Author's response to reviews

Title: Bone management in patients with prostate cancer: Hormonal therapy leads to increase the FRAX score

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Editorial office
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Re: Ms. #1607963481715194, "Bone management in Japanese patients with prostate cancer: Hormonal therapy leads to an increase in FRAX score"

Dear Editor:

Thank you for your letter concerning the above-mentioned manuscript. We are pleased to note the favorable comments of the reviewers and have revised the manuscript. Our point-by-point revisions are described on the following pages.

We would like to thank again the Editor and reviewers for helpful comments and hope that the revised manuscript is acceptable for publication in BMC Urology.

Sincerely yours,

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Again, we appreciate your careful consideration of our manuscript as well as the valuable suggestions and comments. Our point-by-point replies are as follows:

BMC Urology: Answers to reviewers’ critiques

Reviewer #1:
The incidence of prostate cancer is increasing in Japan among the elderly. Many of these patients will be treated with Androgen Deprivation Therapy (ADT), which could increase the risk of hip fractures, since androgens are required for bone health. According to the authors, large scale studies on the risk of ADT on fractures is non-existent. Therefore, this study is a large scale investigation on the impact of ADT on fracture risk in elderly Japanese men with prostate cancer. Below are constructive criticisms regarding this project.

Major Revisions
1. The title should be changed to reflect the focus on Japanese men.

Thank you for your suggestion. We changed the title to reflect the focus on Japanese men.

2. The last sentence, starting with …… “A comparison between the ADT (n=187) and non-ADT (n=399) groups demonstrated”….., in the abstract is confusing and should be reworded.

Thank you for your pointing out. We rewrote the abstract section to clarify these sentences.

3. What is the incidence of and mortality from prostate cancer in Japan?

We appreciate your pointing out. We added the recent data about the mortality rate in Japanese men with prostate cancer in the part of Background.

4. In Table 2, define the units for patients’ height and weight.

Thank you for your suggestion. We added the units of height and weight, cm and kilogram, in Table 2.

5. Define EBRT

In the present study, EBRT was defined as IMRT. We explained this in the revised manuscript.
6. Provide a reason for including parent fractured hip in your report.

Thank you for your suggestion. We included parent fractured hip because it is a necessary component of the FRAX score. We described this in the revised manuscript.

7. In Figure 1, the comparison between ADT & brachytherapy and brachytherapy alone was not obvious.

We appreciate your comment. In Figure 1, there were no differences between the patients who received ADT and those who did not in brachytherapy group. This means that short-duration ADT did not affect FRAX score. We explained this point in the revised manuscript.

8. What does “ALL” refers too in this figure?

Thank you for your pointing out. In that figure, “ALL” means “Total”. As you pointed this out, it might cause confusion. This point was changed in the revised manuscript.

9. Did the study exclude patients with bone metastasis? This should be stated clearly as it could impact how the data is interpreted.

We appreciate your suggestion. In this study, some patients had bone metastasis at the time of diagnosis in the hormonal therapy group. However, this study excluded the patients with a CRPC status. We commented on this in the revised manuscript.

Minor Revisions

10. In the result section, paragraphs 3-5 were difficult to read. A rewording is recommended in addition to summarizing the percentages (%) in a table.

Thank you for your suggestion. Following your advice, we rewrote these sentences so that they may be more easily understood and summarized our findings in Fig.1.

Reviewer #2:

This is a large and interesting cohort study examining the impact of prostate cancer treatment modalities on risk of skeletal fractures using FRAX in men treated at a single Institution in Japan.

Strengths of the paper includes: number of patients involved and use of a well established tool to assess risk of fractures that has not been extensively used or reported in men with prostate cancer.

Points for consideration:

1) Can the authors better elaborate why DXA data was not used in the actual
FRAX scores?

Thank you for your comment. We added an explanation of why we used FRAX without the use of DEXA.

2) Can the authors describe in the intro or methods the cut off point for clinical significant for the FRAX scores? This will make it easier for those not familiar with the actual scores to interpret FRAX.

Thank you for your pointing out. We added the description of the cut-off point of the FRAX score in the Discussion section of the revised manuscript.

3) Were the measures undertaken at one time point as a cross section study or a prospective observational study? Please add study design to the methods so easier to follow.

We appreciate your suggestion. In this study, FRAX was measured at one time point. We explained this point in the Methods section of the revised manuscript.

4) Correlations between ADT time and major osteoporotic fractures were significant but relatively small (example: R=0.141). Can the authors comment on these values and add a sentence to the discussion?

We thank your comment. As you pointed out, the relationship was significant but small. We speculate that the low degree of correlation come from the assessment of the FRAX score rather than the DEXA score. We commented on this in the revised manuscript.

5) Discussion: The first paragraph is very similar to the last paragraph of the introduction (example: description of FRAX). Suggest this section can be shortened so authors can discuss their actual results main finding upfront in the discussion.

Thank you for your suggestion. As you pointed out, some of the sentences in the Introduction and Discussion sections were surely similar. We deleted some sentences from the Discussion section and focused our discussion on the findings of the study.

6) Line 221/222. Briefly provide examples of fracture prevention in ADT treated patients. For instance weight bearing resistance exercise and other strategies.

We appreciate your comment. We added a comment about preventing fracture.

7) Ethnicity is used in the intro and racial differences in the discussion. Better to use one term (Ethnicity) for consistency throughout the manuscript.

Thank you for your suggestion. We changed the word “racial” to “ethnicity” throughout the manuscript.
8) Conclusion: suggest only describing main results. For example: Large study where ADT have influenced FRAX scores.

We appreciate your point. In accordance with your suggestion, we deleted conclusion and incorporated it in our Discussion section.