Local interventions in oligometastatic breast cancer: systematic review and meta-analysis

Camila Bettoni Molina, Ana Beatriz Athayde Dalama, Danieli Pereira da Silva, Marcelo Rocha de Souza Cruz, Ana Clara Campagnolo Gonçalves Toledo.
Universidade do Oeste Paulista, Brazil

Introduction

Breast cancer is the most common neoplasm among women worldwide. It is estimated that, in the 2023-2025 period, around 22,000 women will develop metastases, of which approximately 20% will have oligometastases. Some evidence suggests that local treatment with radiotherapy or surgery may prolong survival. However, the benefits of this approach are still not fully clear.

To evaluate the effectiveness of local therapies, such as radiotherapy and surgery in combination with systemic therapy in the treatment of patients with oligometastatic breast cancer.

Methods and Materials

A systematic review was carried out with registration in the PROSPERO database (CRD42024525782), Medline via Ovid, EMBASE, Web of Science, Cochrane Library Databases, Scopus and Clinical Trials, until November 2024. RCTs were selected, involving women with oligometastatic breast cancer in systemic treatment associated with intervention, radiotherapy or surgery, compared to standard systemic treatment. The processes of study selection, data extraction, risk of bias analysis and level of evidence were carried out by independent and blind authors. For this, platforms such as Rayyan and a standardized Excel form were used. The methodological quality was analyzed by ROB-2 and the evidence was assessed with GRADE. For quantitative data analysis, the Review Manager – RevMan program (version 5.3) was used.

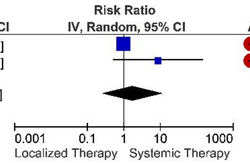
Results

Among 717 studies, 2 randomized controlled trials were included in this review. When comparing the association of radiotherapy or surgery with systemic therapy, overall survival presents RR: 1.78 (CI: 0.26 - 12.17), 162 participants, high risk of bias, very low quality of evidence. For progression-free survival in this same comparison RR: 1.05 (CI: 0.76 – 1.46) 162 participants, high risk of bias, very low quality of evidence. Finally, in this same comparison for the secondary outcome, adverse effects, it was analyzed by subgroups, Grade 3 RR: 1.06 (CI: 0.52 – 2.13) 162 participants, high risk of bias, very low quality of evidence and the subgroup Grade 4 RR:0.42 (CI: 0.10 – 1.80) 162 participants, high risk of bias, very low quality of evidence.

Figure 1. Localized therapy plus systemic treatment versus systemic treatment: Overall Survival.

Study or Subgroup	Localized Therapy Events	Total	Systemic Therapy Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Chimura et al, 2022	39	57	44	62	72.1%	0.96 [0.76, 1.22]
Reddy et al, 2024	4	22	0	21	27.9%	8.61 [0.49, 150.72]
Total (95% CI)		**79**		**83**	**100.0%**	**1.78 [0.26, 12.17]**
Total events	43		44			

Heterogeneity: Tau² = 1.32; Chi² = 2.23, df = 1 (P = 0.14); I² = 55%
Test for overall effect: Z = 0.58 (P = 0.56)



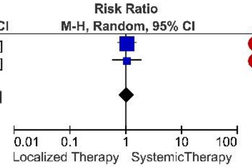


Risk of bias legend
(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Others biases

Figure 2 Localized therapy plus systemic treatment versus systemic treatment: : Progression-Free Survival.

Study or Subgroup	Localized Therapy Events	Total	Systemic Therapy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chimura et al, 2022	27	57	28	62	71.5%	1.05 [0.71, 1.55]
Reddy et al, 2024	11	22	10	21	28.5%	1.05 [0.57, 1.94]
Total (95% CI)		**79**		**83**	**100.0%**	**1.05 [0.76, 1.46]**
Total events	38		38			

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.29 (P = 0.77)





Risk of bias legend
(A) Risk of bias arising from the randomization process
(B) Risk of bias due to deviations from the intended interventions
(C) Missing outcome data
(D) Risk of bias in measurement of the outcome
(E) Risk of bias in selection of the reported result
(F) Others biases

Discussion

Metastatic breast cancer is still considered incurable, with treatment based on continuous systemic therapies. Although radiotherapy is an integral part of the palliative approach, the concept of oligometastatic disease that is, few metastases amenable to local intervention has generated interest in treatments such as surgery or radiotherapy targeting metastatic sites. Only two studies met the selection criteria, which highlights the scarcity of high-quality evidence in this area. The results indicate that local intervention whether through radiotherapy or surgery did not demonstrate statistically significant benefits in overall survival, progression-free survival, or quality of life compared to standard systemic treatment.

Moreover, although observational studies suggest that local treatments combined with systemic therapy could improve outcomes, many of these studies lack control groups, carry a high risk of bias, and have inferior methodological quality. The two randomized trials reviewed presented significant heterogeneity regarding patient profiles, metastasis locations, and other risk factors, which limits the generalizability of the results. In summary, although systemic treatment remains the standard for metastatic breast cancer, there is a strong need for new, well-conducted clinical trials to determine in which subgroups local intervention could truly offer benefit.

Conclusions

There are no benefits from the association of systemic therapy with radiotherapy or surgery in oligomestases compared to systemic therapy for the outcomes of overall survival, disease progression-free survival and adverse events.

Contact:
Giuliano Tosello, InCOP and Unoeste, Brazil
Email: giulianotosello@hotmail.com
Instagram: @giulianotosello
Phone: 55 18 3904-5400

References:

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