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Biomarkers for cancer diagnosis, prognosis, and treatment response: Breast Cancer as a model

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***Abstract*---Background:** The management of invasive breast cancer presents significant challenges, particularly in determining which patients should receive adjuvant chemotherapy. Prognostic and predictive biomarkers play crucial roles in tailoring treatment decisions to individual patients. **Aim:** This article aims to explore the utility of both traditional and molecular biomarkers in optimizing therapeutic strategies for patients with newly diagnosed breast cancer. **Methods:** A comprehensive review was conducted to analyze traditional prognostic factors, including lymph node involvement, tumor size, and tumor grade, alongside emerging molecular biomarkers like Oncotype DX, MammaPrint, and others. **Results:** Traditional factors remain pivotal in breast cancer management, despite the emergence of molecular tests. Notably, lymph node status, tumor size, and tumor grade continue to correlate with patient outcomes. Investigational biomarkers, including circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA), are currently under evaluation for their prognostic capabilities. The Oncotype DX assay,

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which assesses gene expression to predict recurrence risk, has demonstrated substantial impact on clinical decision-making, leading to reduced chemotherapy use in specific patient populations. **Conclusion:** The integration of both traditional and molecular biomarkers is essential for personalized breast cancer management. Ongoing research is crucial for validating the clinical utility of newer biomarkers, ultimately enhancing treatment decision-making processes.

***Keywords*---**breast cancer, biomarkers, adjuvant chemotherapy, prognosis, predictive factors, Oncotype DX, molecular testing.

Introduction

Following the diagnosis of invasive breast cancer, one of the primary challenges is determining which patients should receive adjuvant treatment, particularly adjuvant chemotherapy. Once a decision is made to initiate adjuvant therapy, the subsequent task is to identify the most appropriate therapy or combination of therapies tailored to the individual patient. Prognostic factors and biomarkers can assist in addressing the initial challenge, while predictive biomarkers are valuable for tackling the latter. This article aims to explore how both prognostic and predictive biomarkers facilitate optimized therapeutic decision-making for patients with newly diagnosed breast cancer. Before delving into this, a brief overview of traditional prognostic factors that contribute to the management of early-stage breast cancer will be presented.

Traditional Prognostic Factors

Despite the growing emphasis on molecular prognostic tests in recent years, the significant role of traditional clinical and pathological factors is often overlooked. Among the factors identified, the most commonly utilized include the number of regional lymph nodes affected by metastasis, tumor size, and tumor grade [1], [2]. Even with the emergence of various molecular tests in recent years, these traditional factors remain essential for assessing prognosis and informing treatment decisions for patients newly diagnosed with breast cancer. The principal conventional and investigational prognostic and predictive biomarkers encompass various categories. Conventional biomarkers assessed in tissue include lymph node involvement, tumor size, tumor grade (as indicated by the Nottingham score), estrogen receptor (ER) status, progesterone receptor (PR) status, Ki67 levels, HER2/neu status, Oncotype DX recurrence score (RS), Mammaprint risk assessment, and uPA/PAI tests. Each biomarker contributes to understanding prognosis and predicting responses to therapies. For instance, a positive lymph node status is associated with poorer outcomes, while smaller tumor sizes correlate with better prognoses. Furthermore, established risk assessments, such as Oncotype DX and Mammaprint, help stratify patients into high-risk or low-risk categories regarding recurrence post-treatment. In addition, investigational biomarkers—both in tissue and circulation—have garnered attention in recent studies. These include circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA), which are being evaluated for their prognostic

and predictive capacities. Ongoing trials are exploring the relationship between the presence and quantity of CTCs or ctDNA and treatment outcomes, although further research is necessary to validate their utility in clinical practice.

