Peer Review File

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Reviewer A

1. Did the 98 patients with symptomatic BPH have catheters placed just for the study or were they in retention.?

Reply 1:

Thank you for your valuable advice. 98 patients in our study were in urinary retention which was caused by benign prostatic hyperplasia. We are sorry that the screening process of patients was not written down. We were not taking this section seriously. A detailed medical history of 296 patients who visited the Tianjin First Center Hospital for lower urinary tract symptoms or benign prostatic hyperplasia between October 2016 and November 2019 was obtained from our clinical database. All the patients had examined by T2-weighted magnetic resonance imaging (MRI). These patients were diagnosed as urinary retention which was caused by benign prostatic hyperplasia, prostatic cancer, urinary retention, benign prostatic hyperplasia, prostatitis, prostatic cancer and elevated PSA levels, respectively. Among these patients, there were 106 patients who carried a urinary catheter with urinary retention which was caused by benign prostatic hyperplasia. The structure of prostatic urethra was clearly identifiable on their T2MRI. 8 patients whose peripheral zone and/or central gland were impossible to identify were also excluded from this study. Finally, 98 patients who carried a urinary catheter with urinary retention which was caused by benign prostatic hyperplasia were eligible for analysis. We chose those patients

because the structure of prostatic urethra was clearly identifiable on their T2MRI.

2. Is it a routine at your institution to place catheters for all prostate MRI studies? If not, this is not really a retrospective study.

Reply 2:

Thank you for your prompt attention to our manuscript and helpful suggestions. Your suggestion is very good. The retrospective study design was an analysis of past clinical data. Targeted data already exist at the time the retrospective study was conducted. In our study, we analyzed MRI data of patients who had been examined in our institution previously. From the view of time, our study started from the principle of retrospective study. However, the data of retrospective study cannot be controlled such as diagnostic standards, testing standards and judge standards. The Page 8 line 159 to 160 of our manuscript：In order to precisely achieve 3D reconstruction of the prostatic urethra, each patient carried a urinary catheter. It might seem from this sentence that our study has a control condition. The sentence also brings about ambiguity in readers' reading comprehension. We are sorry that the exclusion criteria of patients were not written down. As seen reply 1, we ultimately selected 98 patients who carried a urinary catheter with urinary retention which was caused by benign prostatic hyperplasia. The structure of prostatic urethra of patients with benign prostatic hyperplasia cannot be distinguished on their T2MRI unless they carried a urinary catheter. We want to explore the changes of prostatic urethra in the benign prostatic hyperplasia. Study population of methods was modified as follows.

This retrospective study analyzed clinical database of patients who visited Tianjin first central hospital for lower urinary tract symptoms / BPH from October 2016 to November 2019. A detailed history of 296 patients who underwent T2 MRI was obtained in our study. Exclusion criteria included: history of surgery of lower urinary tract, prostatitis and other non-benign prostatic hyperplasia diseases, patients did not carry a urinary catheter. Patients whose peripheral zone and/or central gland were impossible to identify were also excluded from this study. Finally, 98 patients who carried a urinary catheter with urinary retention which was caused by benign prostatic hyperplasia were eligible for analysis. They were divided into 4 groups by age: 50-60, 60-70, 70-80 and 80-90 ($n_{50\text{-}60}$=14, $n_{60\text{-}70}$=30, $n_{60\text{-}70}$=36, $n_{70\text{-}80}$=18). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by Institutional Review Board (IRB) of the Tianjin First Center Hospital (registration ID2018NO22KY). Individual consent for this retrospective analysis was waived. (See page 8-9 line 166-179).

3. Figure 2 needs more explaining and orientation.

Reply 3:

Thank you very much for your valuable comments on this study. We added Legends regarding the explaining and orientation on figure 2, as shown below.

(A) The highest and lowest point of prostate were analyzed by 3-matic software, the HD was measured from the highest point to the lowest point. The HD is 63.32 mm. (B) The plane of IPP was fitted by 3-matic software according to the straight line

