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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 00068273

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2018-04-04

Date reviewed: 2018-04-11

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

No particular observations. Very interesting and time consuming paper. Any particular limitation in publishing this review.

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 00008736

Reviewer's country: Germany

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-15

Review time: 3 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors present a comprehensive Review on the Topic of obesity and Nutrition in patients with liver cirrhosis. The manuscript is very well written and all relevant aspects are fully covered. To further improve the manuscript, Graphs highlighting the Impact of Body weight, Nutrition and other factors on cirrhosis and liver capacity would be highly



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welcome. A tabular summary of relevant findings might also be helpful. The section on Vitamin D is very Long and may be shortened.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 00054275

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-18

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Nice and exhaustive review: it earns to be published

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer’s code: 02520359

Reviewer’s country: Greece

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-19

Review time: 8 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I read with interest this manuscript entitled “Nutritional issues in patients with obesity and cirrhosis”. The authors explore the impact of obesity in patients with chronic liver disease and its role in inducing liver damage or accelerating pre-existing liver disease. The phenotype of sarcopenic obesity seems to render a higher risk for the patients. They



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also explore the role of various micronutrients in chronic liver diseases and support their supplementation in case of deficiencies. The role of bariatric surgery to treat obese patients with cirrhosis is also discussed. The study is well written, but some changes have to be made before this manuscript is ready for publication. In the first section it is better to state that NAFLD is the hepatic manifestation of metabolic syndrome, instead of obesity. The authors have to present any data regarding the degree of obesity and its impact to the severity of the liver disease. Regarding the role of sarcopenic obesity in cirrhosis the authors have to speculate about the pathophysiologic mechanisms explaining the higher morbidity in these patients. They have also to comment whether the studies conducted in Korean population can be extrapolated in western populations. This sentence, in page 21, is written in duplicate "The recommended dietary pattern is for small, frequent meals evenly distributed throughout the day (every 3–6 h) with a late evening snack containing at least 50 g of complex carbohydrate[117]. Some minor English language polishing is needed.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 03473431

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-21

Review time: 9 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The following changes are needed a)Pag 7, line 4: please specify that the relative risk of cirrhosis increased more than six fold in women with obesity and alcohol consumption (>150 g/week) vs non obese and drinking < 70 g/week women b) Pag 7, line 13: reference number 13 and 14 (Berzigotti et al) please report inserted in the text c) Pag 7,



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line: please specify that obesity increase “substantially” (HR 13.1), “independently” but also “significantly” ($p=0.016$) the risk of portal thrombosis d) Pag 8 line 11: authors state that obese patients have a reasonable long-term outcome after 7) Pag 10: line 24 “hospital stay” could be more appropriate than simply “stay” e) Pag 12: the sarcopenic obesity observed after organ transplantation is well-described, anyway a reference to the possible cause of these condition such as insufficient physical exercise or drugs (calcineurin inhibitor, steroid and rarely mycophenolate) is not done; f) Pag 14: line 5 “(VDD, <20 ng/mL)” should be “(DDD, <50nmol/L; <20 ng/mL)” since in line 9 the measure is “(<75 nmol/L, <30 mg/mL) g) Pag 14 line 12: the severity of VDD is “directely” and non “inversely” related to the severity of liver disease and in cirrhotic patient the presence of HbsAg and HbcAg” for me could be misunderstand in: HBV infection is not a risk factor for mortality h) Pag 15 line 19: the abbreviation “MRS” should be “Magnetic Resonance Spectroscopy” i) Pag 16: vitamin D deficiency is discussed; what about disbiosys in cirrhosis as a cause and an effect of VDD? l) Pag 17 line 17: Please clarify that the guidelines (biblio n 81) recommend calcium and vitamin D as a general preventive treatment in patients with cirrhosis and severe cholestatic disease and not in all patients with chronic liver disease m) Pag 18 line 25: It should report “primary biliary cholangitis” and not t “primary biliary cirrhosis” even the reference id should be updated n) Pag 19 line 15: ADL is f “advanced liver disease” o) Pag 20 line 102: in the study by Mousa (biblio 102) the treatment group was treated not only with zinc and antioxidant but also with lactulose p) Pag 22 line 5: clarify that magnesium uptake is increased in the condition of magnesium depletion q) Pag 22 line 15: vitamins B are needed to prevent also anaemia, Korsakoff’s syndrome and neuropathies r) Lines 16-18 are repeated s) Pag 28 line 10 and 15: “TIPS” is more currently used than “TIPSS” t) Pag 29 line 6 and 20: in line 6 and not in 20 should be explained the significance of “RYGP” u) Pag 29 line 20; “LABG” is laparoscopic