Lymph Node Metastasis

The presence and quantity of axillary lymph node metastases continue to be the most critical prognostic determinant in breast cancer. A clear correlation exists between the number of metastatic axillary lymph nodes and the risk of systemic metastasis, independent of tumor size [3]. Most studies focusing on lymph node metastases and other commonly employed histological prognostic indicators for predicting patient outcomes were conducted decades ago, prior to the advent of modern breast cancer treatments. Nevertheless, a recent multicenter study conducted in Canada revealed that lymph node status—whether node-negative or node-positive and the number of nodes dissected—serves as a significant predictor for local recurrence, regional recurrence, distant metastasis, breast cancer-specific survival, and overall survival [4]. Importantly, the prognostic value of lymph node status was independent of other variables such as tumor size, tumor grade, surgical intervention type, chemotherapy regimen, and patient age. However, as a prognostic marker, the extent of axillary node involvement is not entirely reliable. This limitation arises from the observation that nearly 50% of patients with nodal metastases are successfully treated through local therapy, while around 30% of untreated patients without nodal involvement may develop recurrent or metastatic disease within ten years [5].

Tumor Size

Similar to lymph node metastases, tumor size assessment is crucial in determining prognosis for breast cancer. The risk of metastasis correlates positively with tumor size, regardless of the number of lymph node metastases [3]. Data indicate that patients with tumors smaller than 1 cm exhibit a 5-year overall survival rate nearing 100%, compared to 89% for those with tumors ranging from 1 to 3 cm, and 86% for tumors measuring 3 to 5 cm [3]. In the aforementioned Canadian multicenter study [4], tumor size was similarly recognized as an independent prognostic factor for local recurrence, regional recurrence, distant metastases, breast cancer-specific survival, and overall survival [3].

Tumor Grade

Tumor grade, along with lymph node metastases and tumor size, is widely utilized to assess prognosis in breast cancer patients [1][2]. Tumor grading evaluates the microscopic resemblance of breast cancer cells to normal breast tissue. The Nottingham grading system is among the most commonly employed and validated grading systems [6][7][8][9]. It assesses three microscopic features: nuclear pleomorphism, gland or tubule formation, and the count of dividing cells. Each characteristic receives a score of 1 to 3 (with 1 indicating the closest resemblance to normal breast tissue and 3 the furthest). The total score determines the tumor grade: scores between 3 and 5 denote grade 1; scores of 6 or 7 designate grade 2; and scores of 8 or 9 classify the tumor as grade 3. In 2017, the Nottingham grading system was integrated into the American Joint Committee on Cancer

staging for breast cancer [10]. While tumor grade is frequently used to predict prognosis, it has two notable limitations. The first limitation is the variability in grading consistency among pathologists. However, studies have reported that the Nottingham grading system is more reproducible compared to some earlier systems [11][12][13]. The second limitation is that the majority of tumors are categorized as grade 2, which is a highly heterogeneous group concerning patient outcomes [14].

Molecular Prognostic Biomarkers

While the number of lymph node metastases, tumor size, and tumor grade provide essential prognostic information for newly diagnosed breast cancer patients, it is increasingly recognized that these factors alone are insufficient for optimal patient management, particularly in the era of personalized treatment [15][16]. Consequently, extensive research has been dedicated to the development and validation of molecular biomarkers that offer prognostic insights and, crucially, predict treatment responses. Over the last decade, several new prognostic tests have emerged for breast cancer [15][16]. Unlike single analyte measurements, most of these tests assess multiple analytes, particularly mRNA species, and are commonly referred to as multi-gene, multi-analyte, or multi-parameter tests. Several of these tests have garnered recommendations from expert panels [17][18][19][20] and are increasingly integrated into clinical practice. Among the most validated tests are Oncotype DX, MammaPrint, and uPA/PAI-1 (Femtelle), which are briefly summarized below.

A summary of gene and protein signatures previously proposed for predicting outcomes in patients with newly diagnosed breast cancer is presented, specifying the required tissue type, measured molecules, number of analytes, and whether they have been studied in prospective randomized trials. The table outlines various tests, including uPA/PAI-1, Oncotype DX, MammaPrint, Prosigna, GGI, BCI, Mammostrat, IHC4 score, EndoPredict, Rotterdam Signature, OncoMasTR, and Curbest 95GC. Furthermore, data summarizes the recommendations of these tests in clinical guidelines issued by ASCO, NCCN, and EGTM, as well as their inclusion in AJCC staging. The recommendations indicate that tests like Oncotype DX and MammaPrint are recognized as beneficial in clinical decision-making, while others, such as uPA/PAI-1 and Prosigna, have varying levels of endorsement across guidelines. Overall, the development of molecular prognostic biomarkers represents a significant advancement in personalized breast cancer management, enabling more tailored therapeutic approaches for patients.

