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Meta Analysis

Can axillary radiotherapy replace axillary dissection for patients with positive sentinel nodes? A systematic review and meta-analysis

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Abstract

Objective: To compare the efficacy of axillary radiotherapy (ART) with that of completion axillary lymph node dissection (cALND) in clinically node-negative breast cancer patients with a positive sentinel lymph node.

Methods: A literature search was performed in PubMed, EMBASE and Cochrane Library by using the search terms "breast cancer", "sentinel lymph node biopsy", "axillary radiotherapy" or "regional node irradiation" for articles published between 2004 and 2016. Only randomized controlled trials that included patients with positive sentinel nodes were included in the meta-analysis.

Results: Two randomized controlled trials and three retrospective studies were identified. The reported overall survival rate (hazard ratio [*HR*] = 1.09, 95% confidence interval [*CI*]: 0.75−1.43, *P* = 0.365), disease-free survival rate (*HR* = 1.01, 95% *CI*: 0.58−1.45, *P* = 0.144), and axillary recurrence rate (1.2% and 0.4%, and 1.3% and 0.8%, respectively) were similar in both groups. The absence of knowledge on the extent of nodal involvement in the ART group appeared to have no major impact on the administration of adjuvant systemic therapy.

Conclusions: ART is not inferior to cALND in the patients with clinically node-negative breast cancer who had a positive sentinel lymph node. Information obtained by using cALND after SLNB may have no major impact on the administration of adjuvant systemic therapy.

Keywords: Breast cancer; Sentinel lymph node biopsy; Completion axillary lymph node dissection; Axillary radiotherapy; Meta-analysis

Introduction

Sentinel lymph node (SLN) biopsy (SLNB) is accepted as an alternative method to evaluate axillary lymph node status in clinically node-negative breast cancer.[1] Completion axillary lymph node dissection (cALND) is the standard of care for patients with a positive SLNB. A cALND provides additional

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prognostic information, optimizes regional control and potentially improves overall survival (OS).[2,3] However, some patients do not need cALND because of a low risk of residual disease or recurrence. In 15–20% of cases, a cALND leads to long-term complications such as pain, paresthesia due to intercostobrachial nerve injury, impairment of shoulder function, or lymphedema.[4,5] The 2009 St. Gallen Consensus Panel did not recommend the use of cALND in patients with SLN-detected micrometastases or isolated tumor cells, and those who had small and well-differentiated tumors.[6]

Axillary radiotherapy (ART) is a possible alternative for cALND. Some retrospective studies examined the use of ART to decrease the rate of regional failure in node-positive disease.[7–9] However, it is unclear if it could be used as a therapeutic substitute for cALND in patients with low burden of axillary disease. A prospective study was conducted at the Massachusetts General Hospital and Brigham and Women's Hospital in Boston between 2000 and 2004 to examine breast plus axillary radiotherapy after positive SLNB.[10] Forty-eight of the 73 patients in the study had SLN macrometastasis, but only one had more than one positive SLN. With a median follow-up of 32 months, one patient had axillary failure 17 months after treatment; she was disease-free 2.5 years after salvage dissection. The AMAROS trial[11] was a prospective randomized controlled trial (RCT) involving patients with cT1-2N0 breast cancer up to 5 cm and clinically node-negative axilla who underwent either breast conservation or mastectomy with SLNB. Of the patients with positive lymph nodes, 744 received cALND and 681 received ART. After 5 years of follow-up, the axillary recurrence rate (ARR) was lower in the cALND than in the ART group. No significant differences in disease-free survival (DFS) rate and OS rate were found between the two groups. The incidence rate of lymphedema in the cALND group was twice that in the ART group.[12] The OTOASOR trial,[13] another prospective RCT, conducted between August 2002 and June 2009, involved 244 patients who were randomized to undergo cALND and 230 patients who were randomized to undergo SLNB plus ART. The mean length of follow-up was 70 months, and the ARRs were 1.6% and 1.7% in the cALND and ART groups, respectively ($P < 0.05$). The 5.8-year OS rates were 84.9% and 91.2%, and the 5-year DFS rates were 79.9% and 85.6% in the cALND and ART groups, respectively. The 5-year follow-up data of the OTOASOR trial suggest that ART without cALND does not increase the risk of axillary failure in patients with positive SLNs.

The aim of this review was to compare the efficacy of ART with that of axillary lymph node dissection (ALND) in clinically node-negative breast cancer patients with a positive SLN.

Methods

Literature search

A literature search was performed in PubMed, EMBASE, and the Cochrane Library by using the search terms “breast cancer”, “sentinel lymph node biopsy”, and “axillary radiotherapy or regional node irradiation” from 2004 to 2016. Articles published in English alone were considered. The complete search strategy is presented in Fig. 1 according to the PRISMA statement.[14] The search was performed independently by two reviewers who selected potentially relevant papers based on the title and abstract.

Review inclusion and exclusion criteria

Two persons independently reviewed abstracts and full-text articles. Eligibility criteria for the studies were defined a priori and are presented in Table 1. Studies whose populations had positive SLNs and those that compared ART with cALND were included. Only RCTs were included in the meta-analysis. A secondary analysis included some observational studies. Studies that included negative SLNs or SLNB alone were excluded from this study. Several studies such as the ACOSOG Z0011 trial, which failed to determine how the positive SLNB was impacting radiation practice patterns, were excluded.

Study selection and quality assessment

The RCTs were assessed with a score assigned for each item identified according to the Consolidated Standards of Reporting Trials (CONSORT) checklist.[15] The studies were assessed for risk of bias according to the *Cochrane Handbook for Systematic Reviews of Interventions*[16] (Table 2).

Outcome measures

The primary outcome measures for this study were OS and DFS, reported as hazard ratios (*HR*s) with confidence intervals (*CI*s), and overall percentage. The *HR*s for DFS and OS in the two studies by Donker et al[12] and