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Approaches and advances using biomarkers for diagnosis in breast neoplasms.

Approach and advances using biomarkers for diagnosis in breast neoplasms

Focus and advances using biomarkers for the diagnosis of breast neoplasms

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SUMMARY

The search for more efficient and early diagnoses in cases of breast cancer is necessary due to its high frequency among women, which, worldwide, represents a significant public health problem, mainly due to the increasing incidence after age 50 and inequalities in access to screening, contributing to high mortality rates. A literature review was conducted using the PubMed, Google Scholar, and CAPES Periodicals Portal databases, analyzing articles published between 2020 and 2025. Twenty-one articles that met the eligibility criteria were selected. Evidence shows that markers such as Ki-67, ER, PR, and HER2 are fundamental for predicting therapeutic response, since elevated Ki-67 levels are associated with greater tumor aggressiveness and worse outcomes, while the analysis of hormone receptors and HER2 status allows for more precise stratification and the selection of more effective therapies. Given the limitations of traditional prognostic markers, the incorporation of molecular biomarkers and gene expression profiles has emerged as an indispensable tool in personalized medicine, contributing to the individualization of treatment, the reduction of overtreatment and undertreatment, and the improvement of clinical outcomes in the management of breast cancer. Although tumor classification still largely depends on invasive approaches, such as tissue biopsy, liquid biopsy, and circulating biomarkers,

Including CTCs, ctDNA, miRNAs, exosomes, and serum proteins, liquid biopsy and circulating biomarkers emerge as promising alternatives. These markers allow for a better understanding of tumor heterogeneity, real-time therapeutic monitoring, and greater treatment personalization, contributing to earlier diagnoses, identification of therapeutic resistance, and early detection of relapses.

Descriptors: Early diagnosis, Biomarkers, Monitoring and Breast Neoplasms

1 INTRODUCTION

Breast cancer is the most common type of cancer among women worldwide and in Brazil. representing approximately 28% of new cancer cases among them, with a progressive increase in Incidence after age 50. Although it has a good prognosis when diagnosed early, It remains a significant public health problem due to the global increase in cases and... inequalities in access to diagnosis and treatment, especially in countries where development (Inca, 2022).

Variations in the incidence and mortality of breast cancer reflect differences socioeconomic factors and exposure to multiple risk factors, such as changes in reproductive profile, Obesity, alcohol consumption, and higher life expectancy. In less developed regions, the lower The incidence contrasts with high mortality rates, attributed to low awareness, to

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The absence of effective screening programs and late diagnosis reinforces the need of more efficient early detection strategies (Królewska et al., 2025).

Traditional methods of monitoring tumor recurrence, such as imaging tests. and serum markers, have limitations in terms of sensitivity, specificity, and cost. In this context, non-invasive biomarkers emerge as promising alternatives, allowing Real-time monitoring of tumor biology and contributing to the advancement of medicine. precision in breast cancer (El-tanani et al., 2025).

From a biological standpoint, breast cancer results from carcinogenesis associated with It is characterized by the accumulation of genetic mutations and exhibits high histopathological and molecular heterogeneity. Biomarkers such as ER, PR, HER2, and BRCA mutations are fundamental for classification. of tumor subtypes and for therapeutic definition, although the diagnosis still depends predominantly through invasive methods. In this scenario, circulating biomarkers and vesicles Extracellular molecules stand out for reflecting tumor heterogeneity more comprehensively. (Ferreira et al., 2023; Silva, 2024; Li et al., 2021).

The clinical application of liquid biopsy, through the analysis of CTCs, cf/ctDNA, miRNAs, Exosomes and serum proteins have shown great potential for early diagnosis. Molecular stratification and therapeutic monitoring. Studies show that certain miRNAs and protein panels exhibit high sensitivity and specificity, and can complement traditional methods, such as mammography, and reduce diagnostic errors (Effatpanah et al., 2025; Sadzeviciene et al., 2025; Fredolini et al., 2020).

