Author's response to reviews

Title: A prostate biopsy strategy based on a new clinical nomogram reduces the number of biopsy cores required in high-risk patients

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Author's response to reviews: see over
Title: "A prostate biopsy strategy based on a new clinical nomogram reduces the number of biopsy cores required in high-risk patients"

Dear Editor:

Thank you very much for your attention and the referee’s evaluation and comments on our paper “A prostate biopsy strategy based on a new clinical nomogram reduces the number of biopsy cores required in high-risk patients”. We have revised the manuscript according to your kind advices and referee’s detailed suggestions. In order to improve the style of written English. Our manuscript has been revised by a professional editing service (Edanz) again. All main changes have been highlighted with red text in revised manuscript. We sincerely hope this manuscript will be finally acceptable to be published on BMC Urology. Thank you very much for all your help and looking forward to hearing from you soon.

Please find the following Response to the comments of referees:

Response to the referee’s comments

Referee1
Comment 1: Why reduced the number of cores from 12 to 6? Is 12 associated with significant complications or pain? In my practice, no this is not the case.

Response: Thanks for the referee’s suggestion. Because of the shortage of the beds in our hospital and developing medical insurance, most of our prostate biopsies were performed in the clinic. And we did not give the patients any anesthesia. Experience of thousands of biopsies has shown that playing prostate biopsy in the clinic without any anesthesia is safe and cheaper, but patients were uncomfortable during biopsy process. Reducing cores from 12 to 6 may reduce half of the biopsy time approximately. Furthermore, reducing cores may reduce bleeding in prostate biopsy.

Comment 2: 13 core or 12 core performed? using a scheme based on the results of the first stage.

Response: In first stage we used a biopsy scheme of 12+1. In second stage, every patients were evaluated by our predictor formula, patients with higher risk based on our forecasting model were advised to accept a scheme of 6+1. We have described in which patients should reduce cores
Comment 3: As the researchers state numerous nomograms are available but may not be applicable to Chinese cohort. But we must specific do we need a nomogram to tell us the risk of harboring prostate cancer and thus when to biopsy or do we need a nomogram to tell us the number of cores to biopsy? I believe the former is more necessary.

Response: We are sure that we need a nomogram to tell us the risk of harboring prostate cancer and thus when to biopsy. The basic application of the nomogram developed in our research is prediction of the risk of prostate cancer. Screening out the patients in which biopsy cores may be reduced is an additional application of our nomogram.

Comment 4: Why were patients seen? Elevated psa? Abnormal DRE? What?

Response: Thanks for the referee’s kind advice. A part of the patients were seen by elevated psa or abnormal DRE in routine physical, the others were seen by lower urinary tract symptoms (LUTS) with elevated PSA. We added this point in revised manuscript.(page5; line1-3)

Comment 5: Move ethics statement to the beginning of this section.
Response: We have moved ethics statement to the beginning of this section.

Comment 6: So it says 12 core biopsy but it seems like everyone had 12 core + 1 (hypoechoic or apex), correct? Perhaps state 13 core then. Otherwise it is a little confusing. New biopsy scheme? If its not the 6 core then how was the new scheme developed? I think you mean the nomogram. Your data analysis section does not describe a new biopsy scheme.

Response: Thanks for the referee’s suggestion. In first stage we used a biopsy scheme of 12+1(13-core). 12-core biopsy and 6-core biopsy are hypothetical. We supposed that every patients in first stage received two biopsy scheme (6-core and 12-core), and compared the detection rate between 12-core and 6-core in different risk degrees. In second stage, every patients were evaluated by our predictor formula, patients with higher risk (cutoff>0.5) based on our forecasting model were advised to accept a scheme of 6+1core. We have described how to screen out the patients with no necessary to accept 12+1 core biopsy in revised manuscript.(page6; line 3-8)
Comment 7: Cacoethic biopsy effect? Text font should be the same.

Response: Thanks for the referee’s suggestion. We have changed “cacoethic biopsy effect” to “cacoethic biopsy result”(page7; line18) and made the text font same.

Comment 8: AUROC 0.761 is from?

