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Diagnostic and Prognostic Role of HER2 Genes in Breast Carcinoma

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Abstract

HER2 (human epidermal growth factor receptor 2) is a pivotal biomarker and therapeutic target in breast carcinoma, overexpressed or amplified in approximately 15-20% of cases. Its presence is associated with aggressive disease behavior and poor prognosis. Accurate assessment of HER2 status through immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) is essential for diagnosis and treatment planning. HER2-targeted therapies, such as trastuzumab, have revolutionized the management of HER2-positive breast cancer, significantly improving patient outcomes. However, challenges such as resistance to therapy and tumor heterogeneity persist, necessitating ongoing research. This review discusses the diagnostic and prognostic roles of HER2 in breast carcinoma, highlighting the impact of targeted therapies and the need for further advancements in treatment strategies.

Keywords: HER2, Breast Carcinoma, Diagnostic, Prognostic.

1. INTRODUCTION

According to the WHO, malignant neoplasms are the greatest worldwide burden for women, estimated at 107.8 million Disability-Adjusted Life Years (DALYs), of which 19.6 million DALYs are due to breast cancer(1). . Breast cancer is the most frequently diagnosed cancer in women worldwide with 2.26 million [95% UI, 2.24–2.79 million] new cases in 2020. In the United States, breast cancer alone is expected to account for 29% of all new cancers in women(2). The 2018 GLOBOCAN data shows that age-standardized incidence rates (ASIR) of breast cancer are strongly and positively associated with the Human Development Index (HDI)(3) . According to 2020 data, the ASIR was the highest in very high HDI countries (75.6 per 100,000) while it was more than 200% lower in medium and low HDI countries (27.8 per 100,000 and 36.1 per 100,000 respectively).

Besides being the most common, breast cancer is also the leading cause of cancer death in women worldwide. Globally, breast cancer was responsible for 684,996 deaths [95% UI, 675,493–694,633] at an age-adjusted rate of 13.6/100,000 . Although incidence rates were the highest in developed regions, the countries in Asia and Africa shared 63% of total deaths in 2020. Most women who develop breast cancer in a high-income country will survive; the opposite is true for women in most low-income and many middle-income countries. HER2, also known as ERBB2, is a proto-oncogene located on chromosome 17 that encodes a transmembrane tyrosine kinase receptor involved in cell growth, differentiation, and survival. HER2 overexpression or gene amplification occurs in a subset of breast cancers, leading to aggressive tumor behavior characterized by increased proliferation and metastatic potential. The identification of HER2 status is crucial for determining appropriate treatment strategies, as HER2-positive breast cancers require targeted therapies in addition to standard chemotherapy(4) .

2. DIAGNOSTIC ROLE OF HER2

The determination of HER2 status is a critical component in the diagnostic workup of breast carcinoma. The two primary methods for assessing HER2 status are:

2.1. Immunohistochemistry (IHC):

IHC evaluates the level of HER2 protein expression on the surface of tumor cells. It is scored on a scale from 0 to 3+, with 3+ indicating HER2 positivity. HER2-positive tumors are eligible for targeted therapies, which significantly improve outcomes(5).

2.2. Fluorescence In Situ Hybridization (FISH):

FISH detects HER2 gene amplification in tumor cells, particularly important in cases where IHC results are equivocal (2+), providing definitive HER2 status. HER2 amplification correlates with a more aggressive disease course but also identifies patients who may benefit from HER2-targeted therapies (6).

Accurate HER2 testing is essential as the treatment and prognosis of HER2-positive breast cancer differ significantly from HER2-negative cases. HER2 testing not only aids in diagnosis but also plays a pivotal role in guiding treatment decisions, ensuring that patients receive the most effective therapies available.

3. Prognostic Role of HER2

HER2 status is a powerful prognostic marker in breast carcinoma. Before the advent of HER2-targeted therapies, HER2-positive breast cancer was associated with a poor prognosis, characterized by higher recurrence rates and reduced overall survival compared to HER2-negative breast cancers(6). The aggressiveness of HER2-positive tumors is attributed to the gene's role in promoting cellular proliferation and inhibiting apoptosis.

3.1. Impact of HER2-Targeted Therapies:

The introduction of HER2-targeted therapies, such as trastuzumab, pertuzumab, and ado-trastuzumab emtansine (T-DM1), has significantly improved the prognosis for HER2-positive breast cancer patients(7). Trastuzumab, in particular, has shown remarkable efficacy in improving disease-free survival (DFS) and overall survival (OS) in these patients, transforming a previously high-risk diagnosis into one with significantly better outcomes (8).

3.2. Challenges and Future Directions:

Despite the success of these therapies, some patients develop resistance, leading to disease progression. Ongoing research aims to identify the mechanisms behind this resistance and develop new strategies to overcome it. Additionally, the heterogeneity within HER2-positive breast cancer, such as differences in hormone receptor status and other genetic factors, poses challenges in treatment and underscores the need for personalized therapeutic approaches(9) .

CONCLUSION

HER2 is a critical gene in the diagnosis and prognosis of breast carcinoma. The accurate determination of HER2 status is essential for guiding treatment decisions and improving patient outcomes. The introduction of HER2-targeted therapies has transformed the management of HER2-positive breast cancer, leading to significantly improved survival rates. However, challenges such as treatment resistance and tumor heterogeneity remain, highlighting the need for continued research and the development of new therapeutic strategies. The future of HER2-positive breast cancer treatment lies in further refining targeted therapies and understanding the underlying mechanisms of resistance to enhance patient outcomes.

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