Oncotype DX

Oncotype DX is recognized as one of the most validated and extensively utilized multigene signatures for predicting outcomes in breast cancer. This assay employs reverse transcription polymerase chain reaction (RT-PCR) to quantify the expression of 21 genes at the mRNA level. Among these genes, 16 are associated with cancer, while 5 function as reference or control genes. The recurrence score (RS) is derived from the relative expression levels of the 16 cancer-related genes compared to the 5 reference genes. This score is continuous and stratifies

patients into three risk categories for disease recurrence: low risk (RS < 18), intermediate risk (RS 18–30), and high risk (RS ≥ 30) [21].

The Oncotype DX test serves two primary purposes in breast cancer management: it predicts the likelihood of disease recurrence and identifies patients who may benefit from adjuvant chemotherapy [22]. The test's capacity to predict disease recurrence has undergone extensive validation across a range of studies, including large population-based cohorts and both prospective and retrospective trials, with two prominent prospective trials providing further insight [22]. In the TAILORx trial (NCT00310180), Sparano et al. [23] demonstrated that lymph node-negative, estrogen receptor (ER)-positive, and human epidermal growth factor receptor 2 (HER2)-negative patients with an RS of less than 11 exhibited a remarkably low risk of recurrence, with 93.8% of participants remaining free from invasive disease and 99.3% avoiding distant recurrence after five years. Additionally, a large prospective trial revealed that the three-year disease-free survival rate for patients with a low RS (≤11) was 98%, even without adjuvant chemotherapy, highlighting the favorable prognosis for node-negative or node-positive (1–3 positive nodes) patients with low Oncotype DX RS [24]. Although follow-up is still somewhat limited, these findings suggest that patients with low RS are unlikely to derive significant clinical benefits from adjuvant chemotherapy.

While less frequently studied than its prognostic capabilities, Oncotype DX has also been found to predict the potential benefits of combining adjuvant chemotherapy with endocrine therapy. In analyses of archival samples from clinical trials (NSABP B20 and SWOG 8814) involving ER-positive and HER2-negative patients, those exhibiting high RS benefited from adjuvant chemotherapy, whereas those with low RS showed minimal to no benefit from this intervention [25][26]. However, the efficacy of chemotherapy in patients with an intermediate RS remains ambiguous, with ongoing evaluations in the TAILORx trial focusing specifically on ER-positive, lymph node-negative patients. Meanwhile, the RxPONDER trial (NCT01272037) is investigating whether adjuvant chemotherapy is advantageous for ER-positive, HER2-negative patients with node-positive (1–3 positive nodes) disease and RS ≤ 25.

Numerous studies have indicated that Oncotype DX significantly influences clinical decision-making, particularly among ER-positive, HER2-negative, lymph node-negative patients [22][27]. A meta-analysis encompassing four prospective studies from various European nations reported that the implementation of the Oncotype DX test resulted in revised treatment recommendations for 32% of patients assessed [28]. Consequently, the recommendation for chemotherapy decreased from 55% to 34%, with the most substantial changes occurring in patients initially advised to receive chemotherapy and those presenting with grade II tumors. In alignment with its capability to lower the rates of adjuvant chemotherapy administration, Oncotype DX has also demonstrated cost-effectiveness, and in certain healthcare settings, it has been shown to result in cost savings. A systematic literature review conducted by Rouzier et al. [27] identified 18 studies that examined the cost-effectiveness of Oncotype DX among ER-positive, HER2-negative early breast cancer patients. All studies evaluated revealed that the test was cost-effective according to established cost-effectiveness thresholds, applicable to both lymph node-negative and node-positive patient

cohorts, as well as mixed groups. In the United States, Oncotype DX was found to be cost-saving, likely due to the high expenses associated with chemotherapy, which is frequently utilized in that context.

