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Review

A meta-analysis of the prognosis in patients with breast cancer with ipsilateral supraclavicular lymph node metastasis versus patients with stage IIIb/c or IV breast cancer

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Abstract

Objective: To systematically evaluate the prognosis in patients with breast cancer with ipsilateral supraclavicular lymph node metastasis (SLNM) versus patients with stage IIIb/c or IV breast cancer, so as to provide evidence for clinical practice and research.
Methods: Computer retrieval from PubMed, Cochrane Libratory, CNKI (China National Knowledge Infrastructure), CBM and Wanfang Database with the assistance of other retrieval tools. All the studies evaluating the prognosis in patients with breast cancer with ipsilateral supraclavicular lymph node metastasis versus patients with stage IIIb/c or IV breast cancer were collected. Quality assessment was performed for the included data based on the quality assessment criteria appropriate for this study. Meta-analysis was performed using RevMan 5.3 software.
Results: A total of four references (1277 patients) were included. Assessment of influences on prognosis: As compared to the stage IIIb/c group, the 5-year survival rate was slightly lower in the SLNM group (relative risk (*RR*) 0.79; 95% confidence interval (*CI*) 0.59−1.06; $Z = 1.55$, $P = 0.12$), but there was no statistical significance; in contrast, the 5-year survival rate was significantly increased in the SLNM group as compared to the stage IV group ($RR = 2.70$; 95%*CI*: 1.36−5.37; $Z = 2.84$, $P = 0.005$). As compared to the stage IIIb/c group, the 5-year disease-free survival rate was lower in the SLNM group ($RR = 0.65$; 95%*CI*: 0.40−1.05; $Z = 1.75$, $P = 0.08$); however, there was no statistical significance.
Conclusions: In patients with advanced breast cancer receiving combined therapy, the prognosis in patients with breast cancer with ipsilateral SLNM was significantly better than in those with stage IV breast cancer, and slightly worse than those with stage IIIb/c breast cancer. However, with the scarcity and poor quality of these observational studies, the long-term prognosis remains to be further verified in large-sample, high-quality studies.

Keywords: Breast cancer; Supraclavicular lymph node metastasis; Ipsilateral; Meta-analysis

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The incidence of breast cancer with ipsilateral supraclavicular lymph node metastasis (SLNM) without distant metastasis is as low as 1−4%.[1] In the 5th edition of the AJCC-TNM breast cancer staging system, the stage assigned to breast cancer with SLNM was modified from N3 to M1, possibly because ipsilateral SLNM in breast cancer is typically a sign of a poor prognosis as the majority of the patients would develop distant metastasis within one year.[2−4] In the early 21st century, Brito et al[5] reported for the first time a significantly better prognosis in patients with breast cancer with ipsilateral SLNM than in those with distant metastasis after receiving combined therapy including surgery, radiotherapy and chemotherapy. In the 6th edition of the AJCC-TNM breast cancer staging system, breast cancer with ipsilateral SLNM, which was no longer regarded as distant metastasis, was reclassified as stage IIIc instead of stage IV.[6,7] Nevertheless, such a staging has not been adequately evidenced, and no consensus has yet been reached on the selection of the treatment regimen for breast cancer with ipsilateral SLNM. Through meta-analysis of the literature on breast cancer with ipsilateral SLNM, this study was intended to explore its clinical relevance, in an attempt to provide references for further clinical practice and research.

Methods

Our meta-analysis was conducted in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-analysis' (PRISMA) guidelines.[8]

Reference search strategies

Computer retrieval for the references published from 1 January, 2000 to 21 December, 2015 was performed from Pubmed, Cochrane Library, CNKI (China National Knowledge Infrastructure), CBM and Wanfang Data. All the studies comparing the prognosis in patients with breast cancer with ipsilateral SLNM vs. stage IIIb/c or IV breast cancer were collected by manual tracing or internet searching at Google Academics. Search items including Medical Subject Headings (MeSH) words and text words were related to breast cancer, ipsilateral supraclavicular lymph node metastasis, outcome and prognosis. References published during the years 2000−2015 and written simply in English were to be collected. To indentify more studies, we manually searched the reference lists of selected articles or review articles. We also contacted authors for additional data if necessary.

Inclusion criteria

Studies that satisfied the following criteria were included in this meta-analysis: 1) prospective or retrospective studies with the follow-up duration more than five years; 2) breast cancer patients with ipsilateral SLNM without distant metastasis and patients with stage IIIb/c or IV breast cancer as evidenced by imaging or pathological diagnosis; 3) reference must provide 5-year overall survival (OS) rate or 5-year disease-free survival (DFS) rate between two groups; 4) reference must have a sample size of at least 30 patients in each group. References published on the same population were to be reduced so that only the study with the best quality or the largest sample size was to be included in the study.

Data extraction

The references were selected by two reviewers (Xu-Hong Liu, Lei Zhang) independently according to the pre-defined inclusion criteria. Discrepancies were resolved through discussion with Bo Chen. The following data were extracted in each study, including the first author's name, the year of publication, country, the follow-up duration, method of outcome assessment, the diagnosis measurement of breast cancer, whether combined therapy was used or not, and the sample size.

Reference quality assessment

Our meta-analysis used the Newcastle−Ottawa Quality Assessment Scale (NOS) to evaluate the quality of each included study.[9] The studies were assessed in three areas: the selection of exposed and unexposed participants; the comparability of the groups; and the assessment of the outcome. Total scores of each study range from one to nine; with nine being the maximum and $\geq$7 scores was considered high quality.

Statistical analyses

An I^2 test was used for evaluating heterogenicity between different studies' results. When statistical homogenicity was found between different studies ($I^2 < 50\%$), a fixed-effect model was used for analysis; a random-effect model was used when statistical heterogenicity was found between different studies ($I^2 \geq 50\%$).[10] Potential publication bias was evaluated by a funnel plot. All analyses were performed with RevMan 5.3 software.