

Tuesday, April 7, 2015

Dear Editor in Chief of *World Journal of Gastroenterology*,

Please find enclosed the revised manuscript in Word format.

Title: Allocation of patients with liver cirrhosis and organ failure to intensive care units:
– a systematic review of the literature and a proposal of a scoring system for clinical practice.

Author: *Katrine Prier Lindvig (KPL), Ane Søgaaard Teisner (AST), Jens Kjeldsen (JK), Thomas Strøm (TS), Palle Toft (PT) Valentin Furhmann (VF) and Aleksander Krag (AK).*

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 17022

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

1 Revision has been made according to the suggestions of the reviewers

2 References and typesetting were corrected

Thank you again for considering our manuscript for publication in *World Journal of Gastroenterology*.

On behalf of all authors,

Sincerely yours,

Katrine Prier Lindvig
Corresponding author
Denmark

Reviewer no. 3024171

Dear authors

In this manuscript "Allocation of patients with liver cirrhosis and organ failure to intensive care – Systematic review and a proposal for clinical practice", the authors aimed to perform a systematic review regarding allocation of patients with liver cirrhosis to ICU. They also proposed a scoring system to help identify the patients as candidates for ICU therapy. The subject matter of current study is of interest. And the manuscript is written fairly well. This review may help clinicians choose the more suitable treatments. It is suitable for publishing in the journal.

Reviewer no. 3024216

Title: i would change it with "Allocation of patients with liver cirrhosis and organ failure to intensive care units: a systematic review of the literature and a proposal of a scoring system for clinical practice".	Title is changed as suggested.
Abstract: the abstract requires some improvements, both regarding grammar/syntax and the content. For example, you must specify that this is a systematic review of the literature (the term "systematic review" does not adequately explain what has been assessed). Furthermore, the "Methods" section lacks some fundamental information: you should add some details regarding the research methodology (for example, which terms have been used during the search and which inclusion criteria have been chosen to include the articles). Finally, the "Results" section should be more focused on the results actually derived from your systematic review rather than generically describe the SOFA score. Moreover, you should mention your proposed clinical system to identify candidates for ICU.	Abstract is revised in accordance with the suggestions.
Introduction: there are some grammatical and syntax errors (for example, "ranges from" at line 22 should be changed with "ranges between").	Introduction is revised.

<p>Pay attention to the use of abbreviations (for example, "Intensive Care Unit" at line 9 should be followed by an appropriate abbreviation - "ICU" - and used in this way in the rest of the text, for example at line 18; "EASL - CLIF" should be explained).</p>	<p>Abbreviations are corrected.</p>
<p>Methods: adequate.</p>	
<p>Results: you must explain the reasons that led to the exclusion of some papers from your literature review (for example, why did you excluded 505 articles "during the initial title screening process"?).</p> <p>"Figure 1" should be put in brackets. Please introduce table 1 before the detailed description of the included studies.</p> <p>Paragraph "Included cohort studies in the field": I would change the title with "Cohort studies". You must delete the term "at our institution" (papers should be as anonymous as possible). You must better specify what you meant with "increasing organ failure" (I assume that you meant the number of organ involved by multi-organ failure).</p> <p>Paragraph "Included reviews within the field": I would change the title with "Reviews".</p> <p>Please specify which "general ICU prognostic scores" and "liver specific scores" have been evaluated in the study by Saliba et al.</p>	<p>The titles of 505 articles where screened and evaluated by the first author, and found not relevant for the specific topic of this article.</p> <p>Figure 1 is in brackets, and introduced properly.</p> <p>Corrections are implemented.</p> <p>Corrections are implemented in the text.</p> <p>Implementations has been specified.</p>
<p>Paragraph "Scoring systems": you must fully explain the abbreviations "APACHE" and "WHO". Table 2 should be briefly introduced at the top of this paragraph. Table 3 should be introduced at the top of the "Child-Pugh Score" section.</p> <p>The MELD score formula must be better explained.</p> <p>Table 4 should be briefly introduced at the beginning of the "The World Health Organisation Performance Score" section.</p>	<p>Corrections are implemented.</p> <p>Corrections are implemented.</p> <p>Corrections are implemented. Tables are introduced properly.</p>

<p>Please provide a full explanation of the abbreviations included in the “The Acute Physiology and Chronic Health Evaluation scores” (for example, “AaDO₂”).</p> <p>You should briefly introduce table 5 at the beginning of the “Sequential Organ Failure Assessment Score” paragraph. What does “MAP” means?</p> <p>Please provide adequate citations for Table 6 and figure 2.</p>	<p>Corrections are implemented. Tables are introduced properly.</p>
<p>Discussion: you should delete all paragraphs from this section.</p> <p>Table 5 presents the CLIF-SOFA score, I can't see any of your “suggested criteria to determine if a patient is a candidate to intensive care”.</p> <p>Please provide adequate citations for figure 3 and figure 4.</p> <p>How did you develop your “First-CLASS” software?</p> <p>Which are the literature data Did you test your “scoring system” during clinical practice? If so, which are your results?</p>	<p>Paragraphs are deleted.</p> <p>The proposed criteria are shown in figure 3 and based on combined info from CLIF-SOFA score, the Child-Pugh score and the MELD score.</p> <p>The figure 3 and 4 published in this article is a novel approach proposed in this review. It has therefore not previously been published or presented elsewhere. The software has been developed in collaboration with a robot system engineer, who has ties to the project.</p> <p>No we are currently testing the scoring system in clinical practice, and hope to evaluate soon.</p>
<p>Tables: table 1 must be completely rewritten, as in the present form it is extremely difficult to understand and cannot be used to extrapolate useful data.</p>	<p>Table 1 has been rewritten.</p>

Reviewer no. 2942858

Comment on Manuscript no : 17022

I think this systematic review is of good quality and deserve publication and the proposed scoring system needs validation in clinical practice in a wider manner. But this review need minor changes first.