Given its extensive validation, capacity to reduce the use of adjuvant chemotherapy, and demonstrated cost-effectiveness, Oncotype DX is widely endorsed for clinical application in Western nations [19]. The European Group on Tumor Markers (EGTM) asserts that "the Oncotype DX test may provide added value to established factors for determining prognosis and aiding decision-making concerning the administration of adjuvant chemotherapy in newly diagnosed breast cancer patients with lymph node-negative invasive disease that is ER-positive but HER2-negative" [19]. Furthermore, they recommend Oncotype DX for identifying HER2-negative, ER-positive patients with 1–3 involved lymph nodes as candidates for adjuvant chemotherapy. Similarly, the American Society of Clinical Oncology (ASCO) has published comparable guidelines for lymph node-negative patients [17]. According to ASCO guidelines, Oncotype DX may be utilized to inform decisions regarding adjuvant systemic chemotherapy for lymph node-negative patients with hormone receptor-positive, HER2-negative breast cancer. However, in contrast to the EGTM guidelines [19], ASCO does not support the use of RS for lymph node-positive patients.

Despite its recommendations and widespread use, Oncotype DX is not without limitations. Key shortcomings include a lack of validation for ER-negative patients and insufficient long-term follow-up data. Moreover, it remains unclear whether lymph node-negative, ER-positive patients with intermediate RS derive benefits from adding adjuvant chemotherapy to endocrine therapy, or if lymph node-positive (1–3 positive nodes) ER-positive patients with low to intermediate RS gain from adjuvant chemotherapy. It is hoped that forthcoming studies will elucidate the answers to these pressing questions in the near future.

MammaPrint

MammaPrint, akin to Oncotype DX, has undergone extensive validation for its capacity to predict disease recurrence and inform treatment decisions in breast cancer patients [29], [30], [31], [32], [33], [34], [35]. This assay employs microarray technology to quantify the expression of 70 genes associated with critical cancer hallmarks. Based on the gene expression levels, patients are classified into two categories: low risk and high risk for disease recurrence. The clinical efficacy of MammaPrint was substantiated in a prospective randomized trial, referred to as the MINDACT study [36]. This investigation enrolled 6,693 patients with early breast cancer, either lymph node-negative or possessing 1–3 metastatic axillary lymph nodes. The findings revealed that patients deemed at low risk for recurrence per MammaPrint, yet classified as high risk based on traditional clinicopathological criteria, exhibited an impressive 5-year distant metastasis-free survival rate of 94.7%. Additionally, employing MammaPrint in treatment decision-making resulted in a 14% decrease in the administration of adjuvant chemotherapy compared to conventional criteria. Among clinically high-risk patients, utilizing MammaPrint led to a notable 46% reduction in chemotherapy administration.

The outcomes from this randomized prospective trial unequivocally demonstrated that MammaPrint can transform breast cancer management by providing robust evidence for the reduced use of adjuvant chemotherapy in patients categorized as high-risk through clinical and pathological assessments, all while maintaining favorable outcomes. Although MammaPrint has been less extensively investigated than Oncotype DX, evidence suggests that its application can influence the administration of adjuvant chemotherapy [37], [38], [39], [40] and proves to be cost-effective [27]. For instance, in a recent multicenter observational study involving ER-positive, HER2-negative patients under 70 years, the availability of MammaPrint results led to a shift in chemotherapy recommendations for approximately half of the participants [34]. Similar to Oncotype DX, MammaPrint has been affirmed as cost-effective across various healthcare systems [27].

Several expert panels now endorse the implementation of MammaPrint [19]. According to the EGTM guidelines, the MammaPrint test "may be utilized for prognostic assessment and guiding decisions regarding the administration of adjuvant chemotherapy in patients with newly diagnosed invasive breast cancer that is lymph node-negative or lymph node-positive (1–3 metastatic nodes). Patients classified as high risk based on clinical and pathological criteria but low risk according to MammaPrint might be suitable candidates for avoiding adjuvant chemotherapy" [19]. Conversely, ASCO opposes the routine application of MammaPrint for treatment decision-making in breast cancer patients [17]. It is noteworthy that ASCO's guidelines were published prior to the release of the MINDACT trial findings [36]. Nonetheless, the US Food and Drug Administration (FDA) has cleared MammaPrint for breast cancer patients with lymph node-negative stage I or II disease and a tumor size of ≥5.0 cm, asserting that MammaPrint as a prognostic biomarker should be used in conjunction with established clinic-pathological factors.

