Peer Review File

Article Information: https://dx.doi.org/10.21037/tau-22-355

Reviewer A

Comment 1: The authors should specify the type of statistical analysis performed in each of the studies (i.e. Cox Proportional Hazards Model or Kaplan Meier method).
Reply 1: Thank you for your constructive comments. In Almarzouq et al. paper, the Cox proportional hazards model was used. In Tanaka et al. paper, the Kaplan-Meier method was used.
Changes in the text: We added the type of statistical analyses performed in the two studies (see Page 10, line 159-162 and Page 11, line 181-182).

Comment 2: The authors should report on statistical tests of association between sarcopenia and clinical and demographic characteristics of the patients, (age, race, smoking-status, baseline anemia, etc) as well as associations between sarcopenia and tumor stage, grade, lymphovascular invasion, and variant histology.
Reply 2: Almarzouq et al. used Student's T or Wilcoxon Rank test for continuous variables and Chi-Square or Fisher's exact test for categorical variables. Tanaka et al. used Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.
Changes in the text: We added some data regarding statistical tests of associations between sarcopenia and other clinicopathological parameters. (see Page 9, line 150-154 and Page 10, line 174-176).

Comment 3: The authors should report on the salvage treatments for the patients who did not experience complete response; they also should report the percentages of patients in each group (sarcopenic vs. non-sarcopenic) who ultimately underwent radical cystectomy.
Reply 3: Thank you for your suggestion. Although this point is clinically important, no data was available regarding salvage treatments for the patients who did not achieve complete response.
Changes in the text: We could not add any comments to the text.

Comment 4: How many of the cases in the tetramodality therapy study were performed robotically?
Reply 4: No patients undergo partial cystectomy robotically.
Changes in the text: We added a comment to the text as follows:
"A robotic-assisted laparoscopic approach was not used in consolidative partial cystectomy." (Page 10, line 172-173).

Comment 5: Line 159 : should be "pelvic lymph node dissection" Line 177: pelvic lymph node dissection
Reply 5: Thank you for your pointing out.
Changes in the text: We have modified our text and tables as advised (see Page 10, line 166, Page 11, line 188, and Table 2 and 3).

Comment 6: Can the authors provide more detail on the nature of the complications reported in each study?
Reply 6: Thank you for your constructive comment. In Tanaka et al. paper, Clavien-Dindo 3 complications included bladder-anastomotic leaks, lymphoceles, and postoperative hemorrhage. For Fraisse et al. paper, we could not find the details of complications.
Changes in the text: We have modified our text as follows:
"Moreover, the rates of Clavien-Dindo 3 complications that included bladder-anastomotic leaks, lymphoceles , and postoperative hemorrhage were 4.1% and 12.2% in sarcopenic and non-

sarcopenic patients, respectively (p = 0.24).” (see Page 11, line 190-192).

Comment 7: The authors should postulate as to why one study showed higher complication rate in sarcopenic patients and another actually showed lower complication rates.
Reply 7: Thank you for your pointing out. This may be because these two studies reported complication rates of different treatments. Tanaka et al. reported that complication rates of consolidative partial cystectomy. Meanwhile, Fraisse et al. reported complication rates of trimodal therapy. Moreover, the sample number of Fraisse et al. study is only 29. Thus, it is mandatory to validate their results in a larger cohort of trimodal therapy.
Changes in the text: We described in the text as follows:
“Only Fraisse et al. reported complication rates of trimodal therapy in MIBC patients with sarcopenia. Sarcopenic patients showed higher rates of total and severe complications compared with non-sarcopenic patients. However, their cohort included only 29 patients and thus it is mandatory to validate their results in a larger cohort of trimodal therapy.” (see Page 13, line 226-230).

Comment 8: The authors should also state the limitations to their study, including only two articles included and therefore limited cohort size, use of a single method of measuring sarcopenia (PMI), lack of more granular clinicopathologic information about patients included in the study, limited information about the nature of the complications reported, limited followup time (32-48mos) which may impact conclusions of oncologic efficacy. Strengths of the study included the use of multiple thresholds of PMI defined sarcopenia were used.
Reply 8: Thank you for your suggestion. As you mentioned, this study has multiple limitations.
Changes in the text: We have modified our text as advised (see from Page 13, line 245 to Page 14, line 250).

