

## Peer Review File

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### Reviewer A

Comment 1: Dear authors, the manuscript is very interesting, the triple negative is more and more frequent and, as you underlined, it is also widespread in the geriatric population. Here are some suggestions.

Reply 1: Thank you for taking the time to evaluate our manuscript titled "Octogenarians with Triple Negative Breast Cancer." We sincerely appreciate your valuable feedback and suggestions, which have helped us improve the quality and clarity of our article.

Changes in the text: N/A

Comment 2: Breast cancer: BC (abbreviation)

Reply 2: "Breast cancer" was replaced with "BC".

Changes in the text: The term "breast cancer" was abbreviated to "BC" throughout the manuscript.

Comment 3: It is important to reiterate that the standard approach to the triple negative subtype is usually neoadjuvant chemotherapy.

Reply 3: Agreed. The standard approach to TNBC often includes neoadjuvant chemotherapy. However, treatment decisions are highly individualized, and not all TNBC patients will receive neoadjuvant chemotherapy. Factors such as tumor size, stage, patient's overall health, and other clinical considerations will influence the treatment plan.

Changes in the text: Lines 119-121: The standard of care (SOC) to TNBC often includes neoadjuvant chemotherapy, although treatment decisions are highly individualized. TNBC SOC treatment relies on surgical resection, chemotherapy, and radiation.

Comment 4: It is important to specify and write in the discussion which are the scientific reasons why in your population you preferred "primary surgery" instead of neoadjuvant chemotherapy and why the same population was able to perform adjuvant chemotherapy after surgery.

Reply 4: We appreciate the reviewer's thoughtful comment and the opportunity to clarify our approach in the manuscript. The choice of primary surgery over neoadjuvant chemotherapy in our study population was based on tumor characteristics and patient preferences.

Changes in the text: Lines 312-314: If the tumor was relatively small and localized, surgery (e.g., lumpectomy) was the preferred initial treatment, followed by adjuvant therapy to reduce the risk of recurrence.

### Reviewer B

Comment 1: Introduction: Define SOC on first use in the first paragraph.

Reply 1: "SOC" was defined as "standard of care".

Changes in the text: Lines 119-120: The standard of care (SOC) to TNBC often includes neoadjuvant chemotherapy, although treatment decisions are highly individualized.

Comment 2: Methods: When was the ECOG testing performed, prior to surgery or after surgery? Was it reassessed prior to consideration of adjuvant therapies? This needs to be clarified because

it has enormous impact on how these findings can be interpreted, especially when the groups had similar all-cause and breast-cancer related outcomes.

Reply 2: ECOG performance status can indeed be influenced by various factors, including surgery, and this may impact the patient's willingness to undergo further treatment. We apologize for not providing explicit details regarding the timing of ECOG assessment in our manuscript. ECOG performance status assessments were conducted prior to surgery, and this information has now been included in the revised manuscript to provide clarity on this important aspect.

Changes in the text: Line 166: ECOG performance status assessments were conducted prior to surgery.

Comment 3: Results: Significant finding of radiation treatment's association in Non-surgical treatment subheading was not bolded like the other significant findings.

Reply 3: "0.002" was bolded as it was significant, as defined by a p-value of <0.05.

Changes in the text: Lines 243-245: The indications for radiation were similar between groups, with significantly less radiation administered in the ID group (2, 22.2%) than in the SOC group (11, 57.1% P = 0.002).

Comment 4: Discussion: The "indications for chemotherapy and/or radiation therapy" were not explicitly discussed and a general audience member may not understand the nuances of breast cancer treatment. This should at least be mentioned in brief to facilitate this despite included Figure 3 which gives a general overview of the ASCO management guidelines. The manuscript can be greatly shortened with the discussion focusing on the key findings that were the answers to the original hypothesis, and removing some of the more extraneous details.

Reply 4: Thank you for your valuable feedback regarding the clarity of our manuscript's discussion on the indications for chemotherapy and/or radiation therapy in the context of breast cancer treatment. We acknowledge the importance of ensuring that our research is accessible to a general audience while still providing the necessary information. While we understand the suggestion to shorten the manuscript by focusing solely on the key findings related to the original hypothesis, we believe that providing contextual information is essential to fully comprehend the significance and implications of our study.

Changes in the text: Lines 179-183: Chemotherapy is typically considered for larger tumors, lymph node involvement, triple-negative or HER2-positive breast cancer, high-grade tumors, or when there is a risk of metastasis. Radiation therapy is recommended post-surgery (e.g., lumpectomy, mastectomy) to reduce the risk of local recurrence, especially when there is lymph node involvement, incomplete tumor removal, or in cases of inflammatory breast cancer.

