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Baseline absolute lymphocyte count as a prognostic indicator in advanced or metastatic breast cancer: a systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - Jiaxing Maternity and Child Health Care Hospital.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 July 2024 and was last updated on 10 July 2024.

INTRODUCTION

Review question / Objective This study used meta-analysis to examine the role of baseline absolute lymphocyte count (ALC) in the prognosis of advanced breast cancer (ABC) or metastatic breast cancer (MBC).

Condition being studied A comprehensive search encompassing PubMed, The Cochrane Library, Embase, and Web of Science databases was undertaken to identify and screen literature based on predefined inclusion and exclusion criteria. Progression-free survival (PFS), time to treatment failure (TTF), post-progression survival (PPS), and overall survival (OS) were selected as outcome measures.

METHODS

Search strategy The search strategy employed in PubMed was based on the following search string: ((Breast Neoplasms[Mesh]) OR (((((Breast Tumors[Title/Abstract]) OR (Mammary Cancers[Title/Abstract])) OR (Breast Carcinomas[Title/Abstract])) OR (Breast Malignant Neoplasms[Title/Abstract])) OR (Breast cancer[Title/Abstract])))) AND (Absolute lymphocyte count[Title/Abstract]). The retrieval approach combined subject words and free words. Simultaneously, a meticulous manual retrieval approach was employed to meticulously trace and analyze the references included in the selected studies.

Participant or population Advanced breast cancer (ABC) or metastatic breast cancer (MBC).

Intervention The baseline ALC thresholds applied in the studies were 1500/μL, 1258/μL, and 1000/μL. Baseline ALC is determined using laboratory data obtained before the initiation of treatment, ensuring that patients have not yet been affected by myelotoxicity from treatments, particularly chemotherapy. Therefore, baseline ALC may provide a more accurate representation of the immune status of the patient.

Comparator Advanced breast cancer (ABC) or metastatic breast cancer (MBC).

Study designs to be included All studies were designed as retrospective cohort studies.

Eligibility criteria The inclusion criteria for this study were as follows: (1) publication in the English language; (2) cohort studies; (3) focus on the correlation between baseline ALC and ABC or MBC; (4) provision of outcome indicators such as hazard ratio (HR) and 95% confidence interval (CI). Exclusion criteria were as follows: (1) reviews, case reports, animal studies, conference abstracts, and other studies that did not meet the specified requirements; (2) studies where data extraction was not possible; (3) studies containing repeated data; (4) studies in which no specific cut-off point for baseline ALC threshold is mentioned.

Information sources A comprehensive search for relevant articles from four databases was carried out, namely PubMed (https://pubmed.ncbi.nlm.nih.gov/), The Cochrane Library (https://www.cochranelibrary.com/), Embase (www.embase.com/), and Web of Science (https://www.webofknowledge.com/), spanning from the inception of the databases to June 2023.

Main outcome(s) A meta-analysis of 14 studies, involving 2540 patients and employing Review Manager 5.3 and Stata 14.0, was conducted. Notably, 12 of these studies originated from Japan. The findings indicated that patients with ABC or MBC exhibiting high ALC had significantly improved PFS, TTF, PPS (hazard ratio [HR] = 0.53, 95% confidence interval [CI]: 0.45–0.62, P < 0.00001; HR = 0.57, 95% CI: 0.51–0.64, P < 0.00001), and OS (HR = 0.44, 95% CI: 0.33–0.58, P < 0.00001; HR = 0.68, 95% CI: 0.60–0.77, P < 0.00001) juxtaposed with low ALC individuals. These findings were corroborated by both univariate and multivariate analyses. Furthermore, subgroup analysis based on breast cancer subtype unveiled that high ALC was associated with prolonged PFS (HR = 0.35, 95% CI: 0.21–0.56, P < 0.0001), TTF, and PPS (HR = 0.45, 95% CI: 0.29–0.71, P = 0.0006) in both human epidermal growth factor receptor 2 (HER-2)-positive and -negative ABC or MBC patients. Additionally, high ALC correlated with prolonged OS in all BC subtypes (HR = 0.73, 95% CI: 0.61–0.88, P = 0.0008) and HER-2-negative ABC or MBC patients (HR = 0.65, 95% CI: 0.55–0.78, P < 0.00001). Subgroup analysis was conducted on chemotherapy regimens, with and without eribulin. Despite variations in chemotherapy regimens, patients with ABC or MBC and high ALC exhibited longer PFS and PPS (HR = 0.45, 95% CI: 0.30–0.67, P < 0.0001), PFS and TTF (HR = 0.39, 95% CI: 0.20–0.78, P = 0.008), and OS (HR = 0.71, 95% CI: 0.62–0.82, P < 0.00001; HR = 0.5, 95% CI: 0.35–0.70, P < 0.0001).

Quality assessment / Risk of bias analysis The quality of the included studies was assessed utilizing the Newcastle–Ottawa scale (NOS).

Strategy of data synthesis Data analysis was conducted employing the inverse variance method utilizing both Review Manager (version 5.3; Cochrane) and Stata (version 14.0; StataCorp LP).

Subgroup analysis Subgroup analysis was conducted to investigate factors affecting heterogeneity and to evaluate the impact of grouping factors on the results.

Sensitivity analysis Heterogeneity between studies was assessed utilizing Cochran's Q test and the I2 test . P >0.10 or I2 <50% indicated low heterogeneity among the studies, and the fixed-effect model was utilized for data analysis. In addition, P 50% suggested significant heterogeneity among the studies, prompting the utilization of the random-effects model.

Country(ies) involved China.

Keywords Advanced breast cancer, metastatic breast cancer, absolute lymphocyte count, eribulin, meta-analysis.

Contributions of each author

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