which was used to measure IPP on 2D plane. The highest point of IPP was taken as the endmost of IPP tangent to a plane which is parallel to the plane of IPP. The IPP is 27.02 mm. (C) BWT was analyzed by 3-matic software. The biggest BWT is 12.6489 mm. (D) The central line of proximal prostatic urethra and distal prostatic urethra，the highest and lowest point of prostatic urethra were determined by 3-matic software, respectively. The angle of central line of the proximal prostatic urethra and distal prostatic urethra with respect to the coronal plane was defined as the A-angle and C-angle, respectively. The distance from the highest and lowest point of prostatic urethra to the coronal plane was defined as the A-Distance and C-Distance, respectively. The A-angle, C-angle, A-Distance and C-Distance were 44.74°, 8.06°, 23.04 mm and 5.92 mm respectively. (E) The angle between the two central lines was defined as PUA. The PUA is 142.84°. Surface distance from proximal endpoint of prostatic urethra to distal endpoint of prostatic urethra was defined as PUL. The PUL is 53.86 mm. (F) The plane of bladder was fitted by 3-matic software based on the basilar part of bladder neck. The angle between the plane of bladder and the central line of proximal prostatic urethra was E-Angle. The E-Angle is 76.71°. HD, the highest diameter of prostate; IPP, intravesical prostatic protrusion; BWT, bladder wall thickness; PUA, Prostatic urethra angle; PUL, Prostatic urethra length. (See page 25-26 line 536-557).

4. The authors should provide an illustration with IPPV, intravesical prostatic protrusion surface area (IPPS), IPPT, PV, prostate thickness (PT), prostate surface

1 area (PS), central gland volume (CGV), central gland thickness (CGT), central gland surface area (CGS), peripheral zone volume (PZV), peripheral zone thickness (PZT), peripheral zone surface area 1(PZS), prostatic urethra thickness (PUT) and BWT to make it easier for the reader to understand the article.

Reply 4:

We appreciate your constructive comment. We had added Figure 3. We added figure Legends regarding this section on figure 3. Figure 2C shows the result of analysis of Bladder wall thickness. Volume and surface area of these 3D entities were calculated automatically by the Mimics software. As shows in Figure 3F, the volume and surface area of peripheral zone can be viewed on the property of peripheral zone. The volume of peripheral zone is 24886.58 mm^3; the surface area of peripheral zone is 8070.86 mm^2.

Figure Legends of figure 3, as shown below.

Figure 3 3D analysis of thickness, volume and surface area. (A) Schematic diagram of analysis of PT. The biggest PT is 42.1402 mm. (B) Schematic diagram of analysis of CGT. The biggest CGT is 38.2654 mm. (C) Schematic diagram of analysis of PUT. The biggest PUT is 6.0679 mm. (D) Schematic diagram of analysis of IPPT. The biggest IPPT is 20.3372 mm. (E) Schematic diagram of analysis of PZT. The biggest PZT is 13.1391 mm. (F) Schematic diagram of property of peripheral zone. The PZV is 24886.58 mm^3. The PZS is 8070.86 mm^2. PT, prostate thickness; CGT, central gland thickness; PUT, prostatic urethra thickness; IPPT, intravesical prostatic protrusion thickness; PZT, peripheral zone thickness; PZV, peripheral zone volume;

PZS, peripheral zone surface area. (See page 26 line 559-568).

5.Agree with the limitations mentioned by the authors. A study with a control group of asymptomatic men would have enhanced the significance of all the parameters measured in this study in understanding the biomechanics of symptoms of BPH.

Reply 5:

Thanks for your valuable suggestions. On the one hand, the number of asymptomatic men who visited our institution is relatively small. They usually did not receive a MRI examination. Thus, the result of MRI of asymptomatic men is almost impossible to get. It is difficult to take asymptomatic men as control group. On the other hand, asymptomatic men do not carry a catheter. If they do not carry a catheter, the structure of prostate urethra cannot be identified on the MRI. The prostate of asymptomatic men hardly protrudes into the bladder. For these reasons, the parameters related to prostate urethra, the volume, surface area and thickness of intravesical prostatic protrusion cannot be analyzed in our study. Above all, it is difficult to find comparative cases. But this is indeed a good suggestion.

Reviewer B

This manuscripts presents an interesting retrospective study that quantified the prostate volume from MR images in patients of different ages.

Unfortunately the manuscript Is difficult to follow and would benefit from a strict gramatical edition.

Reply:

Thank you very much for your sincere help and reminder. We will modify it carefully according to your suggestions. Thanks again for your help.

Some specific comments include:

- The abstract does not have any background. The subsection background only has the purpose of the study.

Reply:

Thank you for your careful review and effective help of our manuscript. The background was modified as follows.

The volume and thickness of intravesical prostatic protrusion and other characteristics of benign prostatic hyperplasia have not been investigated. We determine the effects of age and prostate volume on anatomical features of benign prostatic hyperplasia using three-dimensional measurement in this study. (See page 4-5 line 87-90).

