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1144 – Intratumoral heterogeneity and therapeutic response in breast cancer: a systematic review

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Introduction: Intratumoral heterogeneity in breast cancer represents a significant challenge in oncology, influencing therapeutic response, disease progression, and clinical outcomes. It is characterized by the presence of cell subpopulations with different molecular, genetic, and phenotypic profiles, resulting in variability in treatment sensitivity and the development of resistance. It can occur at the molecular, spatial, and temporal levels, associating with clonal evolution and tumor adaptation to therapeutic pressures, with a negative impact on response, especially in HER2-positive and triple-negative subtypes.

Methodology: A systematic literature review, conducted through the LILACS and PubMed databases. Twenty articles published in the last 5 years were selected. The question was structured using the PICO strategy, and the review followed the PRISMA guidelines. Original studies that evaluated intratumoral heterogeneity in breast cancer and its relationship with therapeutic response and clinical outcomes were included. After applying the criteria, 304 articles were identified, and 20 were selected after screening.

Results: The studies showed that tumor heterogeneity results from the interaction between genetic, epigenetic, and microenvironmental alterations, promoting clonal diversity. Heterogeneous HER2 expression, the presence of distinct subclones, and epigenetic regulation mediated by KDM5, associated with therapeutic resistance, were observed. These differences were evaluated by single-cell sequencing, ctDNA analysis, immunohistochemistry, and gene signatures, evidencing clonal selection throughout treatment. More heterogeneous tumors presented lower rates of pathological complete response and reduced survival.

Conclusion: Intratumoral heterogeneity is a key determinant of therapeutic variability and clinical evolution in breast cancer. Clonal diversity and epigenetic mechanisms favor the selection of resistant subpopulations, negatively impacting prognosis. Molecular stratification strategies and dynamic monitoring are essential for more precise clinical decisions.

Ethics: Public data – Literature review.

Keywords: breast neoplasms; intratumor heterogeneity; tumor prognosis.