

Format for ANSWERING REVIEWERS

August 8, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 10993-edited.doc).

Title: Functional and Metabolic Complications of Prostate Cancer

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Name of Journal: *World Journal of Clinical Urology*

ESPS Manuscript NO: 10993

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated. Language evaluation has been performed. We made pertinent changes according to the suggestions of all editors.

2 Revision has been made according to the suggestions of the reviewer

(1) **Reviewer 724492:** No changes were suggested.

(2) **Reviewer 2471477:** We updated the cancer statistics. We added the definitions of the abbreviations. In regards to the third paragraph of the "Cardiovascular Complications" section, yes, it is intentionally there. We refer to the fact that if we recommend exercise training (for cardiovascular purposes), the benefit seems to be better if we prescribe a supervised routine.

(3) **Reviewer 2976953:** We would like to be clear in the fact that this is not a systematic review. It is a critical review (as we were asked to do) that offers the latest information available, oriented to urologists/other physicians who face this matter in a day-to-day basis and wish to improve their patient's care. For this reason, we did not follow the PRISMA guidelines. The use of SEER analysis was done when considered appropriated. Certainly SEER analyses do not offer the best level of evidence because much information is not available in this type of databases. Anyhow, we used the information when referring to descriptive analysis or rather simple comparison. At any moment did we say it was an absolute true, we just presented the information.

The purpose of the review was to present functional and metabolic complications. We did not review the performance of the different types of ADT in terms of oncologic or mortality outcomes. We added the study done in Denmark referring to survival. We agree, there is an important variation among the results from different centers; we try to bring the information to the reader in a clear and practical form. We cannot show homogeneous data from all centers, and we clarify that there are many things that remain inconclusive with the present information. We do not wish to present ADT as the standard treatment for prostate cancer. We did describe survival or oncologic outcomes. We changed the "title" and the "running title" to clarify this matter.

We did not mean to discuss the indications of ADT, only functional and metabolic complications. We added information about abiraterone acetate and enzalutamide. We did not mention bone metastasis complications because it was not the objective of the present review. We changed the titles to clarify.

We did mention that the results of exercise are better when prescribing supervised training. Either way, even though we agree in the fact that it is hard to convince a patient to do exercise or quit smoking, we show the evidence supporting such habits. As we mentioned before it is better when supervision is available, but still, the recommendation should be done independently whether the patient decides to follow it or not. We know it is hard for a "frail" patient to do exercise (bad prognosis with or without

prostate cancer), but "vulnerable" patients can benefit for such recommendations.

Thank you for recognizing the effort. As you say, we mostly used PubMed. We did not follow the PRISMA guidelines.

When we mentioned mortality in comparison with other cancer sites, we referred to both genders. In males, prostate cancer mortality is only surpassed by lung cancer. Changes have been made within the final manuscript. We changed the sentence "Prostate cancer and ADT is nowadays a combined subject. ADT perhaps represents the most utilized therapy for PCa" to "Prostate cancer and ADT is nowadays a common combination. ADT represents one of the most utilized therapies for PCa and can be implemented in nearly every stage of the disease."

The final sentences were modified to "Adherence to guidelines has great implications on patients. Individual patient selection, surveillance of complications and educational strategies (for both patient and urologists) are important cues in treatment."

(4) Reviewer 468214: A professional English language translator performed language evaluation. Evidence acquisition methodology was extended. We must be clear in the fact that this is not a systematic review. It is a critical review that offers the latest information available, oriented to urologists/other physicians who face this matter in a day-to-day basis and wish to improve their patients care.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Clinical Urology* and thanks to the authors for their useful comments.

Sincerely yours,



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