Given the word limit of abstract, we deleted “the diameter of prostate,” of page 5 line 97, “Two-dimensional measurements included the diameter of prostate, prostate volume and intravesical prostatic protrusion.” of page 5 line 100 to 101 and “There were significant differences between the two-dimensional and three-dimensional measurements in the measurement of the widest diameter and the longest diameter of

the prostate (p< 0.0001, 0.05, respectively).” of page 6 line 113 to 116 without influencing abstract content. The sentence “Peripheral zone index and intravesical prostatic protrusion index were significantly lower of prostate volume > 80 ml group than these in prostate volume < 80 ml group (both p < 0.05).” was changed to “Peripheral zone index was significantly lower of prostate volume > 80 ml group than these in prostate volume < 80 ml group (p < 0.05).” without influencing abstract content. (See page 5 line 106-108).

- Introduction.

-line 113 plane should be planes

Reply:

Thank you very much for your sincere help and reminder. We modified it according to your suggestion. (See page 6 line 127). Page 17 line 359 plane also be changed to planes by us.

-line 114 there us a word missing, non-invasive and convenient what?

Reply:

Thank you very much for your sincere help and reminder. We modified the sentence as follows.

The parameters are characterized by non-invasive and convenient comparison. (See page 6 line 128).

-Line 115. The sentence that starts with under pathological ... can be organized differently for clarity.

Reply:

Thank you very much for your sincere help and reminder. The sentence was modified as follows.

During the hyperplasia process of prostate, the length of prostatic urethra and prostatic urethra angle will be altered. (See page 6 line 131-132).

- line 116 the word prostatic does not need to start with capital P.

Reply:

Thank you very much for your sincere help and reminder. We modified it according to your suggestion. (See page 6 line 131-132).

- line 127 the paragraph is redundant with purpose and aim.

Reply:

Thank you for your careful review and effective help of our manuscript. We modified the paragraph as follows.

We measured conventional parameters in 2D plane, as well as other features of BPH using three-dimensional measurement in this study. The purpose of this research is to better understanding the lower urinary tract anatomy of male and to provide references for clinical diagnosis and treatment of BPH. (See page 7 line 148-151).

Methods.

line 172: which straight line? this is the first time I see this concept.

Reply:

Thank you for your careful review and effective help of our manuscript. We are sorry that we expressed our method inarticulately. A straight line which appears on page 10 line 199 was determined while we measured IPP on 2D plane. We modified the method as follows.

The straight line which was used to measure IPP on the 2D plane previously was imported into 3-matic software. (See page 10 line 216 to 217).

Results.

- a table with discrete values and p values would make this section easier to follow.

Reply:

Thank you for your valuable advice. We modified tables according to your suggestion. We use standard deviation to represent discrete values. Specific P values are also indicated in tables that were modified by us. All data was shown as Mean ± standard deviation in modified tables. (See all tables that were resubmitted by us).

Minor modifications were made with regards to discussion based on modified tables. The detailed modifications of methods, results, discussion are as follows.

At page 11 line 239, the sentence “Values were shown as Mean ± standard deviation or median (interquartile range).” was changed to “Values were shown as Mean ± standard deviation.”

At page 12 line 255, the sentence “Table 1 showed the mean or quartile measurements of all BPH parameters.” was changed to “Table 1 showed the mean measurements of all BPH parameters.”

At page 13 line 265, the sentence “the WD was significantly higher in 3D measurement than it in 2D measurement (mean 57.79 ± 8.85 vs 50.42 ± 9.06, $p < 0.0001$).” was changed to “the WD was significantly higher in 3D measurement than it in 2D measurement (mean 57.79 ± 8.85 vs 50.42 ± 9.06, $p < 0.001$).”

At page 16 line 342 to 345, the sentence “Comparing to 50-59 years age group, 60-69 years age group and 70-79 years age group, the PZV for 60-69 years age group, 70-79 years age group and 80-89 years age group increased about 2.21ml, 4.45ml and 2.29ml, respectively.” was changed to “Comparing to 50-59 years age group and 60-69 years age group, the PZV for 60-69 years age group, 70-79 years age group increased few.”

At page 16 line 350-351, the sentence “Comparing to PV < 80 ml group, the PZV of PV > 80 ml group increased about 6.8ml.” was changed to “Comparing to PV < 80 ml group, the PZV of PV > 80 ml group increased also few.”

At page 18 line 381, the sentence “However, the PUT was measured as 11.63 (6.91-17.41) mm in this study.” was changed to “However, the median (IQR) value of PUT was measured as 11.63 (6.91-17.41) mm in this study.” Thanks again for your valuable suggestion.

Discussion.

- there is some information about the software that is not necessary here.

Reply:

Thank you very much for your feedback and comments. Some information about the software was removed from the discussion according to your suggestion. Specific modifications of discussion are as described below.

Page 13 line 281 was removed. Related literature of the line was also removed.

Page 13 the word “Mimics” of line 284 was changed to “3D measurement.”

Page 14 line 303 to 305 was removed. Related literature of the line was also removed.