Reviewer B
Comment 9: The manuscript should do a much better job of highlighting the issues with chemotherapy regimens in TMT. For example, the Almarzouq et al. paper had 76 deaths out of 141 patients. The patients that survived did have a good response to TMT but many of these patients may have passed away to due poor functional status and having difficulty tolerating some of the toxic regimens given in TMT. In the Tanaka et al. study the overall survival is poorly reported, while patients may have been disease free, their handling of chemotherapy may have been problematic. Neither study really demonstrates the issues that patients have with chemotherapy using TMT.
Reply 9: Thank you for your pointing out about chemotherapy. In Almarzouq et al, paper, gemcitabine alone (weekly at a dose of 100 mg/m2), was the main systemic agent used (66.7%) followed by cisplatin alone (weekly at a dose of 40 mg/m2) as the second most common drug (19%). In Tanaka et al, paper, 2 cycles of intravenous cisplatin (20 mg/body) for 5 days were administered.
Changes in the text: We have modified our text as follows:
“Almarzouq et al. showed the oncological outcomes of trimodal therapy, including TURB, chemotherapy (cisplatin alone [weekly at a dose of 40 mg/m2], or gemcitabine alone [weekly at a dose of 100 mg/m2]), and radiotherapy (total dose: 44–66 Gy), using a cohort of 141 MIBC patients.” (see Page 9, line 143-147).
“Tanaka et al. compared the oncological outcomes between sarcopenic and non-sarcopenic patients in 126 MIBC patients treated with tetramodal therapy, which includes TURB, chemotherapy (2 cycles of intravenous cisplatin [20 mg/body] for 5 days), radiotherapy (total dose: 40 Gy), and consolidative partial cystectomy with pelvic lymph node dissection.” (see Page 10, line 162-167).

Comment 10: I think the discussion with immunotherapy is valid because these patients often have cachexia and the tolerance of immunotherapy is better. The paper needs to better support this by discussing how toxic the chemotherapy regimens may be especially in patients that have sarcopenia/poor functional status.

Reply 10: Thank you for your suggestion. As you mentioned, I added the comment about the toxicity of chemotherapy in sarcopenic patients.
Changes in the text: We added the following sentence to the text:
"Given that chemotherapy is toxic in sarcopenic patients, other immunogenic therapy such as near-infrared photoimmunotherapy rather than chemoradiotherapy may be suitable for sarcopenic patients in combination with ICIs." (see Page 13, line 238-241).

Editorial comment
Comment 11: a. The article already followed a Checklist for reporting standards. Please place "Y" in the "Submission Checklist".
Reply 11: Thank you for your comment. We placed "Y" in the Submission Checklist.
Changes in the text: None.

Comment 12: "Data Sharing Statement" is not required for this paper.
Reply 12: Thank you for your comment.
Changes in the text: Data Sharing Statement was not included in the text.

Comment 13: c. Conflict of Interest (COI) Form must be provided, as suggested by ICMJE: (http://www.icmje.org/conflicts-of-interest/). Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. COI form download link: https://cdn.amegroups.cn/static/public/coi_disclosure.docx.
Please collect all forms from each author, number all forms in the line-up of authorship and submit them to the editorial office. We also attached two templates for your reference.
Reply 13: Thank you for your comment. We filled COI Forms out and submitted them.
Changes in the text: None.

Comment 14: d. Please indicate if any of the authors is serving as a current Editorial Team member (such as Editors-in-Chief, Editorial Board Member, Section Editor) for this journal.
Reply 14: Thank you for your comment.
Changes in the text: We indicated that Hiroshi Fukushima is serving as a current Editorial Team member.

Comment 15: e. Please confirm that all figures/tables/videos in this manuscript are original; if not, permission is needed from the copyright holder for the reproduction.
Reply 15: Thank you for your comment. We confirmed they are original.
Changes in the text: None.

Comment 16: f. We are using the "Submission Checklist for Authors" to double-check your manuscript, place "Y" on blank space if you confirm your manuscript has followed the requirement. Place "N/A" if not applicable. If further explanation is needed on a certain item, you can copy the Item and write explanations down below. A filled "Submission Checklist for Authors" should be submitted to the editorial office, along with other required documents.
Reply 16: Thank you for your comment.
Changes in the text: We filled in the Submission Checklist for Authors.

Comment 17: g. If available, please update your reference list by including related literatures published within a year. Some of the references are outdated.
Reply 17: Thank you for your comment. Although some of the references may be outdated, we could not find more recent alternative references.
Changes in the text: None.