Mortality comparison between axillary lymph node dissection (ALND) and sentinel lymph node biopsy (SND) among breast cancer patients: A meta-analysis and systematic review study

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ABSTRACT

Introduction: Axillary lymph node dissection (ALND) is a crucial surgical procedure for breast cancer. It has guaranteed locoregional control of the disease, guided adjuvant therapy, and functioned as a staging tool. However, over the past 25 years, a more conservative approach has become the standard for surgical management of the axilla. While accurate axillary staging can be achieved with ALND, there is a risk of pain, lymphedema, numbness, and restricted shoulder movement.1–3

Because sentinel lymph node biopsy (SNB) is less invasive and less morbid than ALND, it has become the standard surgical procedure for axillary staging of clinically node-negative breast cancer. Until recently, the accepted method in cases of macro-metastatic sentinel lymph node (SLN) was ALND.1,4

In the past ten years, researchers have questioned the usefulness of ALND in patients with metastatic sentinel lymph nodes, laying the groundwork for the surgical management of node-positive patients to forego axillary dissection now. The purpose of this study was to compare the mortality rates of patients with breast cancer who underwent SNB and ALND procedures.

METHODS

Eligibility criteria

Our review includes randomized controlled trials of breast cancer patients undergoing ALND or SNB surgical procedures. A systematic literature search was performed from PubMed on December 2023 to search for articles reporting on survival rates between ALND vs SNB among breast cancer patients. The data obtained then underwent statistical evaluation, and a meta-analysis was conducted using Review Manager 5.4. In order to represent primary outcomes, the risk ratio was estimated using an inverse variance technique with a random-effects model. Heterogeneity was presented with total values, 95% confidence intervals (CI), and I2 values.

Results: As many as 208 articles were found in the PubMed database search, and only six studies were included in this study. The six included trials all used chemotherapy and radiotherapy for systematic treatment. The length of follow-up varied from 33 months to 15 years. The total number of patients in the trials was 3,585, and the study period was from 2011 to 2023. The pooled analysis of the mortality outcomes showed that the heterogeneity of the data was low (I2 21%, p = 0.4). In the pooled analysis, the mortality of patients with SNB for surgical treatment was not significantly different compared to patients with ALND (OR:0.88; 95% CI:0.65-1.19).

Conclusion: The mortality of patients undergoing SNB and ALND does not differ significantly, according to this pooled study. It demonstrates that the group without axillary dissection had a primary survival outcome that was not inferior to that of the dissection group.

Keywords: axillary lymph node dissection, breast cancer, mortality, sentinel lymph node biopsy.


INTRODUCTION

Axillary lymph node dissection (ALND) is a crucial surgical procedure for breast cancer. It has guaranteed locoregional disease control, guided adjuvant therapy, and functioned as a staging tool. However, over the past 25 years, a more conservative approach has become the standard for surgical management of the axilla. While accurate axillary staging can be achieved with ALND, there is a risk of pain, lymphedema, numbness, and restricted shoulder movement.1–3

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techniques. Populations are breast cancer patients in the first and second stages. The outcomes were mortality of breast cancer patients. Excluded studies included non-RCT studies.

**Information sources**
A systematic computerized literature search was performed from PubMed on December 2023 to search for articles reporting on survival rates between ALND vs SNB among breast cancer patients. The search keyword includes terms related to PICO. The population (P) was breast cancer patients; the intervention (I) was SNB; the control (C) was ALND; and the outcomes (O) as mortality.

**Study selection process**
The 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in the conduct of this systematic review and meta-analysis. The keywords used to search the database are compiled in Table 1.

**Data extraction**
Eligibility criteria were used to screen all studies from the PubMed database that matched the keyword. Screening for titles and abstracts was conducted independently based on these criteria. Duplicate studies were removed.

A screening, eligibility, and literature search were carried out by two independent reviewers. Using the inclusion criteria as mentioned earlier, they separately screened abstracts and titles. Furthermore, each reviewer assessed each study separately to determine its eligibility. Disagreements between reviewers were settled through dialogue. Data on authors, publication years, study countries, sample sizes, mean population ages, surgical treatments, adjuvant systemic management, radiation management, events, overall survival rate, hazard ratio, follow-up times, and side effects were extracted by the reviewers from all of the studies.

After that, the data were statistically evaluated, and Review Manager 5.4 was used for a meta-analysis. The studies were divided into groups according to whether they underwent ALND or SNB surgery. The risk ratio was estimated using an inverse variance technique with a random-effects model to represent primary outcomes. We then presented the results with total values, 95% confidence intervals (CI), and I values to analyze heterogeneity. I2 values of 25%, 50%, and 75%, respectively, are linked to low, moderate, and high heterogeneity. Significant heterogeneity is indicated by I2 values higher than 50%. To help with the interpretation of the findings, we employed a forest plot.

**Risk of bias assessment**
The PRISMA 2020 guidelines were used for the literature search. We searched databases for studies, discarded duplicates, assessed inclusion criteria and determined eligibility. As all the papers ready for review were RCTs, we used funnel plot assessment. Inspection level was two-sided and considered significant if P<0.05.