Comment 5: Limitations: As the patients that were included all underwent surgical therapy for TNBC, the authors should speak about how this biases the study (they did mention that 92.8% of the population usually undergoes surgery). They have not included patients who were diagnosed with TNBC but were either not offered or elected not to undergo surgical resection. By this study design, the patients have at least elected for a portion (surgery) of the SOC of TNBC.

Reply 5: We appreciate the reviewer's thoughtful comment and the opportunity to clarify our approach in the manuscript. The choice of primary surgery over neoadjuvant chemotherapy in our study population was based on tumor characteristics and patient preferences.

Changes in the text: Lines 343-345: Additionally, all included patients underwent surgical treatment for TNBC, which may introduce a bias by excluding those who were either not offered or chose not to undergo surgical resection.

Comment 6: Figures: I do not think that Figure 1 or 2 are needed for the purposes of this manuscript. Supplemental Digital Content, Table 2 and Figure 1 is not referenced in the manuscript and does not need to be included.

Reply 6: Thank you for your feedback regarding the figures and supplemental content in our manuscript. We appreciate your input and will make the necessary adjustments.

Changes in the text: Figure 1, Figure 2, SDC Table 2, and SDC Figure 1 were omitted from the manuscript.

Comment 7: Overall: The authors present a pilot study of 21 octogenarians that were diagnosed with TNBC and underwent surgical therapy, with examination and analysis of the other modalities of therapy that typically accompany such as chemotherapy and radiation therapy, deemed as the standard of care (SOC). The study attempts to determine associations with these patients undergoing SOC vs. “informed-deferred” (ID) treatment (or non-standard of care). They found that ID was significantly associated with an ECOG III score, as well as a lower proportion of patients that underwent chemotherapy and radiation therapy. This deferral was most commonly due to patient preference and shared decision-making. They found no significant differences in outcomes between the SOC and ID groups despite this, and no significant associations with tumor characteristics or other factors examined.

Reply 7: Thank you for taking the time to evaluate our manuscript titled "Octogenarians with Triple Negative Breast Cancer." We sincerely appreciate your valuable feedback and suggestions, which have helped us improve the quality and clarity of our article.

Changes in the text: N/A

Comment 8: This study is very limited by its small patient volume. The timing of when the ECOG was assessed is critically important and was not expanded upon within the manuscript. If ECOG was assessed after surgery, patients that had a decline in function due to surgery certainly would be less likely to agree to further treatment that is obviously impacting quality of life. If the ECOG assessment was performed prior to surgery, this would clearly influence the clinician's recommendation to undergo full SOC treatment when poor performance is already apparent. The conclusion that these patients may have benefitted from SOC does not appear to be consistent with the findings, as the overall all-cause and BCR-mortality outcomes were similar for both groups. The finding that the most common reason for deferment was shared decision-making is encouraging. The authors do stress the importance of individualized assessment and offer resources to perform these, but more patient data is needed before definitive conclusions can be made about outcomes between groups.

Reply 8: ECOG performance status can indeed be influenced by various factors, including surgery, and this may impact the patient's willingness to undergo further treatment. We apologize for not providing explicit details regarding the timing of ECOG assessment in our manuscript. ECOG performance status assessments were conducted prior to surgery, and this information has now been included in the revised manuscript to provide clarity on this important aspect.

Changes in the text: Line 166: ECOG performance status assessments were conducted prior to surgery.; Lines 266-268: These results build on previous literature and suggest that individuals

with TNBC over 80 may pursue chemotherapy and radiation, and achieve comparable all-cause and BC-mortality outcomes as those less than 80.

Comment 9: The authors also did not address the bias of their study design by not including patients diagnosed with TNBC that deferred/were not recommended to undergo surgery. As they only included patients that underwent surgery, one may assume that those patients would already have a lower (better) ECOG performance score and be more likely to complete other aspects of treatment (because they completed the first step) compared to those that elected to defer or were not recommended to undergo any treatment including surgery. This should be addressed in the limitations and discussion. Overall, this manuscript highlights an important conversation centered around a vulnerable patient population, but this conversation needs to be redirected into the most important aspects of the answers to their initial hypothesis, as it can be greatly shortened, especially with only a few key significant findings. I believe this manuscript would be suitable for publication after major revision.

Reply 9: We sincerely appreciate your comprehensive review of our manuscript and your thoughtful comments. Your insights are invaluable in enhancing the quality and relevance of our work. Thank you for your feedback regarding the figures and supplemental content in our manuscript. We appreciate your input and will make the necessary adjustments.

Changes in the text: Lines 343-345: Additionally, all included patients underwent surgical treatment for TNBC, which may introduce a bias by excluding those who were either not offered or chose not to undergo surgical resection.