Response: 0.761 is the AUROC of PSA alone. (page7; line20-21)

Comment 9: Please describe your results with the results of other nomogram from China.

Response: Thanks for the referee’s suggestion. We have compared our nomogram with other nomogram from China in revised manuscript.(last section of discussion and table4)

Comment 10: Reference 4 and 16 have typos

Response: We have corrected the typos

Comment 11: Should error bars be on panel B and C?
Response: Thanks for the referee’s suggestion. We also found that the fig should be refined. We have added error bars on panel C. But in panel B, the positive rate in every risk degree is affirmtory, it seems that error bars is not necessary.

Referee2

Comment 1: The word "Multivariate" should be replaced with "multivariable" . (Please refer to Am J Public Health. 2013 January; 103(1): 10.2105/AJPH.2012.300897.)

Response: Thanks for the referee’s suggestion. We have replaced "Multivariate" with "multivariable" in revised manuscript.

Comment 2: The meaning is not obvious in the second last paragraph of the results section. What does "72.9% vs. 78.6%" mean? Is it the detection rate?

Response: Yes, 72.9% and 78.6% is detection rate, we have explained in revised manuscript.(page8, line 12)
Comment 3: In Table 3, what does "384" (right next to 78) stand for? Do you mean 384 cases with a cutoff >0.5 taken the old scheme? or the cases with a cutoff < or = 0.5? With table and the paragraph related with it, I can not get it.

Response: Thanks for the referee’s suggestion. "384" is the number of patients who had a PCP cutoff > 0.5 in first stage. We have changed the “new scheme and old scheme” to “second stage and first stage” to avoid misunderstanding. (table 3, line 1)

Comment 4: As for the last paragraph in the result section, the authors showed that they reduced the number of biopsy core in the group with cutoff >0.5, but it is nonsense that it is already their study design. Even more, they compared the group with cutoff >0.5 with the one with cutoff 0.5 or less. The positive core rate in former is less than that of latter even if there is no statistical significance. Is it the one Urologists really want to reduce the number of Biopsy core? I do not think so. Not to miss the cancer is the most important in the Oncology field. (The real positive detection rate would be around 80%, as you showed in Fig. 1B) The authors should have put the same condition between two groups to see the effect of reducing core numbers. Otherwise, if they want to stick to this study design, they should comment the portion of insignificant cancer in
the "Second stage".

Response: Thanks for the referee’s suggestion. We are so sorry that our description was not clear. In first stage of our research we supposed every patient received two biopsy schemes, 6-core and 12-core. Obviously, a part of prostate cancer detected by 12-core biopsy could not be detected by 6-core. Furthermore, we found that the positive rate of 6-core and 12-core were not significant different in patients with cutoff>0.5, and we inferred that reducing cores in patients with cutoff>0.5 might not decrease the detection rate. In second stage of our research, we verified our inference prospectively. A total of 238 patients were evaluated using our new nomogram; 78 patients of them had a PCP cutoff >0.5. The 78 patients were recommended to accept 6+1 core biopsy. The other patients still accept 12+1 core biopsy. We have rewritten the last paragraph in the result section to avoid the misunderstanding.

Comment 5: In the first paragraph of Discussion, Schroder et al. report the benefit of PSA screening. (Ref. 16) Moreover, their recent report is saying that the benefit become obvious as time goes by. You should make some corrections for it.

Response: Thanks for the referee’s kind advice, we have read their new
research article. We have quoted their new results. (page 9, line 15-16)

Comment 6: Fig. 1 needs to be refined. The letter is too small to read, and some picture is not so informative. You can get rid of some part of the picture.

Response: Thanks for the referee’s suggestion. We also found that the fig should be refined. We have remade fig 1, and enlarged the letter. B, C and D described detection rate, the number of positive cores counted and the percentage of low Gleason scores (<7) for every risk level respectively. Pictures may describe the information more clearly and legibly than a textual description.

Comment 7: You should show us your own nomogram as the other articles do.

Response: Thanks for the referee’s suggestion. We have made our nomogram in fig 2.