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PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Cases*

Manuscript NO: 78859

Title: Branched-chain amino acids supplementation have beneficial effects on progression for patients with liver cirrhosis: A meta-analysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02811953
Position: Editorial Board
Academic degree: PhD
Professional title: Associate Professor, Director
Reviewer's Country/Territory: United States
Author's Country/Territory: China

Manuscript submission date: 2022-07-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-21 03:36

Reviewer performed review: 2022-07-21 04:11

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The manuscript (78859) entitled "Branched-chain amino acids supplementation have beneficial effects on progression for patients with liver cirrhosis: A meta-analysis" is by Jia-yu Du, et al. The authors conducted a Meta-analysis to determine the effects of branched-chain amino acids (BCAA) in patients with liver cirrhosis (LC). They concluded that BCAAs reduce the incidence of complications in patients with LC, ameliorate the nutritional status and liver function. 1. Please use abbreviations when you defined them. Please check the last sentence of your abstract. 2. Please define liver cirrhosis when it appeared for the first time in the Introduction section. 3. Some language editing is needed. For example, "research " is a mass noun (non-count noun). Please revise the sentence in lines 81-82. Another example, if the abbreviation of Branched-chain amino acids is defines as BCAA, then BCAA should be a plural form (lines 104-105). IN factor, you should use BCAAs as there are three amino acids. 4. In the discussion section, please elaborate why there is a rise of glucose.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

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Reviewer's code: 05311389
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor, Research Fellow

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2022-07-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-29 13:12

Reviewer performed review: 2022-07-29 16:17

Review time: 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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SPECIFIC COMMENTS TO AUTHORS

This is a well written meta-analysis about a topic of central interest in hepatology concerning nutrition in cirrhotic patients and management of complications, firstly hepatic encephalopathy. A meta-analysis on BCAA supplementation was necessary because there are several controversial results in literature. I have only few remarks/suggestions: 1) line 89: MELD score includes INR, bilirubin, creatinine and dialysis in last 2 weeks, not etiology; 2) line 267: "varicose vein" - probably it is a mistake during english editing, I suppose you referred to oesophageal varice; 3) In titles of Fig 4b, 4c, 4d, 6b, 7b, 7c, 8b you should specify subgroups. In this way you improve the readability of figures; 4) One of the most interesting result of your meta-analysis is the reduction of "complications rate". You should specify in M&M the cirrhosis-related complications (eg. ascites, jaundice, encephalopathy, gastrointestinal bleedings). If feasible, a meta-analysis for each complication could define the actual utility of BCAA in preventing the above-mentioned complications, causing an increase in morbidity and mortality in cirrhotic patients. This implementation could give a wider appeal of your work in the hepatology community; 5) In the meta-analysis, BCAA supplementation was not correlated with a reduction of serum bilirubin (Fig 7a). I don't understand how a smaller sample size (Fig 7b - studies with <50 patients) or a shorter treatment period (Fig 7c - studies with patients treated for <1 month) could justify a statistical significance in the subgroup analysis you made. Additionally, these are analysis on only 2 studies. It seems a statistical stretch; if not, this decision need to be justified; 6) In the subgroup analysis for ALT (Fig 6b) you excluded the study of Etsushi Kawamura et al. that have a majority of patients with a viral etiology. The pool of antiviral drugs

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available in 2009 could not permit to achieve a well-controlled viremia and consequentially persistent high serum AST/ALT levels. This is a possible bias that could justify the reason why the lack of statistical significance in the meta-analysis (Fig. 6a). This should be specified in the "discussion"; 7) Concerning the "amelioration on liver function", I agree that BCAA supplementation surely has a role in reducing morbidity and mortality in cirrhotic patients and probably a role in improving residual liver function (with a consequential reduction of complications), but following these data is not possible define an actual effect on liver function. Unfortunately, you do not have data on reduction in Child-Pugh and/or MELD score that are objective parameters for evaluation. You correlate an increase in serum albumin (probably due to an amino acids supplementation in patients that are frequently malnourished) and an uncertain reduction in serum bilirubin, but no data are reported on INR, creatinine, regression of ascites, resolution of encephalophaty. AST and ALT that, as you said, are influenced by several concomitant conditions are not utilized in hepatology for the evaluation of residual liver function. So, as a meta-analysis, is not possible to define a correlation between BCAA and liver function.