<p>Title: is accurately reflects the major topic and contents of the systematic review</p>	
<p>Abstract: it gives a clear delineation of the research background, objectives, materials and methods, results and conclusions.</p>	
<p>Introduction: There is a need for clinical tools and a proper triage to help guide the physicians making decision regarding the allocation of patients with ACLF to ICU <u>Better to be changed to</u> There is a need for clinical tools and a proper triage to guide the physicians in decision making regarding the allocation of patients with ACLF to ICU</p>	<p>Changed to: “There is a need for clinical tools and a proper triage to guide the physicians in decision making regarding the allocation of patients with ACLF to ICU.”</p>
<p>Methods: It is clear and well written and Figure 1 – Flowchart of trials is good.</p>	
<p>Results: is well described however it need minor revision</p> <p>In table 1 : IN the result section The heading (Study setting and study period) <u>Better to be changed to:</u> Study setting, study period and/or main target of the study as study period is not present in all of the 5 included studies.</p> <p>Also in table 1 under the heading: Scores: Child-Pugh, MELD, SOFA in Saliba F, 2013, France, review (12) Suggests that ICU scores (SOFA, APACHE II, SAPS II) predict better than liver scores (MELD and Child-Pugh) the outcome of cirrhotic patients admitted to the ICU. <u>Better to be changed to:</u> Suggests that ICU scores (SOFA, APACHE II, SAPS II) predict the outcome of cirrhotic patients admitted to the ICU better than liver scores (MELD and Child-Pugh).</p>	<p>Changed to: “Main target of the study”</p> <p>Changed to: “Suggests that ICU scores (SOFA, APACHE II, SAPS II) predict the outcome of cirrhotic patients admitted to the ICU better than liver scores (MELD and Child-Pugh).”</p>

<p>Table 1 need to be re written with modification. The studies in the table need re arrangement . It is better to start with cohort studies then the reviews to correlate with what is written under the table in the text part.</p> <p>Also it is better to re arrange the review to start with Ginés P, 2012, Spain, review, then Berry P A, 2013, UK, review, then Saliba F, 2013, France, review in table 1 and Also in the text under the title Included reviews within the field. (Chronological sequence is better)</p>	<p>Table 1 is completely rewritten.</p> <p>The order of authors is altered.</p>
<p>Under the title</p> <p>Included cohort studies within the field</p> <p>Shawcross et al performed----- . They assessed resource utilization and found that presence of organ failure resulted in considerable resource expenditure in patients with liver cirrhosis, but had acceptable hospital survival of 59% as illustrated in Table 1 (1). <u>Better to be changed to:</u> Shawcross et al performed----- . They assessed resource utilization and found that presence of organ failure resulted in considerable resource expenditure in patients with liver cirrhosis, but had hospital mortality of 59% as illustrated in Table 1 (1). To be similar with what is written in table 1</p>	<p>Changed to: “They assessed resource utilization and found that presence of organ failure resulted in considerable resource expenditure in patients with liver cirrhosis, but had hospital mortality of 59% as illustrated in Table 1 (1). “</p>
<p>Under Title Scoring system :</p> <p>To assess severity and prognosis due to underlying liver disease before ACLF or acute hospitalization Child-Pugh score and MELD score are the best-validated scores (15).</p> <p><u>Better to be changed to:</u> To assess severity and prognosis due to underlying liver disease before ACLF or acute hospitalization, Child-Pugh score and MELD score are the best-validated scores (15).</p>	<p>Changed to: To assess severity and prognosis due to underlying liver disease before ACLF or acute hospitalization, Child-Pugh score and MELD score are the best-validated scores (15).</p>
<p>Under the title: Sequential Organ Failure Assessment Score</p>	

<p>(SOFA score) and CLIF-SOFA Score</p> <p>Line 6</p> <p>because low increases in s-creatinine levels in cirrhotic patients indicate marked reductions in glomerular filtration rate.</p> <p>I think there is something wrong in this sentence or need explanation or remove word low</p>	<p>Changed to: “...because minor increases in s-creatinine levels in cirrhotic patients indicate marked reductions in glomerular filtration rate.”</p>
<p>Discussion</p> <p>It is well written and well organized</p> <p>Under title Allocation of patients with cirrhosis to ICU</p> <p>Line 6</p> <p>throughout the litterature better changed to -- ----- throughout the literature</p> <p>Cirrhotic patients following surgery</p> <p>Line 5</p> <p>Coagulopatia better changed to ---- Coagulopathy</p> <p>Under title : Proposal of a systematic allocation system</p> <p>line 3</p> <p>In table 5----- changed to Figure 3</p>	<p>Corrections implemented.</p> <p>Corrections implemented.</p> <p>Corrections implemented.</p>
<p>References:</p> <p>appropriate and relevant.</p>	
<p>Tables and figures: The tables and/or figures reflect the major findings of the study, and they are appropriately presented . With the exception in table 3, and 5 need correction as follow (All the changes in yellow color)</p>	<p>Corrections implemented.</p>