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Review

Axillary lymph node dissection versus sentinel lymph node biopsy alone for early breast cancer with sentinel node metastasis: A meta-analysis

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Abstract

Background: In early breast cancer patients with sentinel node metastasis, the effect of axillary lymph node dissection (ALND) is controversial. The purpose of this study is to compare the safety and efficacy of sentinel lymph node biopsy (SLNB) alone versus ALND in patients with early breast cancer and sentinel node metastasis.

Methods: We searched PubMed, Embase, Web of Science, and Cochrane Library databases from 1965 to February 2014. All data were analyzed using Review Manager Software 5.2.

Results: 12 studies, which included 130,575 patients from five randomized controlled trials and seven observational studies, met our inclusion criteria. 26,870 early breast cancer patients underwent SLNB alone and 103,705 underwent ALND. Patients underwent ALND had more paresthesia (risk ratio [RR] 0.26, 95% confidence interval [CI] 0.20–0.33; $p < 0.01$) and lymphedema (RR 0.28, 95% CI 0.20–0.41; $p < 0.01$) than those had SLNB alone. There were no significant differences in overall survival (hazard ratio [HR] 0.95, 95% CI 0.85–1.06; $p = 0.35$), disease-free survival (HR 1.00, 95% CI 0.98–1.02, $p = 0.96$), and locoregional recurrence (RR 0.92, 95% CI 0.59–1.44; $p = 0.73$).

Conclusion: Current evidence indicates that axillary dissection may be omitted in early breast cancer patients with sentinel lymph metastasis.

Keywords: Axillary lymph node; Breast cancer; Dissection; Sentinel lymph node

Introduction

Breast cancer is the most common cancer and the second only to lung cancer as a cause of cancer death, with an estimated 232,340 new cases and 39,620 died of the disease among American women in 2013. Although about 1 in 8 American women will develop breast cancer in her lifetime,[1] the mortality appears to be decreasing due to early detection and more effective treatment. About 36% women diagnosed with breast cancer undergo mastectomy with axillary lymph node dissection (ALND).[2] Although reliably identifies nodal metastasis and maintains regional control,[3] ALND leads to a significant morbidity such as seroma, lymphedema, paresthesia, infection and pain from intercostal and intercostal-brachial nerve injury.[4] If the sentinel lymph node is negative, the axillary nodes are most probably not involved and ALND should not be performed in breast cancer patients.[5] Sentinel lymph node biopsy (SLNB) was introduced for breast cancer in the early 1990s as a method to predict the status of the axillary nodes.[6] Compared with ALND, SLNB alone has been

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demonstrated to decrease unnecessary complications, shorter hospital stay and improve the quality of life of patients.[7,8]

The current NCCN guidelines recommend that the sentinel lymph node-negative breast cancer patients do not require ALND.[9] However, the effect of ALND in sentinel lymph node-positive early breast cancer is controversial in previous studies.[10–12] Moreover, due to small sample size, these studies were not adequately powered to detect whether ALND can be omitted in early breast cancer patients with positive sentinel lymph. Therefore, in order to provide the latest and most convincing evidence, we systematically reviewed the current available studies to compare the safety and efficacy of SLNB alone versus ALND in early breast cancer with sentinel node metastasis. Overall survival, disease-free survival, locoregional recurrence and adverse events were assessed with meta-analytical methods.

Materials and methods

Study selection

We conducted a comprehensive literature search of PubMed, Embase, Web of Science, and Cochrane Library databases from 1965 to February 2014. The following MeSH search headings were used: “sentinel lymph node”, “axillary lymph node”, “metastasis”, “dissection” and “breast cancer”. The related-articles function was used to broaden the search, and all abstracts, articles, and citations were reviewed without language restriction. When the patient’s material was reported more than once, we selected the article with the most complete data in this meta-analysis. If the applicability of an article could not be determined by the title or abstract alone, the full text would be reviewed. Any disagreements were arbitrated by the corresponding author.

Study inclusion and exclusion criteria

These studies would be selected if they fulfilled the following inclusion criteria: (1) Design: randomized controlled trials (RCTs) and observational studies. (2) Patients: clinical T1 or T2 N0 M0 breast cancer women with sentinel lymph node metastasis. (3) Intervention: SLNB alone (4) Comparison: ALND. (5) Outcomes: overall survival, disease-free survival, locoregional recurrence and adverse events. Exclusion criteria: Studies evaluated less than 30 patients, abstracts, letters, editorials and expert opinions, reviews without original data, meta-analysis, and case reports.

Data extraction and management

Two authors independently extracted data from the inclusion studies. The following information was extracted from each study: first author, year of publication, type of study, patient characteristics, tumor stage, number of positive sentinel lymph nodes, tumor grade, type of histology, follow-up, and the outcomes. Agreement regarding study inclusion was assessed using the Cohen kappa statistic.

Types of outcome measures

The primary outcomes evaluated in this review were overall survival, disease-free survival, and the incidence rate of locoregional recurrence, which was defined as recurrence in the axillary, supraclavicular or internal mammary nodes. The secondary outcomes were adverse events (infection, axillary seroma, paresthesia, and lymphedema).

Quality assessment

We used the Cochrane Risk of Bias Tool to assess the risk of bias for each RCT.[13] This tool includes six specific domains: selection bias, performance bias, detection bias, attrition bias, reporting bias and other bias. Quality assessment of the observational studies were assessed using the Newcastle−Ottawa Scale.[14] A star rating from 0 to 9 was allocated to each study based on the patient’s selection criteria, comparability of cases and controls on the basis of the design or analysis, and the exposure. Studies achieving more than 7 stars were considered to be of higher quality. Two reviewers independently assessed the quality of the included studies. Discrepancies were re-examined, and consensus was reached by discussion.

Statistical analysis

The data were analyzed by the Review Manager software 5.2 (updated by the Cochrane Library for Systematic Reviews). Hazard ratio (HR) was used as a summary statistic for censored outcomes (overall survival and disease-free survival) as described by Parmar and colleagues.[15] The logHR and its standard error were required for each study in the meta-analysis. We calculated the logHR using the reported HR and confidence interval (CI). We extracted HR using the generic inverse variance method available. The risk ratio (RR) was used to analyze dichotomous variables, such as localregional recurrence and adverse events. Heterogeneity among studies was evaluated by the I-squared statistic (I^2). The I^2 measures the extent of inconsistency among studies and is interpreted as approximately the proportion of total variation in study estimates. I^2 of less than 25% is considered as low heterogeneity, 25−50% as moderate heterogeneity, and more than 50% as high heterogeneity.[16] If the p value was more than 0.1, the fixed-effects model would be reported, otherwise, the random-effects model would be used. Subgroup analysis was performed according to the type of study (RCTs versus observational studies). Sensitivity analysis (excluding 1 or more studies) was used to explore possible sources of heterogeneity