**Characteristics of studies**
Table 2 presents a summary of the included studies. Randomized controlled trials comprised every study incorporated into the pooled analysis and review. This systematic review excluded meta-analyses, observational studies, and editor’s letters. Radiotherapy and chemotherapy were the standardized treatments used in all six of the included trials. The follow-up periods ranged from 33 months to 15 years. Three thousand five hundred eighty-five patients participated in the trials, which ran from 2011 to 2023.
Table 2. Characteristics of every included study

<table>
<thead>
<tr>
<th>Number</th>
<th>Author</th>
<th>Year</th>
<th>ALND</th>
<th>SNB</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Giuliano⁷</td>
<td>2011</td>
<td>52</td>
<td>49</td>
<td>5 Years</td>
</tr>
<tr>
<td>2</td>
<td>Canavese⁶</td>
<td>2016</td>
<td>13</td>
<td>115</td>
<td>10 Years</td>
</tr>
<tr>
<td>3</td>
<td>Sávolt⁷</td>
<td>2017</td>
<td>34</td>
<td>240</td>
<td>8 Years</td>
</tr>
<tr>
<td>4</td>
<td>Galimberti⁸</td>
<td>2018</td>
<td>45</td>
<td>465</td>
<td>58</td>
</tr>
<tr>
<td>5</td>
<td>Tinterri⁹</td>
<td>2022</td>
<td>4</td>
<td>439</td>
<td>34 Months</td>
</tr>
<tr>
<td>6</td>
<td>Tinterri¹⁰</td>
<td>2023</td>
<td>2</td>
<td>111</td>
<td>33 Months</td>
</tr>
</tbody>
</table>

Outcome
The mortality analysis comprised six studies in total. As many as 3,585 cancer patients received surgery—SNB or ALND—at random. This report presents the mortality odds ratio (OR) between patients who underwent SNB and those who underwent ALND. The data heterogeneity was relatively low, according to the pooled analysis of the mortality outcomes ($I^2=21\%$; $p=0.4$). The range of the OR was 0.65 to 1.19. Patients with SNB for surgical treatment had a non-significantly higher death rate in the pooled analysis when compared to patients with ALND (OR=0.88; 95%CI: 0.65-1.19). The forest plot is shown in Figure 2.

Funnel plot
The funnel plots of 6 studies using the odd ratio result show that all studies are symmetrically distributed, indicating that publication bias in this study is low to non-existent (Figure 3).

Discussion
After lung cancer, breast cancer is the second most common cause of death for women in the United States with cancer. According to the American Cancer Society’s predictions, 41,070 Americans will lose their lives to breast cancer in 2017, and 255,180 Americans will receive a diagnosis of the disease. Patients with invasive or non-invasive breast cancer have a wide range of intricate treatment options.¹¹

Even today, the ALND procedure remains the gold standard for evaluating axillary lymph node metastases and is crucial to the management of breast cancer. Patients benefit from the ALND procedure because it increases overall survival following the surgical excision of microscopic nodal metastases.¹²

Recent years have seen debate surrounding the use of ALND, with the underlying morbidity that follows ALND without directly affecting survival being the source of the controversy. Arm lymphedema, numbness in the arm and chest wall, restricted arm movement, pain, and infection in the arm and chest wall are among the complications that can arise from breast cancer surgery. The NCCN revised its recommendations in Version 1 of The 2017 NCCN Breast Cancer Guidelines regarding when patients with stages I, II, and IIIA breast cancer can forego ALND.¹³–¹⁶

Breast cancer treatment and staging have undergone significant change as a result of the SNB procedure. As an alternative to ALND for breast cancer staging, this procedure has been introduced in breast surgery centers. This less intrusive technique improves morbidity and postoperative recovery. SNB is a minimally invasive and reasonably reliable technique for determining the status of the lymph nodes in a patient’s region when the patient has clinically node-negative invasive breast cancer, according to recent studies. It might be just as accurate as traditional axillary lymph node dissection for determining the status.
of axillary lymph nodes in patients with breast cancer.17-19

A paradigm shift in axillary management has occurred as a result of the past 20 years’ focus on less invasive surgeries for the treatment of early breast cancer. According to the findings of the clinical trials SINODAR-ONE and ACOSOG Z0011, cN0 patients with up to two macroscopically positive SLNs who undergo BCS may be able to avoid ALND. The clinical utility of ALND for mastectomy patients has not been established. It is still unclear whether these results can be safely applied to patients undergoing mastectomy with one or two macro metastatic SLNs, and there is ongoing controversy regarding the downsizing of axillary surgery in these patients.20

Omitting the axillary dissection even when the disease burden is low has been recommended since 2013 after the Z0011 study and the 5-year results of this trial. Even though only 35% of patients had micro metastatic sentinel nodes and most patients had macro metastases, after early and long follow-up, it was found that no differences were found in locoregional recurrence, and overall survival was non-inferior between the axillary dissection and no axillary dissection.21

Our study included 3,585 cancer patients, which is a large sample size and can represent the expected results. However, the weakness of this study is the limited time of searching for studies and language barriers. This causes the studies that we can include in the analysis to be more limited, so international studies involving more authors will be able to overcome the weaknesses of this study.

CONCLUSION

This systematic review and meta-analysis provide additional high-quality evidence that the omission of the axillary dissection in minimal disease burden patients with sentinel nodes is acceptable. This pooled study showed that the mortality of patients undergoing ALND and SNB is not significantly different. It confirms that the primary outcome of the survival of the group with no axillary dissection was non-inferior compared to the dissection group.

ETHICAL CLEARANCE

Not applicable.

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest in this study publication.

FUNDING

None.

AUTHOR CONTRIBUTIONS

All authors contributed equally to creating the concept of the study, literature searching, data analysis, drafting and revising the paper, gave final approval of the version to be published, and agreed to be accountable for all processes.

REFERENCES


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