



Primary tumor surgery in de novo metastatic breast cancer: Game-changer or misinterpretation?

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Abstract

The study titled “Primary tumor surgery in patients with de novo metastatic breast cancer: a nationwide population-based retrospective cohort study in Belgium” opens an important discussion about the potential role of surgery in the treatment of de novo MBC; although the results are promising, they should be interpreted with caution given the limitations of the study design. The question remains whether surgery is truly a game-changer for all patients or whether its benefits are more nuanced depending on individual patient factors and disease characteristics. As the oncology community continues to explore this question, a modern breast surgeon should emphasize the importance of further prospective trials and personalized treatment strategies that consider not only surgery but also the growing arsenal of available systemic therapies.

Dear Editor,

I read with interest the study titled “Primary tumor surgery in patients with de novo metastatic breast cancer: a nationwide population-based retrospective cohort study in Belgium” [1].

The results, obtained on 1.985 cases, show that primary tumor surgery (PTS) in patients with de novo metastatic breast cancer (MBC) leads to a significant improvement in overall survival [1]. However, I think that, while this study provides valuable data, there are several critical considerations that should be addressed to provide a more complete understanding of its implications for clinical practice.

First, the study design, being a retrospective cohort analysis, has inherent limitations; patients who underwent surgery were younger, had better performance status and were more likely to have HER2-positive or triple-negative breast cancer [1]; these factors suggest that the surgery group may have had a more favorable prognosis from the outset; selection bias is known to be a persistent challenge in retrospective studies, particularly when clinical decision

making is influenced by factors such as cancer biology and patient eligibility that can directly impact survival outcomes [2]. Although propensity score matching was used to mitigate this bias, caution should be exercised in interpreting these results as indicative of a definitive benefit of surgery as unmeasured confounding factors may still be at play. Without the rigor of randomized clinical trials, it is difficult to definitively attribute improved survival solely to breast surgery rather than other variables such as systemic treatment efficacy, cancer biology or patient performance status [2]. Furthermore, the authors did not provide an in-depth analysis of the specific type of systemic therapies administered to patients; the rapidly evolving landscape of systemic treatments, particularly with the introduction of targeted therapies and immunotherapy, plays a crucial role in the survival of patients with metastatic breast cancer [3]. Research has shown that the impact of surgery can be strongly influenced by the systemic therapy a patient receives [3]. The interaction between local and systemic treatment is complex and without controlling for specific treatment regimens, it is difficult to isolate the independent effect of surgery on survival outcomes.

Furthermore, this study considers surgery as beneficial within a relatively narrow time frame (up to nine months after diagnosis) [1]. This raises the question of whether surgery is a universal solution or whether it provides significant benefit only for a specific subset of patients with less aggressive MBC. The results are promising but appear to generalize the role of surgery without addressing the underlying

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heterogeneity of metastatic disease. Besides, the timing of surgery (before or after systemic therapy) did not show significant differences in OS; this suggests that the survival advantage observed in the surgery group could be more reflective of other factors than the surgery itself.

Additionally, I would like to draw attention to the broader clinical implications of Authors' conclusions [1]. It is fair to ask whether, in light of modern treatment modalities, it is prudent to continue advocating surgery for all patients with de novo metastatic breast cancer, particularly when survival benefits may be marginal in certain molecular subtypes or in patients with widespread metastatic involvement.

The role of surgery in MBC should be carefully considered on an individual basis, taking into account not only survival outcomes but also potential risks and quality of life (QoL) considerations for breast cancer patient; one area that should strengthen this study is the inclusion of an analysis of QoL post-surgery, particularly in light of the treatment burden associated with metastatic disease; although the survival data are compelling, the question remains if PTS translates into improved QoL or whether it comes at a significant physical and emotional cost for patients already battling widespread disease. The growing importance of QoL in cancer care suggests that this dimension should not be overlooked in studies on the benefits of surgery in metastatic settings; for many patients with stage IV disease, the priority could be to improve their QoL and manage their symptoms rather than perform additional surgery that could compromise their overall well-being.

In conclusion, this study opens an important discussion about the potential role of surgery in the treatment of de novo MBC; although the results are promising, they should be interpreted with caution given the limitations of the study design.

The question remains whether surgery is truly a game-changer for all patients or whether its benefits are more nuanced depending on individual patient factors and disease characteristics. As the oncology community continues to explore this question, a modern breast surgeon should emphasize the importance of further prospective trials and personalized treatment strategies that consider not only surgery but also the growing arsenal of available systemic therapies.

Author contributions Gianluca Franceschini is the Author of this letter to the Editor.

Data availability No datasets were generated or analyzed during the current study.

Declarations

Competing Interests The authors declare no competing interests.

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