

Answering reviewers

Impact and risk factors of post-stroke bone fracture

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We thank the reviewers for their positive comments and constructive suggestions. We have revised the paper accordingly. The changes are highlighted in yellow in the revised manuscript.

Reviewer #1.

1. For completeness and further clinical utility, its relevance should be underlined in male subject, generally neglected for osteoporosis evaluation, detection, prevention and therapy. All that in spite of fact that, as the authors reports 20 % of males have fractures, osteoporosis and relation with stroke.

Response: We agree. Male subjects are often neglected for osteoporosis. We have added the information for male subject in page 8, line 224-227

2. Attention should be also paid to hypertension, a major risk factor for stroke and a risk of fractures and osteoporosis, perhaps sharing the “accelerated ageing process”. The association of hypertension, osteoporosis, and fractures with arterial stiffness has been recently described in several population cohorts such as in J Hypertens. 2015 Apr;33(4):727-35; discussion 735. doi: 10.1097/HJH.0000000000000475. Association of age-dependent height and bone mineral density decline with increased arterial stiffness and rate of fractures in hypertensive individuals. El-Bikai R1, Tahir MR, Tremblay J, Joffres M, ?eda O, ?edová L, Awadalla P, Laberge C, Knoppers BM, Dumas P, Gaudet D, Ste-Marie LG, Hamet P

Response: These are good points. We aware that hypertension is a major risk factor for stroke, bone fracture and osteoporosis. We have added corresponding information in page 8, line 241-245.

3. Furthermore, the discussion of calcium supplementation as a cardiovascular risk should be either supported by citation from literature or ponder with more recent analysis of state of the art: Effects of Dairy Products Consumption on Health: Benefits and Beliefs-A Commentary from the Belgian Bone Club and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases. Rozenberg S, Body JJ, Bruyère O, Bergmann P, Brandi ML, Cooper C, Devogelaer JP, Gielen E, Goemaere S, Kaufman JM, Rizzoli R, Reginster JY. Calcif Tissue Int. 2015 Oct 7

Response: It is a good suggestion. We have added a discussion in page 10, line 290--293, and cited indicated reference.

4. Finally the number of references quoted in the text should be crosschecked, for example ref 55 on line 372 is actually referring to meta-analysis from ref. 54.

Response: We have corrected the mistakes.

Reviewer #2.

1. First of all, the author's name that the author wrote in the manuscript should be indicated just by the last name. For example, "A. Ashburn et al" (line 216) should be changed to "Ashburn et al." and "Yoshifumi Maeno et al." (line 382) should be changed to "Maeno et al."

Response: We apologize and have corrected all mistakes.

2. Second, reference number that the author cited in the manuscript with superscript is shifted for one reference number. The author should check the reference number carefully.

Response: We have checked and have made corrections.

3. Third, the manuscript is not organized. For example, the authors described the issues related to the lack of estrogen and anti-depressant drugs in the "ADDITIONAL MANEGEMENTS....." section. I think these issues should be included in the "RISK FACTOR....." section.

Response: We thank the reviewer for the suggestion and have moved the issues related to the lack of estrogen and anti-depressant drugs to Risk factor section in page 9, line 246-267

4. In spite of the last section entitled ".....AND FUTURE DIRECTION", the authors do not mention the future direction. So I recommend to change Subheadings as follows: For example, 1. Incidence or epidemiology of post-stroke fracture 2. Risk factors 3. Assessment (BMD, metabolic bone markers, TUG, Tinetti test, etc.) 4. Prevention: physical therapy, drug intervention (calcium, vitamin D, bisphosphonate, parathyroid hormone)

Response: We thank the reviewer's suggestion and have changed the subtitles accordingly.

5. Lastly, I think bisphosphonate should be the first-line drug for prevention or treatment of post-stroke osteoporosis, as for primary osteoporosis. The author stressed the side effects of bisphosphonates including BRONJ, atypical femur fractures, esophageal cancer and cardiovascular diseases. However, these side effects are very few, and benefits of bisphosphonates surpass disadvantages for not using them. So, I think the author should recommend to use bisphosphonate as the first-line drug to prevent bone loss for post-stroke patients

Response: We agree and have added discussion regarding the use of bisphosphonate as the first-line drug to prevent bone loss for post-stroke patients. The section is in section in page 14 line 436-441