

Peer Review File

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Reviewer A

This study is important in looking at predictive factors of high-risk prostate cancer. However the landscape of predictive biomarkers have evolved rapidly to involve genomic biomarkers and also next generation molecular imaging and radio-omics. Therefore more needs to be done to show how this article can value add to the current body of literature. More work needs to be done before the manuscript can be reconsidered for publication.

1. The authors describe the entity of "LPPCa" and define it as "PCa that has metastasized distantly by breaking through the envelope unit, and is defined as stage \geq T3." There are many issues with this statement. Firstly, the local progression of prostate cancer by itself has much ambiguity in that it describes the progression of the disease rather than a state of disease. It seems to describe T2 disease that has "progressed" locally to T3 disease. Also, the above statement is inaccurate in using the term "metastasized distantly" and then ending off with \geq T3. T is the local staging and metastasis describes M1 disease. I believe the authors are trying to describe locally advanced prostate cancer which is a more commonly used and accepted term. Also, "envelope unit" is a highly non-medical term, a more anatomical term would be prostate capsule. The authors will need to work on defining the disease entity that they want to study properly.

Reply 1: Thank you very much for your pertinent opinions. As you suggested, we indeed made a spelling error right from the start; our actual intention was to study locally advanced prostate cancer, which aligns perfectly with your advice. We have revised all the content in the document related to local progression of prostate cancer, but this does not affect the subject matter we aim to research and discuss.

Changes in the text: we have modified our text as advised (see Page 1, line 3-4; Page 2, line 46,48,52,64,67-71; Page 3, line 98-99,103,105-106, 122, 127; Page 5, line 220; Page 6, line 238,251; Page 7, line 270; Page 7, line 304-305; Page 7-8, line 308-309)

2. "Body mass index (BMI) is associated with several types of cancer (7), but its connection with PCa has not been clarified."

BMI defines obesity and Obesity has clear linkages to prostate cancer. (recent SRMA <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9666096/>)

([https://www.nature.com/articles/s41585-023-00764-9](https://www.nature.com/articles/s41585-023-00764-9#:~:text=Obesity%20is%20associated%20with%20aggressive,cells%20in%20the%20tumour%20stroma.)#:~:text=Obesity%20is%20associated%20with%20aggressive,cells%20in%20the%20tumour%20stroma.)

9#:~:text=Obesity%20is%20associated%20with%20aggressive,cells%20in%20the%20tumour%20stroma.)

Reply 2: Thank you very much for your pertinent opinions. Thank you very much for providing us with the latest research progress. Based on the literature you provided, we have added some content on the relationship between BMI and the development of prostate cancer.

Changes in the text: we have modified our text as advised (see Page 3, line 112-118)

3. "We investigated the correlation between the pathologic T stage as an indicator of LPPCa and clinical indicators (BMI, PSA, Gleason score) and indicators of systemic inflammation (neutrophil: lymphocyte ratio (NLR), lymphocyte: monocyte ratio (LMR))."

The sentence is confusing with regard to its syntax. It is methodologically wrong to correlate an outcome, in this case, the pT stage with LPPCa when pT stage defines LPPCa. This sentence needs revision.

Reply 3: Thank you very much for your pertinent opinions. we have modified our text as advised.

Changes in the text: we have modified our text as advised (see Page 3 , line 124-126)

4. what is microscopic radical prostatectomy?

Reply 4: Thank you very much for your pertinent opinions. We sorry about the mistake we made while our original mean is Laparoscopic radical prostatectomy.

Changes in the text: we have modified our text as advised (see Page 4, line 140)

5. "Postoperative specimens were confirmed to be PCa through a combination of histopathological and clinical diagnoses"

What is the clinical diagnosis here? And why is it needed when histopathological diagnosis is the final arbiter of cancer?

Reply 5: Thank you very much for your pertinent opinions. We are sorry for the confusion caused by our inappropriate statement . We have modified our text as advised.

Changes in the text: we have modified our text as advised (see Page 4, line 141-142)

6. Relevant publications to this topic should be cited as above and below:

- [https://www.clinical-genitourinary-cancer.com/article/S1558-7673\(19\)30364-7/fulltext](https://www.clinical-genitourinary-cancer.com/article/S1558-7673(19)30364-7/fulltext)

- There is no mention of the imaging used for the initial staging of these cancers and whether there is significant pathological upstaging post-prostatectomy. There is evidence that imaging biomarkers have come out as strong independent predictors of high-risk prostate cancer. PSMA PET has the highest accuracy in the primary staging

of prostate cancer. This recent SRMA should be cited to make this manuscript and discussion more contemporary and relevant. (<https://pubmed.ncbi.nlm.nih.gov/37032189/>)

Reply 6: Thank you very much for your pertinent opinions. Based on the literature you provided, we have refinished our content to make the article look more complete. we have added some content in our text about inflammatory indexes and PSMA PET. Changes in the text: we have modified our text as advised (see Page3, line126; Page 6-7 line 262-266; Page 7 line 275-289)

Reviewer B

the job is well done. The topic is interesting even if it isn't the most popular.

Reply: Thank you very much for your encouragement and support for our work. It gives us more confidence to continue our in-depth research.