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Updated meta-analysis of randomized trials: pathological complete response as a prognostic marker for survival in breast cancer treated with neoadjuvant chemotherapy

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Objective: To present an updated meta-analysis including only randomized clinical trials (RCTs) evaluating the prognostic impact of pathological complete response (pCR) on overall survival (OS) and disease-free survival (DFS) in breast cancer patients treated with neoadjuvant chemotherapy, expanding on previous meta-analyses that combined RCTs and real-world evidence data. **Methods:** A systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. RCTs reporting pCR after neoadjuvant chemotherapy and survival outcomes (OS and DFS) were included. Hazard ratios (HR) and 95% confidence intervals (CI) were extracted or estimated. Heterogeneity was assessed using the I^2 statistic, and publication bias was evaluated through funnel plots, Egger's, and Begg's tests. The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO), under CRD42024558811. **Results:** Thirteen RCTs (n=6,977 patients) were included; pCR was significantly associated with improved OS (15% higher survival) and DFS (45% higher survival) compared to non-pCR patients. The benefit was greater in triple-negative breast cancer (TNBC) and human epidermal growth factor receptor-type 2 (HER2)-positive subtypes. In TNBC, pCR was linked to a 45% increase in OS and a 71% increase in DFS; in HER2-positive tumors, pCR was associated with a 13% increase in OS and a 23% increase in DFS. The pooled analysis showed significant associations (OS: Z=10.3, p=0.03; DFS: Z=20.2, p=0.02). Moderate-to-high heterogeneity was observed (OS: I^2=60%; DFS: I^2=75%). **Conclusion:** This updated meta-analysis, based exclusively on RCTs, confirms that pCR is a strong prognostic marker for survival in early-stage breast cancer, especially in TNBC and HER2-positive subtypes, providing robust evidence beyond previous analyses that mixed RCTs with real-world evidence.

Keywords: breast neoplasms; neoadjuvant therapy; pathologic complete response; randomized controlled trial; survival rate.