

48. Breast

Authors

Gabriel N. Hortobagyi, James L. Connolly, Carl J. D’Orsi, Stephen B. Edge, Elizabeth A. Mittendorf, Hope S. Rugo, Lawrence J. Solin, Donald L. Weaver, David J. Winchester, Armando Giuliano

Emerging Prognostic Factors for Clinical Care

The authors have not noted any emerging prognostic factors for clinical care at this time.

Risk Assessment Models

Prognostic models will continue to play an important role in 21st century medicine for several reasons.¹ First, by identifying which factors predict outcomes, clinicians gain insight into the biology and natural history of the disease. Second, treatment strategies may be optimized based on the outcome risks of the individual patient. Third, because of the heterogeneity of disease in most cancers, prognostic models will play a critical role in the design, conduct, and analysis of clinical trials in oncology.¹ If developed and validated appropriately, these models will become part of routine patient care, decision-making trial design, and conduct.

The AJCC Precision Medicine Core (PMC) developed and published criteria for critical evaluation of prognostic tool quality,² which are presented and discussed in Chapter 4. Although developed independently by the PMC, the AJCC quality criteria correspond fully with the recently developed Cochrane CHARMS Checklist for critical Appraisal and data extraction for systematic Reviews of prediction Modeling Studies.³

Existing prognostic models for breast cancer meeting all of the AJCC inclusion/exclusion criteria and meriting AJCC endorsement are presented in this section. A full list of the evaluated models and their adherence to the quality criteria is available on www.cancerstaging.org.

The PMC performed a systematic search of literature for prognostic models/tools in breast cancer published from January 2011 to December 2015. The search strategy is provided in Chapter 4. The PMC defined “prognostic model” as a multivariable model where factors predict a clinical outcome that will occur in the future. Each tool identified was compared against the quality criteria developed by the PMC as guidelines for AJCC commendation for prognostication models (see Chapter 4).

Thirty prognostication tools for breast cancer were identified and reviewed against a checklist derived from the PMC guidelines. Only two tools, Adjuvant! Online^{4,5} and PREDICT-Plus^{6,7} were found to have met all predefined AJCC inclusion and none of the exclusion criteria. Table 48.6 presents information

48. Breast

about these two models. One tool, CancerMath, looked promising, but not all the criteria could be evaluated with the available information in the scientific article and on the author's website.

TABLE 48.6. Prognostic tools for breast cancer that met all AJCC quality criteria

Approved Prognostic Tool	Web Address	Factors Included in the Model
Adjuvant! Online	www.adjuvantonline.com/	Tumor size, number of positive lymph nodes, ER status, age, menopausal status, comorbidity, adjuvant therapy
PREDICT-Plus	www.predict.nhs.uk/predict.html	Age, number of positive lymph nodes, tumor size, tumor grade, mode of detection, chemotherapy, hormone therapy; separate models for ER-negative and ER-positive; HER2 added in PREDICT-Plus

Adjuvant! Online⁴ is primarily a tool to assist in making decisions about adjuvant therapy for women with early-stage breast cancer. Outcome estimates are made from projections based on U.S. population-based SEER data, and adjuvant therapy efficacy estimates are from randomized trial overviews. These probability estimates are combined according to a proprietary system. Input data used to predict outcomes are periodically updated. PREDICT-Plus⁷ was developed to predict outcome in women treated for early breast cancer in the United Kingdom. Estimates are based on a Cox proportional hazards regression model fit to data from a population-based registry. Both tools were externally validated with good calibration and acceptable levels of predictive accuracy.

Recommendations for Clinical Trial Stratification

The authors have not provided any recommendations for clinical trial stratification at this time.

Bibliography

1. Halabi S, Owzar K. The importance of identifying and validating prognostic factors in oncology. Paper presented at: Seminars in oncology2010.
2. Kattan MW, Hess KR, Amin MB, et al. American Joint Committee on Cancer acceptance criteria for inclusion of risk models for individualized prognosis in the practice of precision medicine. *CA: a cancer journal for clinicians*. 2016.
3. Moons KG, de Groot JA, Bouwmeester W, et al. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. *PLoS medicine*. 2014;11(10):e1001744.

48. Breast

4. Ravdin PM, Siminoff LA, Davis GJ, et al. Computer program to assist in making decisions about adjuvant therapy for women with early breast cancer. *J Clin Oncol*. 2001;19(4):980-991.
5. Olivotto IA, Bajdik CD, Ravdin PM, et al. Population-based validation of the prognostic model ADJUVANT! for early breast cancer. *J Clin Oncol*. 2005;23(12):2716-2725.
6. Wishart GC, Azzato EM, Greenberg DC, et al. PREDICT: a new UK prognostic model that predicts survival following surgery for invasive breast cancer. *Breast cancer research : BCR*. 2010;12(1):R1.
7. Wishart GC, Bajdik CD, Dicks E, et al. PREDICT Plus: development and validation of a prognostic model for early breast cancer that includes HER2. *Br J Cancer*. 2012;107(5):800-807.