Finally, the incorporation of biomarkers has significantly impacted the Personalization of treatment and prognosis for breast cancer patients. The use of Molecular profiling allows for the selection of targeted therapies, identification of therapeutic resistance, and... To detect relapses early, including through minimally invasive methods. Biomarkers derived from miRNAs, especially those associated with extracellular vesicles, They reinforce this progress by enabling more precise stratification and more accurate predictions of clinical evolution of the disease (Colomer et al., 2024; Kim et al., 2021).

In light of this, the study aims to analyze the advances in the use of Biomarkers in breast cancer diagnosis, highlighting their importance for personalization. of treatment, early diagnosis, and comparison between traditional and innovative biomarkers. Regarding clinical efficacy.

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2 METHODOLOGY

This study is an integrative review. It includes a literature review of...
August 2025 to June 2026, with a structured search in the PubMed and Google databases.
Academic and CAPES Journals. Articles published in the last five years were included, without
Language restriction. Using the following descriptors obtained from the search in the Descriptors
in Health Sciences (DeCS): *"Early Diagnosis", "Biomarkers",* "Monitoring" and "Breast
Neoplasms", combined with the Boolean operator AND.

Articles from official documents of health organizations, such as the Institute, were included.
National Cancer Institute. The selection of studies considered criteria of relevance, timeliness, and relationship.
direct analysis with genetic, protein, epigenetic, histopathological, and biopsy-derived biomarkers
liquid. Contributions on clinical practice, prevention, and diagnosis were also analyzed.
early, as well as studies on low-abundance serum biomarkers; the data were
organized and synthesized in a critical manner, allowing for comparison of evidence and identification of advances.
Technological factors in the discussion of clinical applicability in early diagnosis and stratification.
molecular model of breast neoplasms.

All articles that did not present qualitative information were excluded from the analysis.
sufficient to support the discussion on the use of biomarkers in breast cancer, without
Studies lacking adequate methodological description or critical analysis of the findings were excluded.
They specifically addressed triple-negative breast neoplasms, as this is a subtype with...
A distinct biological profile with biomarkers exhibiting differentiated behavior, which
This could compromise the homogeneity of the review. Furthermore, they were removed from the corpus of...
Search for incomplete articles, such as abstracts without access to the full text, manuscripts with sections
missing or publications that did not provide sufficient results for careful evaluation.

The research included studies published between 2020 and 2025, with filters applied.
such as available full texts, studies in humans and, where applicable, peer-reviewed articles
peers. This strategy made it possible to identify relevant and current scientific publications, ensuring a
A consistent theoretical basis for analyzing advances in the use of biomarkers in diagnosis and in
Breast cancer monitoring.

