed in the clinical practice [17];
  - section "*Acoustic radiation force impulse -ARFI - Clinical applications, normal and pathological values*": "As above mentioned, liver biopsy is often not recommended in patients with non-alcoholic fatty liver disease (NAFLD), because of its cost, the potential risk of complications and the absence of consensus regarding the histopathological criteria that firmly differentiate between the NAFLD entities. ARFI can represent a useful tool in diagnosing the onset of fibrosis in NAFLD and non-alcoholic steatohepatitis (NASH), in which B-mode evaluation can be inaccurate; Fierbinteanu-Braticevici [50] reported a high diagnostic performance in predicting cirrhosis in these patients (AUROC=0.984)";
  - section "*MR elastography (MRE) - Clinical applications, normal and pathological values*": "Kim<sup>[104]</sup> reported that the best cutoff for advanced fibrosis was 4.15 kPa (AUROC = 0.954, sensitivity = 0.85, specificity = 0.929), concluding that MR elastography can be a useful diagnostic tool for detecting advanced fibrosis in NAFLD. Chen<sup>[109]</sup> reported that the mean hepatic stiffness for patients with simple steatosis (2.51 kPa) was lower than that for patients with inflammation but no fibrosis (3.24 kPa). The mean hepatic stiffness for patients with inflammation but no fibrosis was lower than that for patients with hepatic fibrosis (4.16 kPa). Liver stiffness had high accuracy (AUROC= 0.93) for discriminating patients with NASH from those with simple steatosis, with a sensitivity of 94% and a specificity 73% by using a threshold of 2.74 kPa; the author concluded that in patients with NAFLD, hepatic stiffness measurements with MR elastography can help identify individuals with steatohepatitis, even before the onset of fibrosis; NAFLD patients with inflammation but no fibrosis have greater liver stiffness than those with simple steatosis and lower mean stiffness than those with fibrosis";

- we have therefore provided 2 more references; references list has been modified.
- 4- we put reference numbers at the end of each citation content or after the cited author's name;
- 5- we have provided the requested modifications to references.

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

Sincerely yours,

Riccardo DE ROBERTIS, MD  
Mirko D'ONOFRIO, MD  
Department of Radiology  
University of Verona - G.B. Rossi Hospital  
Piazzale L.A. Scuro, 10, 37134, Verona  
Italy  
Fax: +39-45-8027490  
E-mail: [riccardo.derobertis@hotmail.it](mailto:riccardo.derobertis@hotmail.it), [mirko.donofrio@univr.it](mailto:mirko.donofrio@univr.it)