

To the Editorial Team of *World Journal of Gastroenterology*,

On behalf of my co-authors, I submit the enclosed **Reviewer's comments** together with the modifications in the **Revised manuscript 20675**, for consideration by the Journal in response to your invitation ID 00724474. There are not possible conflicts of interest (including financial and other relationships) for each author.

All authors send this letter as confirmation that they have read and approved all the manuscript modifications, including responses to reviewers.

They also have met the criteria for authorship as established by the International Committee of Medical Journals Editors, believe that the paper represents honest work, and are able to verify the validity of the results reported. The present manuscript has been reviewed by native English speaker from Language Services of the Universitat de Barcelona, Michael Maudsley, whose department have performed the Language certificate.

Note that some references have not DOI and one reference have not PMID.

We think our manuscript conforms to the journal style and our files are correctly formatted. We have followed editor's suggestions in the **edited manuscript file**. We claim for help to the editorial team of *WGJ* for subjecting the present manuscript to *CrossCheck* analysis since our institution does not provide this service and Ze-Mao Gong - Science Editor of *WGJ*- offered us their help. If we have done any mistake, please contact us in order to correct it.

I hope it will be of your interest. Thank you for the opportunity of re-submitting our report.

If you need further information, please contact us. Sincerely, on behalf of all authors,

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Peer reviewer's comments.

Reviewer 1: The topic highlight by Lopez-Delgado and co-workers reviews the outcomes of abdominal surgery in patients with liver cirrhosis. This is an interesting and well written review of an important clinical (surgical) problem. Although there have been previous reviews of this topic, the current manuscript adds valuable information.

There are a few comments: The authors state that “the prevalence of LC is increasing due to the global higher rates of hepatitis C (HCV), hepatitis B (HBV) and alcohol-related LC”. Could the authors provide a reference for this? First of all, thank you very much to the present reviewer for their judicious comments.

The statement of first paragraph of introduction has been modified. Despite the statement can be referenced by means of [3] and [4], it is difficult to firmly state that the prevalence of LC is increasing due to the lack of reliable epidemiological data. However, there are studies suggesting that due the higher incidence in alcohol consumption and the high prevalence of HCV and HBV, the prevalence of LC is expected to increase during the next ten years at least. We have included two new references for this new statement.

“[...]. Despite the lack of reliable epidemiological data, the prevalence of LC is expected to increase due to higher rates of hepatitis C (HCV), hepatitis B (HBV) and alcohol-related LC, even in European countries ^[3, 4]. [...]”

[3] Hatzakis A, Wait S, Bruix J, Buti M, Carballo M, Cavaleri M, Colombo M, Delarocque-Astagneau E, Dusheiko G, Esmat G, Esteban R, Goldberg D, Gore C, Lok AS, Manns M, Marcellin P, Papatheodoridis G, Peterle A, Prati D, Piorkowsky N, Rizzetto M, Roudot-Thoraval F, Soriano V, Thomas HC, Thursz M, Valla D, van Damme P, Veldhuijzen IK, Wedemeyer H, Wiessing L, Zanetti AR, Janssen HL. The state of hepatitis B and C in Europe: report from the hepatitis B and C summit conference. *J Viral Hepat* 2011; **Suppl 1**: 1-16 [PMID: 21824223 DOI: 10.1111/j.1365-2893.2011.01499.x]

[4] Harris RJ, Thomas B, Griffiths J, Costella A, Chapman R, Ramsay M, De Angelis D, Harris HE. Increased uptake and new therapies are needed to avert rising hepatitis C-related end stage liver disease in England: modelling the predicted impact of treatment under different scenarios.

The review does not follow the PRISMA statement; this shortcoming should be acknowledged in the Methods section.

The acknowledgement of not following the PRISMA statement is explained appropriately in the last paragraph of Introduction (methods have been joint at the end of the Introduction section due to Editor's advice).

Reviewer 2: This is an interesting review of the literature.

Thank you very much for your comments. They have served to modify some mistakes/ transcription errors that have happened during the development of the present review.