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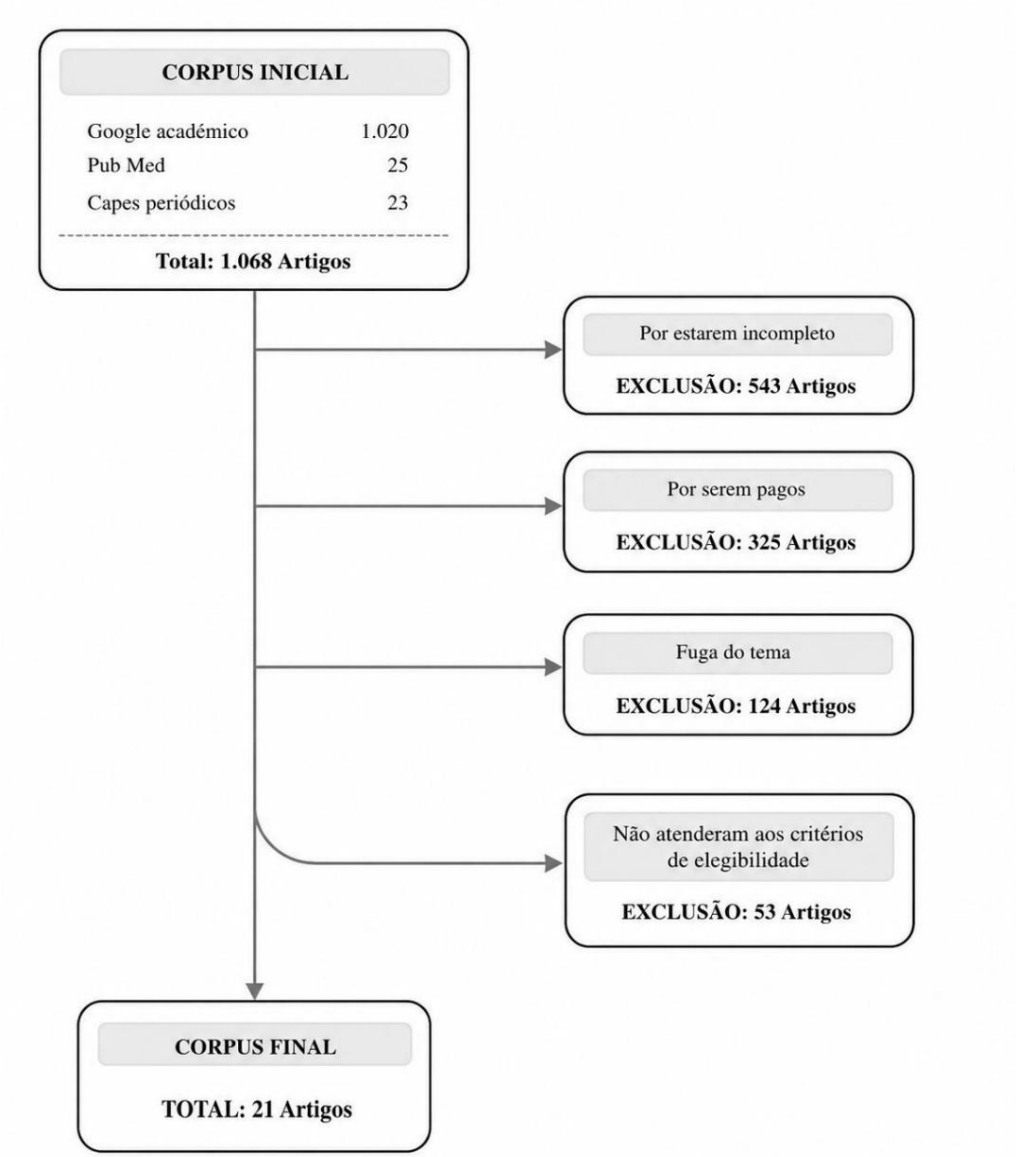
3 RESULTS

Figure 1. Flowchart of article selection included in the integrative review, 2026.



Source of figure 1: author's own work, 2026.

Table 1 of the articles selected for the article, 2026

Article title	Author/Year	Objective	Key results
Shotgun proteomics coupled to nanoparticle-based biomarker enrichment reveals a novel panel of extracellular matrix proteins...	FREDOLINI et al., 2020	Identify extracellular matrix proteins using a method put nanotechnology.	Discovery of a new panel of serum proteins for early-stage detection.

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Multi-miRNA panel of tumor-derived extracellular vesicles as promising diagnostic biomarkers of early-stage breast cancer	KIM et al., 2021	Analyze multi-miRNA panel in tumor-derived vesicles.	The vesicle panel has shown promise as a screening tool for initial diagnosis.
Protein biomarkers in breast cancer-derived extracellular vesicles for use in liquid biopsies.	LI et al., 2021	To study the proteins present in in the extracellular vesicles from of liquid biopsies.	Specific proteins found in vesicles serve as less invasive diagnostic markers.
Cancer Control Mama	INCA, 2022/2023	To guide breast cancer control in Brazil.	Emphasis on early detection and guidelines for healthcare professionals in the Brazilian Unified Health System (SUS).
Overview of breast cancer care in the Brazilian public health system (SUS).	ALMEIDA, 2023	To present an the overview of cancer care within the Brazilian Unified Health System (SUS).	It maps the difficulties of access and the bottlenecks in public healthcare.
Biomarkers in breast cancer: an old story	ALVES et al., 2023	To discuss the historical evolution of biomarkers.	It contextualizes how the history of markers has incorporated new analytical technologies.
Early detection and prevention of breast cancer: knowledge, attitudes, and practices of primary health care professionals...	FERREIRA et al., 2023	Evaluate the practices of professionals from the Family Health Strategy (ESF).	Identified gaps in knowledge of professionals on prevention and detection.
Multidisciplinary clinical guidelines in proactive monitoring, early diagnosis, and effective management of T-DXd...	WEKKING et al., 2023	Guidelines for the management of drug-induced lung disease (T-DXd).	It establishes safety protocols for the use of new targeted therapies.
Biomarker-targeted therapies and in for breast cancer: a literature review	ARAÚJO et al., 2024	Review the relationship between targeted therapies and biomarkers.	It highlights that you biomarkers are they are essential for indicating the most appropriate biological therapy.