uPA and PAI-1

In contrast to Oncotype DX and MammaPrint, the assessment of uPA and PAI-1 is a simpler and less costly procedure. This test quantifies two proteins through ELISA in extracts from fresh or freshly frozen breast cancer tissues [35]. Patients exhibiting elevated levels of these proteins face significantly poorer outcomes compared to those with lower levels. The validation of the uPA/PAI-1 test for patients with lymph node-negative disease has been achieved through both a multicenter prospective randomized trial and a pooled analysis of individual patient data encompassing 18 distinct datasets totaling 8,377 patients [41], [42], [43], [44]. Consistent with findings from Oncotype DX and MammaPrint, the measurement of uPA and PAI-1 has demonstrated the ability to reduce the use of adjuvant chemotherapy and has been deemed cost-effective [45].

The evaluation of uPA and PAI-1 is now widely advocated for prognostic determination and therapeutic decision-making, particularly in lymph node-negative breast cancer patients [17], [19]. The EGTM guidelines affirm that “levels of PA and PAI-1 protein may be integrated with established prognostic factors to identify ER-positive, HER2-negative, and lymph node-negative breast cancer patients unlikely to benefit from adjuvant chemotherapy” [19]. Similarly, ASCO guidelines suggest that for node-negative patients with ER/PR-positive, HER2-

negative breast cancer, the uPA/PAI-1 assessment may be utilized to inform decisions regarding adjuvant systemic therapy [17].

Other Prognostic Biomarkers

While multigene signatures such as those previously discussed are increasingly integrated into the clinical management of early breast cancer patients, their high costs render them prohibitively expensive in numerous countries. Consequently, significant efforts have been dedicated to the development and validation of affordable and straightforward prognostic biomarker tests. One of the most commonly utilized inexpensive biomarkers is Ki67. Despite existing methodological challenges in its determination—such as poor inter-laboratory precision and the absence of a validated cutoff point—numerous studies, including retrospective evaluations of randomized clinical trials and meta-analyses, have demonstrated that elevated Ki67 levels are independently associated with adverse outcomes in breast cancer patients.

Due to its established clinical utility, wide availability, and relatively low costs compared to multianalyte signatures, Ki67 is extensively employed in various countries. The European Group on Tumor Markers (EGTM) expert panel suggests that "Ki67 may be used in combination with established prognostic factors for determining prognosis, particularly if values are low (e.g., <10% cell staining) or high (e.g., >25% cell staining)." However, other expert panels, such as the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN), oppose the utilization of Ki67 as a prognostic biomarker for breast cancer. In addition to Ki67, other promising inexpensive prognostic biomarkers for breast cancer include IHC4, which assesses estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67; a risk score combining ER, PR, grade, and tumor size; or a risk score that incorporates ER, PR, Ki67, tumor size, and the Nottingham Index. Nonetheless, these multiparametric tests require further validation prior to clinical recommendation.

All the prognostic biomarkers discussed necessitate tumor tissue for their evaluation, indicating a clear need for robust and clinically validated circulating prognostic biomarkers. While elevated levels of circulating biomarkers such as CA 15-3, carcinoembryonic antigen (CEA), and tissue polypeptide specific antigen (TPS) have been associated with poor outcomes in breast cancer patients, they are not widely employed for prognostic assessment in clinical settings. The limited clinical use of these biomarkers may stem from a lack of validation in clinical trials and the absence of evidence demonstrating that their measurement can influence patient management. Nevertheless, given that these biomarkers are simple and relatively inexpensive to measure, further research, including clinical trials, is warranted.

Predictive Biomarkers

In contrast to prognostic biomarkers, which estimate the risk of disease recurrence, predictive biomarkers serve to identify patients likely to respond to specific therapies. Breast cancer is a pioneer in utilizing therapy predictive biomarkers. For instance, the assessment of estrogen and progesterone receptors

(ER, PR) to anticipate response to endocrine therapy has been in clinical practice for over 40 years, while HER2 measurement for predicting response to trastuzumab (Herceptin) has been routine for more than 15 years. The clinical relevance of these three biomarkers is discussed in the following sections.