Comments:

1. The manuscript appears a little bit too long and sometimes difficult to read. It may be shortened without losing impact.

Manuscript has been shortened as much as possible. Reviewer must be tend into account that trying to summarize abdominal surgery in the cirrhotic scenario from preoperative, intraoperative and postoperative point of view has been challenging. We have tried to do our best in order to make easier for readers.

2. The statement on antibiotic perioperative treatment is not totally embraceable. Why the authors suggest perioperative coverage and not simply prophylaxis. Is there evidence for prolonged antibiotic treatment?

See response 3.

3. In the same line of thought, why 3rd generation cephalosporins? And coverage of Gram negative bacteria? This group of antibiotics have a high risk of selecting resistant bacteria. Any strong evidence for choosing the class?

We state that perioperative antibiotics should be given in the presence of ascites to prevent a postoperative Spontaneous Bacterial Peritonitis (SBP) or bacteremia secondary to SBP. Our aim was to suggest SBP prophylaxis which is current clinical practice with LC patients who have ascites. We have modified this

sentence in order to avoid misunderstandings.

In the same line, the most frequent infections in SBP are produced by Gram-negative bacteria and quinolones (norfloxacin) are the most current antibiotic regimen for SBP prophylaxis. We have modified this statement because there is an obvious transcription error. We have added a final comment regarding the emergence of multidrug-resistant agents in SBP appropriately referenced.

"[...]. Perioperative antibiotic prophylaxis should be given in the presence of ascites to prevent a postoperative SBP or bacteremia secondary to SBP that may occur during procedure and the most frequent microbiological causes, such as Gram-negative bacteria, must be covered. Despite quinolones are the most frequent antibiotic used for SBP prophylaxis, an individual approach is needed due to the emergence of multidrug-resistant agents. [...]"

[66] Biecker E. Diagnosis and therapy of ascites in liver cirrhosis. *World J Gastroenterol* 2011; **17**: 1237-1248 [PMID: 21455322 DOI: 10.3748/wjg.v17.i10.1237]

[-] de Mattos AA, Costabeber AM, Lionço LC, Tovo CV. Multi-resistant bacteria in spontaneous bacterial peritonitis: a new step in management? *World J Gastroenterol* 2014; **20**: 14079-14086 [PMID: 25339797 DOI: 10.3748/wjg.v20.i39.14079]

4. Epidural analgesia has many benefits (Nimmo SM, et al. *Cont Edu Anaesth Crit Care and Pain* 2014; **14: 224-9). Do the authors have strong evidences or guidelines suggesting that this should be avoided in LC with normal coagulation and platelet count?**

From our point of view it seems reasonable that epidural analgesia may be used due to the benefits not only in terms of pain control during and after surgery, even it can reduce pulmonary, cardiovascular, thromboembolic, and gastrointestinal complications enhancing recovery of gut function occurring after abdominal surgery. Thus, we agree with the present reviewer and in our opinion it seems reasonable that epidural analgesia should not be avoided in LC with normal coagulation and platelet count, especially if evaluated preoperatively. However, it is strongly recommended not to use epidural analgesia in LC when coagulation and/or platelet count is abnormal, even in

the setting of minimal variations, despite there is a lack of strong evidence. Based on reviewer comments, we have modified this statement accordingly within the manuscript. We also have added a reference (**Nimmo SM**, Harrington LS. What is the role of epidural analgesia in abdominal surgery? *Contin Educ Anaesth Crit Care Pain* 2014; **14**: 224-229 [DOI: 10.1093/bjaceaccp/mkt062])).

“[...]. Some authors argue that epidural anesthesia must be avoided in LC patients due to the complications derived from the coagulopathy. However, epidural analgesia has many benefits not only in terms of pain control during and after surgery, even in terms of reducing pulmonary, cardiovascular, thromboembolic and gastrointestinal complications, enhancing recovery of gut function after abdominal surgery. In our opinion, epidural anesthesia may be safe in the absence of abnormal coagulation and/or platelet count, especially if evaluated preoperatively by means of TEG, due to the lack of evidence in avoiding its use in LC patients without coagulopathy. [...]”