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Biomarkers in breast 2024: Cancer an updated consensus statement by the Spanish Society of Medical Oncology...	COLOMER et al., 2024	Update the consensus on biomarkers (Spain).	Update of clinical guidelines for the use of biomarkers in routine oncology.
Advances in in tumor markers in the diagnosis and treatment of cancer. Mom.	FREITAS et al., 2024	Reviewing progress on markers to diagnosis and therapy.	It concludes that the evolution of markers allows for treatments. less aggressive.
Breast cancer: histopathological aspects and treatment. and	Silva et al., 2024	Describe the histopathological aspects and types of treatment.	It details how the characteristics of cells influence the choice of therapy.
The cost of breast cancer treatment per patient in the Brazilian public health system (SUS).	SIMÃO, 2024	Analyze the cost of treatment put patient in the SUS (Brazilian public healthcare system).	It demonstrates the high financial impact and importance of efficiency. node treatment.
It is estimated that Brazil will register 73,610 new cases of cancer. Breastfeeding until 2025.	COFEN, 2025	To publish estimates of new cases in Brazil.	An estimated 73,000 new cases are expected. This reinforces the need for proactive nursing.
Circulating miR-6165 and miR-182-3p as Non-Invasive Biomarkers for Early Breast Detection Cancer.	EFFATPANAH et al., 2025	Investigate miR-6165 and miR-182-3p as biomarkers.	specific These miRNAs offer high accuracy in early cancer detection. in
Advancements in non-invasive biomarkers for the detection and monitoring of breast cancer recurrence.	EL-TANANI et al., 2025	To evaluate advances in biomarkers for the detection of recurrence.	Promising invasive they biomarkers are not to monitor for without relapses biopsies.
Breast cancer	FEMAMA, 2025	To inform patients about their rights and their journey.	Focus on supporting the patient and and emphasizing the nothing importance of information for diagnosis.

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Cancer mortality is projected to increase by 98.5% by 2050.	INCA/IARC, 2025	Projecting mortality data and global disease burden.	A projected drastic increase (98.5%) in mortality by 2050 necessitates new services.
The assessment of breast Cancer biomarkers in diagnosis, prognosis, and treatment monitoring: integrated analysis.	KRÓLEWSKA-DASZCZYÿSKA et al., 2025	Analyzing integrated biomarkers to for diagnostic and prognostic purposes. and	Integrating multiple of biomarkers improves monitoring of treatment.
Identification of cell-free circulating epigenomic biomarkers for early diagnosis and response to therapies...	RATRE et al., 2025	Identify circulating epigenomic biomarkers.	Cell-free DNA allows for early diagnosis and anticipation of therapeutic response.
Liquid biopsy-based DNA methylation biomarkers for precision medicine in breast cancer.	SADZEVICIENE et al., 2025	Analyze DNA methylation for the precision medicine.	DNA methylation helps personalize treatment according to the genetic profile.

Source: Author's own work, 2026.

