

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39923

Title: Beta-blockers and physical frailty in patients with end-stage liver disease

Reviewer's code: 00034151

Reviewer's country: South Korea

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-19

Date reviewed: 2018-05-29

Review time: 9 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	(High priority)	<input checked="" 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 checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input 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

Kuo et al. have investigated beta blocker (BB) side effects on physical frailty in patients with cirrhosis. They found BB use was not associated with increased odds of frailty, exhaustion, or low physical activity. BB use was, however, significantly associated with a decreased adjusted risk of mortality. Thus, they claimed BB should not deter their



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utilization when indicated in patients with cirrhosis. This manuscript was interesting in general and well written. Major comments are as below: 1. The authors dichotomize patients into BB users and non-users. The dose dependent effects should be investigated or discussed. 2. In considering recent debates on the BB usage in decompensated cirrhosis, the BB effects should be investigated or discussed in terms of severity of liver cirrhosis.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

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- ☐ Plagiarism
- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39923

Title: Beta-blockers and physical frailty in patients with end-stage liver disease

Reviewer's code: 02152124

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2018-05-19

Date reviewed: 2018-06-01

Review time: 12 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

This manuscript aimed to support the concept that beta-blockers (BB) use in end stage liver disease was not associated with physical frailty. The goal appears to be clear, but there are some concerns that need to be clarified: 1. The acronyms in the abstract should be specified (MELD, BB). Furthermore the aim should be reformulated, adding

survival among the objectives. Instead of "...Fatigue and weakness are commonly reported with beta-blocker use in the general population..", the Authors have to focus their attention on "frail phenotype or frailty index", such as cited in the title. 2. The concepts of "Fatigue and weakness" should be replaced by more appropriate definition of frailty index. The introduction should be focused on frailty phenotype and exhaustion (Targeting Cognitive Frailty: Clinical and Neurobiological Roadmap for a Single Complex Phenotype. J Alzheimers Dis. 2015;47(4):793-813) and eventually 3. The work lacks of an adequate background concerning the role of nonselective beta-blockers in cirrhotic patients with ascites; however, definitive evidence in this regard is still lacking; furthermore references should be updated (Curr Treat Options Gastroenterol. 2018 Jun;16(2):215-225. doi: 10.1007/s11938-018-0179-x. Frailty in Patients With Cirrhosis) 4. The clinical description of the sample lacks of illness's duration. The great debate about this topic led to an interesting "window hypothesis" for beta-blocker therapy, in which Krag et al. proposed that beta-blockers improve survival within only a narrow window in the natural history of cirrhosis and are either ineffective or harmful outside of this window (The window hypothesis: haemodynamic and non-haemodynamic effects of betablockers improve survival of patients with cirrhosis during a window in the disease. Gut. 2012;61:967-969) 5. No reference was cited about dietary patterns.

INITIAL REVIEW OF THE MANUSCRIPT

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