Estrogen and Progesterone Receptors

Despite being the oldest biomarkers, ER, specifically ER-alpha, remains the most critical biomarker for breast cancer. Measurement of ER is essential in all newly diagnosed breast cancer cases and, where feasible, in recurrent or metastatic lesions. Although ER provides both prognostic and predictive information, its primary clinical application is as a predictive biomarker for endocrine therapy. Patients who test positive for ER should be considered for endocrine treatment, whereas those lacking ER should not receive such therapies. ER serves as a predictive marker for endocrine therapy across neoadjuvant, adjuvant, and advanced disease contexts.

The rationale for using ER as a predictive marker for endocrine therapy is grounded in observations made decades ago indicating that certain breast cancers are estrogen-dependent, particularly on estradiol. Estrogens are believed to promote breast cancer cell proliferation by binding to regulatory genomic elements, thereby enhancing the transcription of oncogenes like MYC and cyclin D (CCND1). Given that estrogens stimulate tumor growth through ER activation, it was postulated that the levels of this receptor in breast tumors would correlate with the efficacy of anti-estrogenic therapies. Early studies in the 1970s demonstrated that approximately 50% of ER-positive patients with advanced breast cancer experienced objective tumor regression when treated with then-available endocrine therapies such as ovariectomy and adrenalectomy. Conversely, patients with ER-negative tumors rarely showed tumor regression with these treatments.

Currently, while ER is still utilized to predict response to endocrine therapy in advanced breast cancer, its primary role lies in identifying patients with early breast cancer for adjuvant treatment with agents like selective estrogen receptor modulators (tamoxifen), aromatase inhibitors (anastrozole, letrozole, or exemestane), LH-RH agonists (leuprolide, goserelin), pure selective estrogen receptor downregulators (SERDs) (fulvestrant), and oophorectomy. These therapies ultimately target ER, inhibiting its ability to promote breast cancer proliferation. Consequently, they are only administered to patients with ER-positive tumors. However, due to their distinct mechanisms of action, resistance to one drug does not imply resistance to all related compounds. Therefore, various classes of endocrine therapy may be employed sequentially for treating ER-positive breast cancers.

The progesterone receptor (PR) is typically assessed concurrently with ER. The initial rationale for measuring PR alongside ER was based on the observation that PR is induced by estrogen. Consequently, PR was proposed as an indicator of a functional ER. While ER stimulates PR expression, PR, in the presence of progesterone, has been shown to interact with ER, altering its chromatin binding location. This altered binding results in a shift from regulating genes associated

with proliferation to modulating genes linked to cell cycle arrest, apoptosis, and differentiation. This mechanism, coupled with the "functional" receptor hypothesis, may elucidate why PR presence in ER-positive breast cancer correlates with favorable outcomes.

In line with these findings, several studies involving early or advanced breast cancer patients have indicated that those with ER-positive and PR-positive tumors are more likely to respond to endocrine therapy compared to those with ER-positive/PR-negative tumors. However, other studies, particularly in the adjuvant setting, have concluded that PR provides no additional predictive value beyond ER. Conflicting findings may stem from variations in cutoff values for defining PR positivity, the duration of patient follow-up, and whether adjuvant chemotherapy was administered. While the independent predictive value of PR for adjuvant endocrine therapy remains uncertain, numerous studies in ER-positive patients have reported that it provides independent prognostic information for recurrence risk. Consequently, expert panels recommend measuring both ER and PR in all newly diagnosed breast cancer cases, with most advocating for their assessment in recurrent or metastatic lesions when feasible.