4. DISCUSSION

The results show that the main biomarkers used in diagnosis and in Monitoring of breast neoplasms is converging towards an integrated model, in which markers hormonal, cell proliferation, tumor growth and, more recently, biomarkers Molecular and circulating factors act in a complementary way in clinical decision-making. According to consensus among the studies analyzed, hormone receptors, especially the receptor of Estrogen (ER) remains the most solid pillar in prognostic and therapeutic definition, being unanimously recognized as essential in both initial diagnosis and follow-up. of the disease. The presence of ER is associated with a better prognosis and the indication for endocrine therapies. effective, while the progesterone receptor (PR) convergently emerges as a marker. assists in the functionality of the estrogenic pathway, contributing to the stratification between subtypes. luminal A and B and for predicting response to hormonal treatment (Alves et al., 2023; Araújo et al., 2024; Colomer et al., 2024; Królÿwska-Daszczyÿska et al., 2025).

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Despite this consensus, a relevant point of contention can be observed in the interpretation. quantitative assessment of hormone positivity. More recent guidelines introduce intermediate categories, such as the low expression of RE (1–10%), which requires an individualized analysis, since these Tumors can exhibit biological behavior similar to that of ER-negative carcinomas, which reduces the expected benefit of conventional endocrine therapy (Colomer et al., 2024). This This aspect highlights that, although hormonal biomarkers are well established, their application... Clinical practice demands a continuous refinement of interpretation.

Another point widely discussed and agreed upon by the authors is the relevance of HER2. as a predictive and prognostic biomarker. Overexpression or amplification of this receptor is associated with more aggressive tumors, but, paradoxically, it also represents an opportunity. therapeutic methods using monoclonal antibodies and tyrosine kinase inhibitors, which modified significantly alters the natural history of the disease (Alves et al., 2023; Królÿwska-Daszczyÿska et al., 2025). In contrast, recent studies highlight the emergence of the HER2-low subtype, expanding the spectrum of patients potentially benefiting from targeted therapies, such as conjugates This reinforces the need for continuous monitoring and reassessment of antibody-drug interactions, highlighting the need for continuous monitoring and reassessment of status. HER2 levels throughout tumor progression (Colomer et al., 2024).

With regard to Ki-67, there is consensus regarding its usefulness as a dynamic marker of cell proliferation and as a relevant tool in monitoring therapeutic response, especially in neoadjuvant settings and in recurrence risk stratification. However, the Studies also converge in pointing out important limitations related to the lack of standardization. methodological and interlaboratory variability compromises reproducibility and application. isolated in clinical practice (Alves et al., 2023; Araújo et al., 2024; Colomer et al., 2024). Thus, Ki-67 presents more consistent clinical value when interpreted in conjunction with others. biomarkers and clinicopathological data.

Moving beyond classic markers, the most recent studies highlight a transition. Clear for precision oncology, with the incorporation of genetic platforms, of mutations specific (BRCA1/2, TP53, ESR1) and circulating biomarkers. While there is consensus that These tools enhance prognostic and predictive capabilities; however, in contrast, it is observed that... The limitation of its universal applicability, whether due to cost, technological availability, or... need for more robust clinical validation in certain contexts (Freitas et al., 2024; Królÿwska-Daszczyÿska et al., 2025).

In addition, traditional serum biomarkers such as CA 15-3, CA 27-29, and CEA, They are generally recognized as having low sensitivity for early diagnosis, but are useful. in monitoring metastatic disease and detecting relapses. In contrast, technologies

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emerging factors, such as liquid biopsy, circulating tumor cells, circulating tumor DNA, and proteins. Regulatory agents, such as galectins and progranulin, are emerging as promising alternatives for a less invasive and more dynamic monitoring of tumor evolution (Freitas et al., 2024; Królÿwska-Daszczyÿska et al., 2025).

Thus, an integrated analysis of the literature demonstrates that no single biomarker is sufficient to fully meet the demands of diagnosis and monitoring of neoplasms mammary. The common point among the studies lies in the defense of multimodal panels, which combine hormonal markers, HER2, proliferative indices, genetic signatures and circulating biomarkers. The counterpoints, in turn, focus on technical limitations, in Standardization and clinical interpretation of these markers. Even so, the convergence of findings... argues that the integrated use of these biomarkers represents the most consistent path to Therapeutic individualization, early detection of resistance, and improvement of clinical outcomes. Aligning breast cancer management with the principles of personalized medicine.

