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World Journal of Orthopaedics

19/05/2021

Dear Reviewer/Editor,

RE: Summary of revisions

Thank you for reviewing our paper titled "Current concepts in the management of bisphosphonate associated atypical femoral fractures."

We have reviewed your comments and made appropriate revisions. Please find a reply to each comment in turn in our document attached.

Many thanks in advance.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Branavan Rudran', with a horizontal line underneath the name and a period at the end.

Dr Branavan Rudran
The MSk Lab, Imperial College London

<p>"1. The risk factors of bisphosphates associated atypical femoral fractures needed more emphasis because it is important for clinical screening practice"</p>	<p>“Risk factors for atypical femoral fractures</p> <p>Despite the common use of bisphosphonates for the treatment of osteoporosis, atypical femoral fractures remain rare. The majority of patients who are treated with bisphosphonates will not sustain a stress change in their femur. However, the consequence of an atypical femoral fracture can have significant impact of mortality and morbidity. Therefore it is imperative that risk factors are identified and screened accordingly.”</p>
<p>"2. The role of bone scintigraphy is important, especially for detecting bilateral or multiple lesions. For those locations without obvious symptoms, bone scintigraphy can be helpful and also needs discussion."</p>	<p>“Bone scintigraphy provides clinicians with another imaging adjunct to ensure early detection.⁴³ At present, there are no high quality studies which consider bone scintigraphy compared to MRI for identification of occult fractures in bisphosphonate related atypical femoral fractures. However, a recent meta-analysis on the use of advanced imaging in occult hip fractures of the elderly suggests that CT and bone scan (sensitivity, 79% and 87% respectively) are less sensitive for occult hip fractures compared with MRI.⁴⁴”</p>
<p>"3. Regarding operation, adequate bone grafting also promoted fracture healing. This point was missed."</p>	<p>“Fracture healing in this complex group of patients is an area of consideration to the surgeon. Pathologic by nature, bisphosphonate related atypical femoral fractures are due to chronic osteoclast inhibition, resulting in a site on the femur of reduced remodelling and sclerosis. Autologous bone grafting or bone marrow aspirate may restore the normal bone homeostasis. Currently, the literature is limited in regards to the theoretical benefits. A report by the American Society for Bone and Mineral research found limited evidence to suggest the chronic suppression of osteoclasts may affect the efficacy of bone grafting at the fracture site. Conversely, a study showed no decrease in bone formation after transiliac crest biopsy in a similar patient population. This shows that further research is required regarding femoral fractures improving time to fracture union.”</p>
<p>"4. The authors may provide a clinical check-up suggestion for those patients with high risk of bisphosphates associated atypical femoral fractures."</p>	<p>“We did not feel there was sufficient agreement in the literature regarding time for clinical check up, therefore refrained from passing judgement as to when a check up should happen”</p>
<p>"5. Bone turnover markers status was not discussed. Did those with bisphosphates</p>	<p>S”erum markers provide a clinical value for initiation and monitoring bisphosphonate use. The present definition for osteoporosis is based</p>

批注 [BR1]: Shane E, Burr D, Abrahamsen B, et al: Atypical subtrochanteric and diaphyseal femoral fractures: Second report of a task force of the American Society for Bone and Mineral Research. J Bone Miner Res 2014; 29:1-23.

批注 [BR2]: https://www.nejm.org/doi/10.1056/NEJMc1107029?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%20pubmed

<p>associated atypical femoral fractures have a different turnover status as compared with controls? "</p>	<p>on the value of bone mineral density (BMD) measured by DEXA or occurrence of fragility fracture. BMD response to bisphosphonate use is slow, which makes monitoring bone turnover difficult. Bone turnover markers (BTM) provide a more real time reflection of bone formation and bone resorption through the monitoring of serum and urine. A comprehensive review by Vasikaran et al⁴⁵ demonstrated that high level of BTMs may predict fracture risk independently to BMD for post-menopausal women. Despite the ability of BTM to monitor the pharmacologic effects of osteoporosis, the inconsistency in metrics of measurement and unsuitable trials on the BTM levels with treatment compared to controls."</p>
<p>"Obtain permission for all images"</p>	<p>"Declaration: All unidentifiable patient images were obtained by consent."</p>