Conclusion

The article provides a thorough examination of biomarkers for breast cancer diagnosis, prognosis, and treatment response, highlighting their critical role in guiding therapeutic decision-making. While traditional prognostic factors—such as lymph node involvement, tumor size, and tumor grade—continue to hold significant relevance, the emergence of molecular biomarkers marks a transformative shift in breast cancer management. These advancements enable a more nuanced understanding of individual patient risks and treatment responses, allowing for personalized treatment strategies. The importance of traditional prognostic factors is underscored by their established correlations with patient outcomes. For instance, the number of metastatic axillary lymph nodes significantly impacts the risk of systemic metastasis, serving as a reliable predictor of local and distant recurrence. Similarly, tumor size and grade remain integral to evaluating prognosis, despite some limitations in grading consistency among pathologists. However, these traditional metrics alone may not suffice in the context of increasingly personalized treatment paradigms. Molecular prognostic biomarkers, such as Oncotype DX, MammaPrint, and uPA/PAI-1, represent substantial advancements in the field. These tests assess multiple analytes to provide comprehensive insights into disease recurrence and treatment responses. Notably, Oncotype DX has been pivotal in altering clinical decision-making, leading to reduced chemotherapy recommendations among patients classified as low risk. Its ability to predict the likelihood of recurrence and identify patients who would benefit from chemotherapy positions it as a cornerstone of contemporary breast cancer management. Emerging investigational biomarkers like circulating tumor cells (CTCs) and circulating tumor DNA (ctDNA) hold promise for further enhancing prognostic and predictive capabilities in breast cancer. Ongoing research is crucial to validate these biomarkers' utility in clinical practice, ensuring they contribute meaningfully to patient care. In summary, the integration of both traditional and molecular biomarkers is fundamental to the personalized management of breast cancer. By optimizing therapeutic decision-

making, these biomarkers improve patient outcomes and pave the way for more effective treatment strategies. Future studies should focus on refining the application of these biomarkers and establishing their roles in various clinical settings, ultimately leading to improved patient care and survival rates in breast cancer.

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المؤشرات الحيوية لتشخيص السرطان والتنبؤ به واستجابة العلاج - سرطان الثدي كنموذج

الملخص:
الخلفية :إدارة سرطان الثدي الغازي تطرح تحديات كبيرة، خاصة في تحديد أي المرضى يجب أن يتلقوا العلاج الكيميائي المساعد. تلعب المؤشرات الحيوية التنبؤية والتشخيصية أدوارًا حاسمة في تخصيص قرارات العلاج للمرضى بشكل فردي.
الهدف :يهدف هذا المقال إلى استكشاف فائدة المؤشرات الحيوية التقليدية والجزيئية في تحسين استراتيجيات العلاج للمرضى الذين تم تشخيصهم حديثًا بسرطان الثدي.
الطرق :تم إجراء مراجعة شاملة لتحليل العوامل التنبؤية التقليدية، بما في ذلك انتشار العقد اللمفية، حجم الورم، ودرجة الورم، إلى جانب المؤشرات الحيوية الجزيئية الناشئة مثل Oncotype DX و MammaPrintوغيرها.
النتائج :تبقى العوامل التقليدية حيوية في إدارة سرطان الثدي، على الرغم من ظهور الاختبارات الجزيئية. وتجدر الإشارة إلى أن حالة العقد اللمفية وحجم الورم ودرجة الورم لا تزال مرتبطة بنتائج المرضى. يتم حاليًا تقييم المؤشرات الحيوية قيد البحث، بما في ذلك خلايا الورم المتداولة (CTCs) و DNAالورم المتداول(ctDNA) ، من حيث قدرتها التنبؤية. لقد أظهر اختبار Oncotype DX، الذي يقيم التعبير الجيني للتنبؤ بمخاطر الانتكاس، تأثيرًا كبيرًا على اتخاذ القرارات السريرية، مما أدى إلى تقليل استخدام العلاج الكيميائي في فئات معينة من المرضى.
الخاتمة :إن دمج كل من المؤشرات الحيوية التقليدية والجزيئية ضروري لإدارة سرطان الثدي الشخصية. البحث المستمر أمر حيوي للتحقق من الفائدة السريرية للمؤشرات الحيوية الأحدث، مما يعزز في النهاية عمليات اتخاذ القرارات العلاجية.
الكلمات المفتاحية :سرطان الثدي، المؤشرات الحيوية، العلاج الكيميائي المساعد، التنبؤ، العوامل التنبؤية، Oncotype DX، الاختبارات الجزيئية.