Insulin-like Growth Factor-1 Receptor as a Prognostic Factor for Breast Cancer: A Systematic Review and Meta-Analysis

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Introduction

- Breast cancer is the “malignant proliferation of epithelial cell lining the ducts or lobules of the breast” (1).
- Breast cancer is the most common form of cancer affecting women and the second leading cause of cancer death among women.
- Insulin-like growth factors are potent mitogens that have a role in cell proliferation, differentiation, and apoptosis.
- Overexpression of IGF-1R is thought to cause an increased risk in tumor metastasis and tumorigenesis.
- The aim of this project is to conduct a systematic review of IGF-1R expression in breast cancer and its relationship to patient survival.
- Our hypothesis is that increased insulin-like growth factor-1 receptor expression leads to poor prognosis in breast cancer patients.

Methods

1. Articles were selected based on predefined eligibility criteria using PRISM.
2. Criteria are listed in Table 1.
3. A search string was determined based on the eligibility criteria using standardized search terms and searched through PubMed, CINAHL, Cochrane, and Web of Science databases.
4. Articles were screened independently by four investigators for inclusion, based on eligibility criteria.
5. Data were analyzed by the researchers to determine the association between IGF-1R expression and breast cancer patient survival.

Results

- A total of 175 articles were screened: 56 were provisionally selected, and 17 articles were accepted by concensus of all four investigators.
- Table 2 summarizes the characteristics of the accepted studies.
- Table 3 summarizes the results of the 17 articles screened and reviewed. 6 articles found that IGF-1R expression was associated with better prognosis, 9 articles found that IGF-1R was associated with poor prognosis, 1 found that decreased expression was associated with better prognosis, and 3 articles found no association between expression and prognosis.

Table 1: Eligibility Criteria

• Article in English
• Publication between 2006 and 2016
• Longitudinal study with pretreatment assessment of IGF-1R
• IGF-1R measurement used in the determination of prognosis
• Female patients
• Diagnosis on histological review on breast tissue biopsy
• Survival as a measure of prognosis

Table 2: Study Characteristics

Type of study	Standard of care
Breast cancer type	Most not specified; primary invasive; ductal, lobular; subtypes: Luminal A, Luminal B, HER2, triple-negative
Breast cancer stage	invasive, metastatic, in situ
Survival measures	overall, disease-free, recurrence/relapse-free, breast cancer/disease-specific survival
Other prognostic variables	ER, PR, HER2 positivity; tumor size, histological grade, lymph node status, nuclear grade
Method of IGF-1R measurement	protein by immunohistochemistry; mRNA by RT-PCR; polymorphisms by DNA sequencing; ELISA
Demographics	variable (age ranged from 20-93; groups based on location)
Pre- or post-menopausal	both included
Geographic location	US, China, South Korea, UK, Japan
Comorbidities	None
Therapy treatment	surgery, radiation, chemotherapy, hormonal treatment (tamoxifen)

Table 3: Association of IGF-1R with prognosis

	# of studies
Increased expression, better prognosis	4
Increased expression, worse prognosis	9
Decreased expression, better prognosis	1
No association	3

Discussion

- We found that IGF-1R expression is associated with different outcomes dependending on the patients and methodologies involved. Some studies measured IGF-1R expression while the patients were on hormone therapy or other treatments.

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