Evaluating the contributions of biomarkers to early diagnosis and the Molecular stratification of breast cancer reveals a consistent trend in the literature towards towards less invasive, more sensitive approaches capable of capturing biological complexity. of the disease. Convergingly, the studies analyzed highlight liquid biopsy as an advance strategic in relation to conventional tissue biopsy, especially due to its ability to reflect, In real time, the tumor heterogeneity and evolutionary dynamics of cancer. While the tissue A tumor cell count provides a specific and limited picture of the neoplastic process, circulating biomarkers, MicroRNAs, extracellular vesicles, and epigenetic signatures significantly amplify the potential for early detection and molecular stratification (Lin et al., 2024; LI et al., 2021; Ratre et al., 2025).

One point of consensus among the authors is the limitation of traditional serum markers. such as CEA and CA 15-3, especially in the early stages of the disease, which drives the search for more sensitive molecular biomarkers. In this context, circulating microRNAs emerge as promising tools, with high stability in plasma and high diagnostic accuracy. A a combination of multiple miRNAs, such as miR-9, miR-16, miR-21, and miR-429, as well as the Isolated identification of miR-6165 and miR-182-3p demonstrates sensitivity and specificity. superior for the early detection of breast cancer, in addition to providing relevant information. regarding tumor aggressiveness, cell proliferation and metastatic potential (Kim et al., 2021; Effatpanah et al., 2025). These findings reinforce the idea that early diagnosis does not depend on a single factor. marker, but from integrated molecular panels.

In a complementary way, the analysis of extracellular vesicles is consolidated as a central axis.

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central to molecular stratification. There is convergence in the literature regarding the ability of these structures for carrying protein and genetic information specific to different tumor subtypes, which allows for the discrimination between luminal, HER2-positive, and triple-negative cancers. Proteins EDIL3, EGFR, fibronectin, HER2, and annexin A2 stand out for their diagnostic value and stratifier, while also contributing to the prediction of therapeutic resistance and disease progression (Li et al., 2021). However, a relevant counterpoint refers to tumor heterogeneity and the lack of standardization in methods for isolating and analyzing these vesicles, which still limits its routine incorporation into clinical practice.

Another widely discussed aspect is the incorporation of epigenetic biomarkers. especially DNA methylation profiles and histone modifications, as tools capable of complementing genomic and protein information. The literature converges in pointing out that These epigenetic signatures allow for the early identification of malignancy patterns in plasma, contributing both to the initial diagnosis and to the molecular stratification and to the understanding the mechanisms of chemoresistance and immune response (Ratre et al., 2025; Sadzeviciene et al., 2025). However, the authors also highlight, as a counterpoint, the need robust clinical validation and prospective studies that support its large-scale application.

Molecular and epigenetic biomarkers form the foundation of oncology. precision. If, on the one hand, diagnostic sensitivity has reached unprecedented levels through the On the other hand, the clinical viability of liquid biopsy depends on overcoming methodological challenges and... Consolidation of an evidence base to support the suggested adaptive and personalized management. through contemporary literature.

A comparison between traditional biomarkers and innovative approaches to diagnosis. Breast cancer screening highlights important advances in the search for more sensitive, specific methods. and applicable to clinical practice. In general, traditional biomarkers, such as mammography and Serum markers CA 15-3 and CEA continue to be widely used, but have limitations. relevant, especially in the early detection of the disease. According to Fredolini et al. (2020), although the While mammography has good overall accuracy, its effectiveness may be reduced in dense breasts and in... early-stage tumors, which reinforces the need for complementary diagnostic strategies.

In this context, innovative approaches based on molecular biomarkers have been emerging. standing out for offering greater diagnostic sensitivity. Fredolini et al. (2020) demonstrated that protein signatures identified through biomarker enrichment with nanoparticles They demonstrated superior sensitivity compared to mammography, allowing for the detection of ductal carcinomas. invasive procedures in the early stages. This finding is relevant because high sensitivity reduces the risk of False-negative results can be avoided, contributing to earlier and more effective interventions.

