Peer Review File

Reviewer A: This is an interesting manuscript and is very well written.

Some issues:

Comment 1: The methods could state study design and approach early in the section.
Reply 1: Thank you very much for your positive and precious comments on our manuscript. According to your recommendation, the paragraph of subheading "Data source" was moved to the latter part of PATIENTS AND METHODS section to state study design and approach early in the section.
Changes in the text: The paragraph of subheading "Data source" was moved to the latter part of PATIENTS AND METHODS section, between the subheading "Outcomes measures" and "Statistical analysis" (see Page 7, line 21 – Page 8, line 7).

Comment 2: The authors use the abbreviation ARB without spelling it out / defining it first (abstract). This should be fixed.
Reply 2: Thank you for pointing out our mistake. The abbreviation ARB was spelled out when it was used for the first time in the ABSTRACT.
Changes in the text: "angiotensin receptor blockers" was moved to the first use of the abbreviation ARB in the Background of ABSTRACT (see Page 2, line 2–5).

Comment 3: The ethics comment in the Methods is confusing – did they waive informed consent, so that other ethics approval was granted? Or was there no submission at all? Please expand.
Reply 3: The description regarding informed consent was modified to prevent possible confusion.
Changes in the text: "which waived the need for informed consent" was changed to "and informed consent was waived" in the first paragraph of PATIENTS AND METHODS section (see Page 5, line 14).

Comment 4: The inclusion of Table 1 seems excessive and not relevant.
Reply 4: We agree with you that Table 1 is excessive. Table 1 was removed from the manuscript and Table 2,3, and 4 was revised to Table 1,2, and 3, respectively.
Changes in the text: Table 1 was removed from the current manuscript. Table 2,3, and 4 was revised to Table 1,2, and 3, respectively (see Tables and Page 9–10).

Reviewer B
Comment 1: This is an interesting paper with results that I would don't have anticipated mainly because I was not aware of the potential for ARBs to cause delayed healing and complications. I think that it would be important to stratify based on age and other co-morbidities to eliminate these as potential confounding variables. It may be that elderly patients with co-morbidities are more prone to complications.

Reply 1: Thank you very much for your encouraging comment on our manuscript. We performed multivariable analyses to adjust possible confounders including age, presence of diabetes, and other comorbidities using Charlson comorbidity index score as described in the last sentence of subheading "DTI reconstruction" and "Abdomen-based autologous reconstruction" of RESULTS section. Table 3 summarizes the results of multivariable analyses and indicates that the use of angiotensin receptor blockers was significantly associated with an increased risk of the surgical complications in direct-to-implant reconstruction and complication-related medical cost in abdomen-based autologous reconstruction after controlling confounding variables.
Changes in the text: Not applicable

Reviewer C
Comment 1: This is a retrospective nationwide study assessing potential implications of the ARB perioperative use in breast reconstruction.
The use of ARBs was shown to be associated with surgical complications both in autologous and implant-based subgroups. The authors have previously published on this topic in 2019, with the similar findings in a single-institution cohort.

I think that the current paper, with the limitations that all retrospective study possess, has a solid methodology and a clear message.

The demographic and baseline characteristics of the subgroups are heterogeneous, eg patients on ARBs had diabetes more frequently than the other subgroups, which per se might have an impact on microcirculation. Yet, this is a clinical reality and moreover, the association of ARB and poorer surgical outcomes remained significant in the multivariable regression model after adjusting for diabetes.

How did you deal with bilateral cases, are they excluded at the stage of patient identification? If not, how did you adjust for the bilaterality? Please, specify in methods.
Reply: Thank you very much for taking the time to review our article and give your valuable feedback. As described in the subheading "Study population" of PATIENTS AND METHODS section, we only included unilateral cases to maintain homogeneity of the study population. We added a sentence describing the exclusion of bilateral cases more clearly.
Changes in the text: "Bilateral and contralateral risk-reducing mastectomy cases were excluded to reduce heterogeneity of the study population." was added to the subheading "Study population" of PATIENTS AND METHODS section (see Page 5, line 24 – Page 6, line 1).

I would encourage authors to strengthen the discussion by suggesting a potential practical solution to deal with patients on ARBs scheduled for breast reconstruction (add insights from anesthesiologists and cardiologists? how have the study findings changed your practice?).

Reply 1: Based on the results of this study, we currently cease or replace of ARBs with other classes of antihypertensive medication preoperatively, or consult to cardiologists in patients who have comorbidities. According to your comments, a sentence was added to suggest a potential practical solution for breast reconstruction.

Changes in the text: "In patients undergoing breast reconstruction, the authors recommend preoperative cessation or replacement of ARBs, or preoperative consultation to cardiologists in patients who have comorbidities, because several different classes of antihypertensive medications could easily replace ARB except for some specific indications for ARB." was added to the fourth paragraph of DISCUSSION section (see Page 12, line 23 – Page 13, line 3).