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Peer Review File

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Reviewer A

Comment 1: This is an important paper. As all the pts are likely to have had a TURBT as well, presumably pre-MRI from the way this is written, it would be valuable to have a table with the TURB timing and estimated stage as well.

Reply 1: Thank you for your inspiring comments.

As you kindly pointed out, the interval time between TURBT and RC was calculated, and the clinical stage before RC is summarized in Table 2. It is hoped that readers will gain more information from this table. (Page 9, Line 137)

Changes in the text: The median interval between TUR-BT and RC was 58 days (IQR 43-136). Clinical TNM stages of patients before RC are shown in Table 2.

Comment 2: There are often long delays between initial TURBT and cystectomy and the time issue as well as the accuracy issue should be discussed.

Reply 2: Thank you for your comment.

This topic is very important. Radical cystectomy is delayed for a number of reasons, not only because of diagnostic issues, but also because of patient requests. Inappropriate delay in patients with radical cystectomy indication can lead to poor outcomes. This has been explained in the discussion. (Page 12, Line 198)

Changes in the text: This might also help reduce the interval delay between the initial TUR-BT and RC. In some cases, RC was delayed due to the tight schedule and time required for pathological confirmation. Longer delays from bladder cacner diagnosis to RC can significantly worsen survival outcomes (25). However, this algorithm still requires further discussion.

25. Russell B, Liedberg F, Khan MS, et al. A Systematic Review and Meta-analysis of Delay in Radical Cystectomy and the Effect on Survival in Bladder Cancer Patients. Eur Urol Oncol 2020;3:239-49.

Comment 3: MRI can be used to fast-track pts to cystectomy if clearly MIBC on imaging (plus a suitable tissue confirmation). This should also be discussed.

Reply 3: Thank you for your sharp comment.

If the accuracy of MRI increases and replaces the 2nd TURBT, it will be advantageous to patients in terms of time and cost. Moreover, it can also be useful in places where TURB is difficult, such as diverticulum. However, it is still difficult for MRI to completely replace the role of TURBT. This has been explained in the discussion. (Page 12, Line 194)

Changes in the text: Recently, a new treatment algorithm using VI-RADS for bladder cancer has been proposed (24). If bladder cancer is diagnosed by cystoscopy or urine cytology, it is



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argued that MRI should be performed before TUR-BT and approached according to VI-RADS. In particular, VI-RADS 4 recommends performing neoadjuvant chemotherapy and RC after tissue sampling. This study has the potential to support this perspective.

24. Taguchi S, Watanabe M, Tambo M, et al. Proposal for a New Vesical Imaging-Reporting and Data System (VI-RADS)-Based Algorithm for the Management of Bladder Cancer: A Paradigm Shift From the Current Transurethral Resection of Bladder Tumor (TURBT)-Dependent Practice. Clin Genitourin Cancer 2022;20:e291-e5.

Comment 4: I attach our recent presentation on this topic

Reply 4: Thank you for your consideration. However, the attached presentation could not be verified. Could you please send me a link or presentation files again?

Reviewer B

Minor comments:

Comment 1:

Introduction

The first sentence and the following sentence are repetitive.

Reply 1: Thank you for your comments. We have modified the sentence. (Page 5, Line 57)

Changes in the text: Bladder cancer is the fourth most common cancer among all cancers in the United States, and its incidence is steadily increasing. Especially in men, it accounts for approximately 4% of all cancer-related deaths.

Comment 2:

Discussion

Would you please discuss the weakness of VI-RADS in the discussion? The weakness of VI-RADS is that at VI-RADS 3, the scoring system is optimally sensitive and not specific. The sensitivity drops rapidly when the optimal specificity is reached at VI-RADS 4. This is an ongoing issue with VI-RADS which needs to be addressed in the revised version of the VI-RADS.

Reply 2: Thank you for your important comment. This issue was also of interest to us. We hope to share our thoughts with our readers through this discussion and to improve VI-RADS. (Page 11, Line 165)

Changes in the text: However, VI-RADS still has some weaknesses. One of the weakness is the role of VI-RADS score of 3 in predicting muscle involvement. In this study, the sensitivity of VI- RADS score of 3 was 0.94 and the specificity was 0.68. However, the sensitivity rapidly decreased and reached the optimal specificity in VI-RADS score of 4. Some researchers use tumor contact length to overcome this limitation of VI-RADS (15).

15. Wang X, Tu N, Sun F, et al. Detecting Muscle Invasion of Bladder Cancer Using a Proposed Magnetic Resonance Imaging Strategy. J Magn Reson Imaging 2021;54:1212-21.



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Comment 3: Given that the authors have an extremely valuable data set of RC specimens and mpMRI, would they be able to add minor tweaks/recommendations for VI-RADS that can further improve the performance of the scoring system?

Reply3: It is an honor for us to be able to talk about Improving VI-RADS. In this study, the diagnostic performance of VI-RADS was very good. The problem arises when the three variables (T2WI, DWI, and DCE) do not match. In order to overcome this, it is judged that priorities should be set. This was described in the discussion by referring to the recent study. (Page 11, Line 169)

Changes in the text: Another problem is that the three variables (T2-weighted, diffusion-weighted, and dynamic contrast-enhanced images) in MRI are sometimes inconsistent. In this case, a study have shown that using dynamic contrast-enhanced images is advantageous for predicting muscle invasion (16). These are ongoing issues and reasons to modify VI-RADS.

16. Meng X, Hu H, Wang Y, et al. Accuracy and Challenges in the Vesical Imaging-Reporting and Data System for Staging Bladder Cancer. J Magn Reson Imaging 2022;56:391-8.

Comment 4: Sharing the raw data for future use and meta-analysis is extremely valuable if possible.

Reply 4: Thank you for your good point. I hope my data will be used to produce higher level of evidence.

