

**#1**

**SPECIFIC COMMENTS TO AUTHORS**

This article was well-written. Si-Cong Si et al. investigated the association of BTM levels with severe intracranial and extracranial artery stenosis in patients with T2DM. Clinical studies to date have mainly studied the associations among different BTMs and atherosclerosis, whereas few studies have explored the correlations between BTM levels and severe intracranial and extracranial artery stenosis in T2DM patients. So, this article was interesting and informative regarding with artery stenosis in T2DM. I have several concerns. 1. Although this cross-sectional study included a total of 257 patients, only 33 had some form of stenosis. Will this influence the results of the study? 2. The authors need to clearly define inclusion and exclusion criteria in the text.

**#2**

**SPECIFIC COMMENTS TO AUTHORS**

The manuscript describes the associations among BTM levels, previous stroke, and the burden and location of intracranial and extracranial artery stenosis in T2DM patients. The topic of the review is relevant for clinicians involved in diabetes management. This study is very useful. The title reflects the main subject of the article, abstract and keywords well summarize the arguments. The methodology is described in detail and is well structured. The discussion is well articulated according to results and the authors have clearly underlined the limitations and drawbacks of the manuscript. The tables and figures are representatives and of good quality. The manuscript cites appropriately the latest and authoritative references. However, the only regret is that there is too much content in the DISCUSSION section, and some of the content can be incorporated into the background. DISCUSSION should be focused on what they found and learned, and comparison with previous evidence.

**#3**

**SPECIFIC COMMENTS TO AUTHORS**

The study is aimed to determine whether BTMs are associated with intracranial and extracranial atherosclerosis and investigate the value of BTMs as potential indicators for risk assessment and intervention targets for severe intracranial and extracranial artery

stenosis in T2DM patients. Major comments: The study is well planned and well written. Minor comments: a. Abstract is not very informative, as it does not contain new information. I would include a summary of introduction. b. Authors need to summarize a Core tip to present the core content of the article. c. In some parts of the discussion section, the authors seem repeating the result rather than discussing their findings. The authors can use their findings to add recommendations at the end of the discussion section. d. Additionally, minor language polishing is needed.

Re: Manuscript ID: 83817

March 20th, 2023

Dear Professor

Thank you for your feedback. We have carefully read all the constructive comments on our submitted manuscript "Association of bone turnover biomarkers with severe intracranial and extracranial artery stenosis in type 2 diabetes mellitus patients", and completed the revision according to all reviewers' comments. All the comments are valuable and helpful for improving our manuscript.

1. Although this cross-sectional study included a total of 257 patients, only 33 had some form of stenosis. Will this influence the results of the study?

Response: Regarding the prevalence of severe intracranial and extracranial artery stenosis in type 2 diabetes mellitus population, we have only found few articles and the prevalence is about 40% in a stroke population. Considering that this study is only a general type 2 diabetes mellitus, the prevalence may be limited, but we will include more enrollment in future studies

2. The authors need to clearly define inclusion and exclusion criteria in the text.

Response: define inclusion and exclusion criteria more clearly