

Dear Editor and Reviewers

We thank the referee for fruitful suggestions. We have revised our manuscript entitled “Is Branched-Chain Amino Acid Nutritional Supplementation Beneficial or Detrimental in Heart Failure?” on the basis of the referee’s comments. We look forward to a publication of our manuscript in Scientific Reports. Our responses to the referee’s comments are as follows:

The paper represents mini-review which is answering the question is branched-chain amino acid (BCAA) nutritional supplementation beneficial or detrimental in heart failure. The article is written with the good English-speaking adduction of the arguments. The article is sufficiently novel and very interesting to warrant publication. All the key elements are presented and described clearly.

Thank you for your comment. In addition, we appreciate your careful reviewing our manuscript.

1) Would you please kindly correct all your typos and grammar errors throughout the manuscript

Our manuscript was checked again by native speakers of Enago (<https://www.enago.jp/>).

2) Please provide some statistics for phenomenon of sarcopenia in heart failure. Maybe any value for clinical outcomes (with numbers, please)?!

Thank you for the reviewer’s pertinent comment. We added the description about the statistics for phenomenon of sarcopenia in heart failure in revised manuscript as follows.

(Introduction line2)

“Sarcopenia and cachexia were reported to be present respectively about 20 % in patients with heart failure, however there was a width about the percentage of it among different studies. In addition, both of it sometimes coexist about 10 % in patients with heart failure.”

3) Please, elaborate on the style of your data representation. If you mention any fact from the clinical trials, there must be some numbers/ per cent of the prevalence or outcome.

Thank you for your pertinent comment. We added concise data including numeric data

and outcomes about clinical trials in revised manuscript.

(Introduction line 13)

“Rondanelli M et al. demonstrated nutritional supplementation with whey protein, essential amino acids, and vitamin D for twelve weeks, significantly increasing fat-free mass and muscle strength.”

(Introduction line 19)

“that BCAA levels decreased **by 10%** in sarcopenic adults,”

(Second paragraph line 12)

that BCAA administration **for five weeks** improved several parameters, including **bioelectrical-impedance-analysis-derived skeletal mass index by approximately 10%** and **grip strength by about 10%**.

(Second paragraph line 28)

“For instance, amino acid supplementation increased the six-minute walk test distance by approximately 20%.”

(Third paragraph line 5)

“For instance, in the study of type 2 diabetes patients free of cardiovascular and renal diseases, patients with incident heart failure had 5.6% higher serum BCAAs than those without HF. Serum BCAAs had a positive linear association with incident HF, adjusting for age, sex, and duration of diabetes.”

4) Your figure is great, but can you draw a table just to collect all the studies in the field to one place?

Thank you for your pertinent comment. We added a table including clinical trials about BCAA supplementation.