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Similarly, Kim et al. (2021) point out that traditional serum markers
They rarely rise in the early stages of breast cancer, which limits their usefulness in...
early diagnosis. In contrast, the analysis of microRNA panels derived from vesicles
extracellular molecules showed high sensitivity and specificity, in addition to allowing differentiation.
between molecular subtypes of the disease. This capability expands the clinical value of these approaches.
Innovative, as it facilitates both diagnosis and treatment personalization.

Regarding disease monitoring, Królÿwska-Daszczyÿska et al. (2025)
They highlight technologies such as circulating tumor DNA (ctDNA) and circulating tumor cells.
(CTCs) allow for monitoring of tumor progression in real time. Unlike
Unlike traditional biomarkers, these tools allow for the identification of molecular relapses months earlier.
of changes detectable by imaging tests, which represents a significant advance in
clinical monitoring and in therapeutic decision-making.

Despite the benefits presented by innovative approaches, the literature indicates
limitations to its routine application. As discussed by Colomer et al. (2024), biomarkers
Classic methods, such as hormone receptors, HER2, and Ki-67, remain the gold standard in practice.
Clinical advantages stem from their broad validation, lower cost, and greater availability. Technologies, on the other hand,
Innovative technologies, although more precise, still face challenges related to standardization.
methods, but with high costs and the need for specialized infrastructure.

FINAL CONSIDERATIONS

An analysis of the advances in the applicability of biomarkers in cancer diagnosis.
Mama highlighted the growing importance of these tools for personalizing treatment and
The improvement of clinical outcomes. The literature reviewed consistently demonstrates that...
Contemporary management of breast neoplasms no longer relies on isolated markers.
moving towards an integrated and multimodal model, capable of reflecting biological complexity and
tumor heterogeneity of the disease.

Therefore, the research made it possible to analyze the significant advances in the applicability of
biomarkers in the diagnosis and monitoring of breast cancer, confirming that the
Contemporary oncology is moving towards a precision medicine model. The study showed
although traditional markers, such as hormone receptors (ER and PR) and HER2,
remain indispensable pillars of clinical practice due to their robust validation and cost-
While beneficial, its application today requires continuous interpretative refinement, especially in light of
new categories, such as "HER2-low" and borderline estrogen receptor expression.

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It was also observed that the main evolution in the area lies in the transition of markers.
isolated for multimodal panels and innovative technologies, such as liquid biopsy and the study of
microRNAs and extracellular vesicles. These tools have been shown to overcome the limitations of
Mammography and conventional serum markers (CA 15-3 and CEA) are used in the early detection and treatment of breast cancer.
Real-time monitoring of tumor dynamics. The ability of these new approaches to reflect
the tumor heterogeneity and the ability to identify molecular recurrences even before manifestations in
Imaging exams represent the greatest advancement in improving clinical outcomes and...
Therapeutic personalization.

However, the results also point to relevant counterpoints that limit the
universal applicability of these innovations: high costs, technological availability and need
robust clinical validation in prospective studies. These factors still restrict its incorporation.
routine in clinical practice, especially in resource-limited settings, reinforcing the
The importance of integrated strategies that reconcile innovation, feasibility, and scientific evidence.
lack of methodological standardization, especially observed in the Ki-cell proliferation index
67, and the high costs of genetic platforms and liquid biopsies still restrict their use.
routine, particularly in healthcare systems with limited resources.

In short, highlighting the importance of traditional and innovative biomarkers represents the
The most promising path for improving the diagnosis and management of breast cancer.
Convergence of studies supports the idea that personalized treatment, based on panels of
Multimodal biomarkers have the potential to significantly improve clinical outcomes.
to reduce unnecessary treatments and optimize patients' quality of life. Finally, it should be noted
the need for continuous investment in research, standardization, and clinical validation, in order to
to consolidate the transition from the conventional diagnostic model to a truly [unclear/initiative] approach.
Customized and based on precision.

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Advancements in non-invasive biomarkers for detection and monitoring of breast cancer recurrence.

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