Peer Review File

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Reviewer A

Comment 1: In conclusions of abstract it says "Trimodal leads to longer OS in MIBC".Should be: Trimodal therapy

Reply 1: We have changed Trimodal into Trimodal therapy (see Page 2, line 23).

Changes in the text: Page 2, line 23.

Comment 2: On line 58 it says:"We excluded patients with metastasis..." etc

What about cN1,N2,N3? This is unclear.

Reply 2: We excluded patients with distant metastasis (see Page 5, line 58)., the staging of lymph nodes is supplemented in Table 1(see Table 1).
Changes in the text: Page 5, line 58 and Table 1

Comment 3: Table 1: Questions and remarks
(a) Should say cT and not T
(b) Where do we find cN-stages?
Reply 3: We have modified our text as advised (Table 1)
Changes in the text: Table 1.

Comment 4: The MIBC-subgroup is not clearly described. I want a comparison between MIBC- patients less than 85 years and MIBC-patients 85 or older.
Question [1] : Is there a selection bias with significantly more advanced cancers (T-stage-wise) in the "younger" group?
Question [2]: Is there a selection bias with significantly more nodally advanced cancers (cN-status) in the "younger" group?

Reply 4: There is a lack of evidence-based guidelines for managing all stages of BCa for patients over 85 years of age. The current guidelines for the treatment of BCa do not preclude curative therapies for elderly patients. Therefore, the present study aimed to characterize treatment decisions among BCa patients over 85 years.

Changes in the text: None.

Comment 5: The patients in the younger group - what was the outcome over neoadjuvant chemo (NAC) and NAC-naive- patients?

Reply 5: There is a lack of evidence-based guidelines for managing all stages of BCa for patients over 85 years of age. The current guidelines for the treatment of BCa do not preclude curative therapies for elderly patients. Therefore, the present study aimed to characterize treatment decisions among BCa patients over 85 years.

Changes in the text: None.

Comment 6: What chemo was offered to the "older" patients in that MIBC-subgroup?
Reply 6: We can only find out whether chemotherapy has been done. However, the specifics regarding treatment regimens, including chemotherapy (adjuvant, neoadjuvant, dose, drugs and cycle of chemotherapy and radiotherapy), were not provided by the SEER database. We've added this limitation in the Discussion section (Page 10, line 201)
Changes in the text: Page 10, line 201

Reviewer B

Comment 1: The inherent problem is the rapid change of treatment standards (e.g. adjuvant CPI treatment). Authors should include this in their limitations.
Reply 1: We've added this limitation in the Discussion section (Page 10, line 203-204)
Changes in the text: Page 10, line 203-204.

Comment 2: I would temper the discussion around cancer outcomes in this paper. Several groups have shown that confounders are very difficult to control in this population.
Reply 2: SEER database do not provide information about additional confounding factors, such as renal function, ASA score and Charlson comorbidity score. However, they failed to predict OS in patients over 85 years of age in a recent study (1). The lack of this information prevented us from evaluating whether patients in the three groups had similar health conditions. Therefore, the present study results should be conservatively interpreted. We've mentioned this limitation in the Discussion section (page 9 line 184-193)
Changes in the text: None.

Comment 3: There are several problems linked to this type of analysis: first of all, it remains a persisting problem to define "TMT" as numerous protocols are offered and conducted. In consequence, costs and efficacy of TMT may greatly vary. Thus, the need to define a treatment standard for TMT should be more clearly stated.

Reply 3: There is a lack of evidence-based guidelines for managing all stages of BCa for patients over 85 years of age. The current guidelines for the treatment of BCa do not preclude curative therapies for elderly patients. The present study generally analysed treatment decisions among BCa patients over 85 years. Prospective studies with large cohort are needed to define a treatment standard. We've added this limitation in the Discussion section (Page 10, line 204-205)

Changes in the text: Page 10, line 204-205

Comment 4: Furthermore, retrospective datasets such as SEER-Medicare are intrinsically susceptible to a high degree of confounding by unmeasurable patient characteristics (i.e severity of comorbidities within the CCI score) and therefore are inadequate in addressing questions of comparative efficacy between treatments. Other studies have used IPTW methodology to compare like groups, which wasn't described here. What was the author's way to control for these confounders.

Reply 4: Baseline patient characteristics, as shown in Table 2 and Table 3, were comparable among these groups.As mentioned, SEER database didn't provide important information regarding patients' general physical condition. We've mentioned this limitation in the Discussion section (page 9 line 184-193).Therefore, as far as we're concerned, adopting IPTW, PSM or other methods without balancing important variables might not be helpful.

Changes in the text: None.

Comment 5: Use of claims data limits our ability to account for dose of chemotherapy utilized which is a critical limitation as radiosensitizing chemotherapy is a crucial component of TMT therapy. Furthermore, it is difficult to identify radiation schedules using claims data. What were the radiotherapy fractions used for the TMT cohort? Were they adequate for treatment based on current protocols.

Reply 5: The specifics regarding treatment regimens, including radiotherapy and chemotherapy (adjuvant, neoadjuvant, dose, drugs and cycle of chemotherapy and radiotherapy), were not provided by the SEER database, which may limit the interpretation of radiotherapy and chemotherapy. We've mentioned this limitation in the Discussion section (Page 9-10, line 198-202).

Changes in the text: None.

Comment 6: How was sequencing agents determined (i.e NAC prior to radical cystectomy)

Reply 6: The sequencing agents cannot be determined by SEER database. We've mentioned this limitation in the Discussion section (Page 9-10, line 198-202)

Changes in the text: None.