
**Goals:** Breast cancer is a heterogeneous disease and many variables have been suggested to be prognostic of patient outcome and potentially also predictive of patients' likelihood to respond to different types of adjuvant systemic therapy. This paper evaluates the level of evidence supporting routinely used prognostic and predictive factors in breast cancer including tumor size and grade, Ki-67, Adjuvant! Online (AOL) and the Nottingham Prognostic Index (NPI). It also discusses the implications of these findings to the clinical management of patients with breast cancer.

**Methods:** A systematic search of the scientific literature written in English was performed using PubMed to identify prospective and retrospective studies reporting results for tumor size and grade, Ki-67, AOL, and NPI as either prognostic or predictive factors in breast cancer patients overall and in particular for patients with estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative tumors. The electronic search identified a total of 750 hits and 186 studies were full-text reviewed.

**Results:** The available evidence based on prospective and retrospective data shows that tumor size, tumor grade and Ki-67 provide prognostic information regarding recurrence risk and breast cancer survival. Likewise, AOL and NPI have been extensively validated as prognostic tools in breast cancer patients. As prognosticators, all five factors satisfy Level II evidence. Their prognostic value in ER positive, HER2 negative early breast cancer remains somewhat uncertain since most of the studies included mixed-patient populations and were of retrospective nature. As regards the prediction of chemotherapy benefit, there is no convincing evidence that any of the five routinely used factors possess significant predictive power.

**Conclusion:** Tumor size and grade, Ki-67, AOL and NPI are significant prognosticators in early-stage breast cancer. There is however no robust evidence supporting these markers as predictive of chemotherapy benefit. The findings of this review highlight the need for well-validated tests that demonstrate predictive ability in order to enable more informed treatment decisions in newly diagnosed patients with early-stage ER positive, HER2 negative breast cancer. Juliette Plu-Favreau and Christer Swedman are employees of Genomic Health International. Stefanie Luthman and Johan Mesterton received funding from Genomic Health International to undertake this study.