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adjustable gastric banding and SG is “sleeve gastrectomy”

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 00003629

Reviewer's country: Greece

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-25

Review time: 14 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The review article under consideration by Luigi Schiavo et al, is the result of combined work of authors from specialized centers in Italy, Israel and France with large experience in the subjects of obesity, complications of cirrhosis and liver transplantation. It is very informative, well written and extensively referenced. It covers mainly the subject of



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obesity as cause and driving force of liver disease. However, it extends to several other related important topics as, sarcopenia and sarcopenic obesity of cirrhosis; the outcome of liver transplantation in very obese subjects; the pros and cons of gastric bypass surgery as a long-term treatment of obesity and in the setting of patients awaiting liver transplantation. These, and several other important points are presented and discussed by authors, who apparently have ample experience in the subjects they deal with. I really enjoyed reading this article and I hope the readers of the WJG will feel the same way.

General Comments: 1. It would have been useful to make a reference of how body muscle tissue and body mass fat can be estimated clinically. 2. Authors should also consider the following references: i. Clapp B, et al. Long term (7 or more years) outcomes of the sleeve gastrectomy: a meta-analysis. *Surg Obes Relat Dis* 2018. [Epub ahead of print] PubMed PMID: 29625744. ii. Lemmens L, et al. Banded Sleeve Gastrectomy: Better Long-Term Results? A Long-Term Cohort Study Until 5 Years Follow-Up in Obese and Superobese Patients. *Obes Surg* 2018. [Epub ahead of print] PubMed PMID: 29671124. iii. Noel P, et al. What are the long-term results 8 years after sleeve gastrectomy? *Surg Obes Relat Dis*. 2017;13:1110-1115. iv. Yemini R, et al. Bariatric surgery in solid organ transplant patients: Long-term follow-up results of outcome, safety, and effect on immunosuppression. *Am J Transplant* 2018. [Epub ahead of print] PubMed PMID: 29569341. v. Adams TD, et al. Weight and Metabolic Outcomes 12 Years after Gastric Bypass. *N Engl J Med* 2017;377:1143-1155.

Major Comments: 1. (Page 6 lines 1-4 from top): The ultrasound estimation of steatosis is grossly subjective. 2. (Page 6, line 9 from bottom): Within what interval of observation decompensation of cirrhosis developed?

Minor Comments: 1. (Page 7, line 11 from top): Please give a reference. 2. (Page 20, lines 5-7 from bottom): Duplicated sentence. 3. (Page 29, References): Authors should follow the format of WJG and make sure that all cited references comply.



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39101

Title: Nutritional issues in patients with obesity and cirrhosis

Reviewer's code: 03567380

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-11

Date reviewed: 2018-05-25

Review time: 14 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The review by Schiavo et al. describes how liver cirrhosis and obesity are influenced by nutrient ingestion and absorption. The review initially characterizes these syndromes and discusses major associated complications such as sarcopenia. The authors then discuss micronutrient status and supplementation before discussing macronutrients and



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surgical interventions for these disease states. Overall, the review is well written and encompasses many of the necessary aspects of this field. However, there are a few areas the authors should address to improve this review, which are outlined below: 1) The authors spend a significant portion of the review talking about micronutrient status and supplementation. This section would be improved by discussing alterations, and the subsequent effects, to the microbiome during cirrhosis/obesity. 2) The authors need to include figures or tables to graphically summarize the literature for the major sections of the review (or at minimum a overall summary figure). 3) The sentence “The recommended dietary pattern is for small, frequent meals evenly distributed throughout the day (every 3–6 h) with a late evening snack containing at least 50 g of complex carbohydrate” is repeated twice (once on page 20, and the other on page 21).

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