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Molecular subtypes and organ-specific metastatic patterns in breast cancer: A cross-sectional study at a tertiary referral hospital in West Sumatra

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Abstract
Background: Breast cancer heterogeneity significantly influences the site of distant recurrence. This study aims to analyze the correlation between molecular subtypes and organ-specific metastasis in a major referral center in Indonesia.
Methods: A cross-sectional study was conducted on 96 metastatic breast cancer patients at Dr. M. Djamil Hospital (2023-2025). Molecular subtypes (Luminal A, Luminal B, HER2-enriched, TNBC) and metastatic sites (bone, lung, liver, brain) were analyzed using Chi-square tests.
Results: The HER2-enriched subtype was most frequent (36.5%). Luminal A was strongly associated with bone metastasis (83.3%), while HER2-enriched and Luminal B predominantly spread to the lungs. A significant association (p=0.000) was found between subtype and metastatic site.
Conclusion: Molecular subtypes are predictive of metastatic organotropism, allowing for more targeted clinical surveillance.

Keywords: Breast cancer, molecular subtypes, metastasis, organotropism, Indonesia

Introduction

Breast cancer remains the most prevalent malignancy among women worldwide and a leading cause of cancer-related mortality. In Indonesia, the high death rate is often attributed to late-stage presentation and the aggressive nature of certain biological profiles (World Health Organization, 2020) [8]. The process of metastasis, or the spread of cancer cells from the primary tumor to distant organs, is the primary cause of death in these patients (American Cancer Society, 2024) [1]. The management of breast cancer has shifted from a one-size-fits-all approach to personalized medicine based on molecular subtypes. These subtypes Luminal A, Luminal B, HER2-enriched, and Triple-Negative Breast Cancer (TNBC) are defined by the expression of Estrogen Receptor (ER), Progesterone Receptor (PR), and HER2 (Perou *et al*., 2000) [3]. Each subtype possesses a unique biological behavior that influences not only the patient's prognosis but also the specific organs where the cancer is likely to recur (Prat *et al*., 2015) [4].
Organotropism, the tendency of certain tumors to metastasize to specific organs, is a key feature of breast cancer. For instance, hormone-positive cancers often show an affinity for bone, while hormone-negative and HER2-positive cancers are more likely to involve visceral organs (Xing *et al*., 2021) [9]. In the context of Indonesia, where clinical characteristics may differ due to genetics and delayed diagnosis, understanding these patterns is crucial (Rahmawati *et al*., 2018) [5]. This study investigates the relationship between molecular subtypes and metastatic locations in West Sumatra to provide a basis for improved diagnostic and therapeutic strategies (Susanti *et al*., 2022) [6].

2. Methods

This research utilized an observational analytical design with a cross-sectional approach, conducted at the Department of Surgery, Dr. M. Djamil Hospital, Padang. The study population consisted of patients diagnosed with metastatic breast cancer between January 2023 and December 2025. A total of 96 patients met the inclusion criteria, which required complete histopathological, immunohistochemistry (IHC), and radiological data (Zulma, 2026) [11]. Data collection focused on molecular subtypes categorized into Luminal A, Luminal B (HER2

negative or positive), HER2-enriched, and TNBC. Metastatic sites were identified through imaging modalities such as CT scans, bone scans, or biopsies of the metastatic lesions (Nindita *et al*., 2024) [2]. Statistical analysis was performed using the Chi-square test to evaluate the association between the molecular profiles and the location of organ-specific metastasis, with a p-value < 0.05 considered significant (Zulma, 2026) [11].

3. Results

The demographic profile of the 96 patients showed a distribution where the HER2-enriched subtype was the most frequent (36.5%), followed by Luminal A (31.3%) and Luminal B (29.2%). Only a small percentage were identified as TNBC (3.1%). The most common site of metastasis overall was the lungs (35.4%), closely followed by bone (32.3%), while liver and brain metastasis were less frequent. When analyzed by subtype, Luminal A showed a clear preference for bone metastasis, with 83.3% of Luminal A patients exhibiting bone involvement. In contrast, Luminal B and HER2-enriched patients were more likely to present with lung metastasis (46.4% and 54.3%, respectively). Liver involvement was most prominent in the HER2-enriched group. The statistical analysis yielded a p-value of 0.000, indicating a highly significant correlation between the molecular subtype and the site of distant metastasis.

4. Discussion

The findings of this study confirm that breast cancer subtypes exhibit distinct metastatic "signatures." The strong association between Luminal A and bone metastasis observed in this cohort (83.3%) aligns with the "seed and soil" hypothesis, where hormone-receptor-positive cells find the bone microenvironment particularly conducive to growth due to specific signaling pathways like the RANK/RANKL system (Zhang *et al*., 2025) [25]. Bone metastasis, while often associated with a longer survival compared to visceral metastasis, significantly impacts the quality of life due to skeletal-related events (Xing *et al*., 2021) [9].

The high prevalence of lung and liver metastasis in HER2-enriched and Luminal B patients reflects the aggressive nature of these subtypes. HER2 signaling promotes epithelial-to-mesenchymal transition (EMT), which enhances the ability of cancer cells to invade the circulatory system and colonize visceral organs (Prat *et al*., 2015) [4]. Interestingly, this study found a higher frequency of HER2-enriched cases compared to some Western studies, which may suggest a specific epidemiological trend in the Indonesian population (Widiana & Irawan, 2020) [7].

Furthermore, the significant p-value (0.000) obtained in this research underscores the clinical importance of molecular profiling at the time of initial diagnosis. By knowing the subtype, clinicians can implement more rigorous surveillance for specific organs; for example, prioritizing bone scans for Luminal A patients or chest CT scans for HER2-enriched patients (Rahmawati *et al*., 2018) [5]. This proactive approach is essential in limited-resource settings to optimize the use of diagnostic tools and improve early detection of recurrence (Nindita *et al*., 2024) [2].

5. Conclusion

This study concludes that there is a significant and specific relationship between molecular subtypes and the location of metastasis in breast cancer patients. Luminal A is primarily associated with bone spread, whereas Luminal B and HER2-enriched subtypes are more prone to visceral metastasis, particularly in the lungs and liver. These findings support the integration of molecular biology into routine clinical decision-making to predict metastatic patterns and tailor follow-up protocols for better patient outcomes (Zulma, 2026) [11].

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