



UOC di Gastroenterologia ed Endoscopia Digestiva

Primario Prof. Adolfo Francesco Attili

Prof Manuela Merli

Dear Editor,

Please find enclosed the edited manuscript in Word format (file: 7005review English editing).

Title: Changes in nutritional status after liver transplantation

Running title: Nutrition and liver transplantation

Authors: Michela Giusto MD, Barbara Lattanzi MD, Vincenza Di Gregorio MD, Valerio Giannelli MD, Cristina Lucidi MD, Manuela Merli MD.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7005

After the suggestions of the reviewers the manuscript has been completely revised. At the same time we have submitted the manuscript for English revision and editing . We are rather confident to have reached the modifications required however we would be more happy if we could

2 Revision has been made according to the suggestions of the reviewer

(1)

Authors should mention limitations of literature search e.g. language bias.

This suggestion was taken into account

Could the authors perhaps include a paragraph comparing the effects of malnutrition in liver transplant patients to other patients undergoing major surgery while in a malnourished state i.e. how many of the described physiologic alterations are attributable to the trauma and stress of major surgery and how much is specific for liver transplant patients only?

A paragraph has been introduced as requested by the reviewer

A few parts need minor language and grammar polishing.

All the proposed small changes have been considered in the new version

(2)

English language revision is needed.

The manuscript has been sent to a complete editing and language revision (the certificate is included)

I would expect that the first section after methods contained information on the primary aim. I do not believe it is within the scope of the review to investigate techniques for assessment of





nutrition. I would suggest focusing on the aim of describing nutritional changes after LTX and dropping other aspects of nutrition in liver disease

I would also recommend breaking the following sections: 'nutritional status and the outcome after LTX' and 'modifications of nutritional status after LTX' into shorter sections.

We followed the suggestion by the reviewer and the manuscript has been completely changed in structure considering the reviewer comments

the topic of vitamin and trace element deficiencies is not included in the description of malnutrition.

A Table with regard to vitamins and trace elements has been included

the authors seem to conclude that weight gain after LTX is solely because on increased food intake, whereas the importance of liver related malabsorption, impaired protein synthesis, increased gluconeogenesis and anabolic resistance in end-stage liver disease is not touched upon. The authors offer no (pathophysiological) discussion of the lack LTX on sarcopenia - this otherwise very interesting observation deserves more attention

Physiopathologic considerations have been introduced as suggested by the author

(3)

could be interesting to verify if malnutrition status is related to the etiology of the liver pathology.

due to the comment of reviewer 2 of our original version, the relationship with the etiology of liver disease was previously removed

We have now included two sentences (evidenced in yellow) with the purpose to remember that malnutrition is not linked to a specific etiology but obesity is related to NASH.

(4)

There are several typos and some sentences are not constructed very well and this affects the readability of the manuscript.

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

Sincerely yours,

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Dear Editor,

After the comments of the reviewer we decided to completely modify our manuscript. This makes now somehow difficult to deal with our changes in a point by point reply which we have tentatively added at the end. It is also uneasy to evidence the new parts as very little of the previous version is left.

At the same time we have sent the manuscript for an estimate of English revision and editing and I will tell You as soon as possible the time they require.

We are rather confident to have reached the modifications required however we would be more happy if we could have at least your agreement. We will update the revised version on the Journal web site after the English editing and revision.

Thank You for giving us the opportunity to improve the review

Yours cordially
Prof Manuela Merli

REV 1 → minor revisions

Authors should mention limitations of literature search e.g. language bias.

This suggestion was taken into account

Could the authors perhaps include a paragraph comparing the effects of malnutrition in liver transplant patients to other patients undergoing major surgery while in a malnourished state i.e. how many of the described physiologic alterations are attributable to the trauma and stress of major surgery and how much is specific for liver transplant patients only?

A paragraph has been introduced as requested by the reviewer

A few parts need minor language and grammar polishing.

All the proposed small changes have been considered in the new version

REV2 → major revisions

Thank you for the opportunity to review this manuscript on an important subject. The manuscript is entitled "Changes of nutritional status after liver transplantation". It is a review of the current literature. The authors show a good understanding of the topic. However, I believe that the manuscript can improve substantially by revisions regarding language and structure. Finally, an explanatory section on the pathophysiology of malnutrition in end-stage liver disease, sarcopenia and weight gain after LTX are needed.

MAJOR REVISIONS: English language revision is needed. The authors often forget past tense 'd's, mistakes 'on' versus 'in' and 'a' versus 'an'. Some abbreviations are not spelled out before the abbreviation occurs. The authors use the uncommon phrases 'over nutrition' instead of overweight or obesity, and 'post alcoholic liver disease' instead of alcoholic liver disease. Some sentences are long and unclear and some have a wrong order of words; as a whole the text does not appear fluent and easy-to-read.





The manuscript has been sent to an editing and language revision evaluation which will follow soon

The manuscript structure can be improved. From the section just above "methods" it appears that the primary aim of the review is to examine modifications of nutritional status after liver transplantation. Secondary aims appears to be to examine prevalence of malnutrition in patients with advanced liver disease awaiting LTX and impact of malnutrition on outcomes after LTX. If that is correct, I would expect that the first section after methods contained information on the primary aim. Currently that section instead contains a description of malnutrition in liver disease (not focused solely on transplant list patients but also overall) and a description of imaging techniques for assessing sarcopenia (with only a few lines on hand-grip strength and nothing on other more widely used techniques). I do not believe it is within the scope of the review to investigate techniques for assessment of nutrition. I would suggest focusing on the aim of describing nutritional changes after LTX and dropping other aspects of nutrition in liver disease that have been extensively described already. For example, the section 'prevalence and consequences of nutritional alterations...' can be dropped and the description of malnutrition in end stage liver disease shortened and moved to the introduction. I would also recommend breaking the following sections: 'nutritional status and the outcome after LTX' and 'modifications of nutritional status after LTX' into shorter sections. E.g. with focus on the different aspects of malnutrition: sarcopenia, osteopenia, underweight, changes in fat mass versus lean body mass.

We followed the suggestion by the reviewer and the manuscript has been completely changed in structure considering the reviewer comments

Finally, the manuscript does not touch on several topics that I would expect from a review on LTX and nutrition. Firstly the topic of vitamin and trace element deficiencies is not included in the description of malnutrition.

A Table with regard to vitamins and trace elements has been included

Second, the authors seem to conclude that weight gain after LTX is solely because on increased food intake, whereas the importance of liver related malabsorption, impaired protein synthesis, increased gluconeogenesis and anabolic resistance in end-stage liver disease is not touched upon. The authors offer no (pathophysiological) discussion of the lack LTX on sarcopenia - this otherwise very interesting observation deserves more attention (see also Dasarathy, Dig Dis Sci 2013 Nov; 58(11):3103-11)

Physiopathologic considerations have been introduced as suggested by the author

Rome 08/03/2014

