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REVIEW

Association of a high versus low number of negative lymph nodes removed with survival and recurrence-free survival after lymph node dissection in breast cancer: a systematic review and meta-analysis of observational studies

Mansour Bahardoust[1,2] · Danyal Yarahmadi[3] · Fatemeh Naseri Rad[3] · Mohammad Mehdikakoienejad[3] · Benyamin Kazemi[3] · Babak Goodarzy[3] · Adnan Tizmaghz[4]

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Abstract
Although most studies have reported that a high number of negative lymph nodes (NLNs) at surgery can be associated with improved overall survival (OS) in patients with breast cancer (BC), the effect size was reported differently in several studies, which may be due to the small sample size of the primary studies. This systematic review and meta-analysis aimed to investigate the association of a high number of NLNs removed during surgery with OS and recurrence-free survival (RFS) in BC patients who are candidates for axillary lymph node dissection. We searched the PubMed, Embase, Scopus, Google Scholar, and Web of Science databases, as well as study references, to identify related articles published from the beginning of 2000 to October 2024. Based on sensitivity analysis, the removal of ≥ 10 NLNs was defined as the high number of NLNs removed group, and the removal of < 10 NLNs was defined as the low number of NLNs removed group. The heterogeneity between studies was assessed using Cochran's Q and I2 tests. Publication bias was assessed using Egger's test. Ultimately, 14 studies encompassing 36,576 BC patients were included. A pooled estimate of 14 studies showed that a high number of NLN removed compared to a low number of NLN removed was significantly associated with improved 5-year OS (HR: 0.82, 95% CI: 0.74, 0.90), I2 = 93.8) and RFS rate (HR:0.76, CI: 0.765, 0.86), I2 = 86.3). A higher number of NLNs removed during surgery in BC patients who are candidates for axillary lymph node dissection appears to be associated with improved OS and RFS.

Keywords Five-year survival rate · Surgery · Breast cancer · Recurrence-free survival

Introduction

Breast cancer accounts for 36% of all cancer cases and is the most commonly diagnosed malignant tumor and the leading cause of cancer-related death in women worldwide [1]. According to recent studies, in 2018, more than 2 million patients were diagnosed with breast cancer, and its incidence and prevalence are increasing worldwide [2, 3]. The incidence of BC is higher in developed countries, and more than half of the cases occur in industrialized countries [4]. Although the improvement and progress of diagnostic and therapeutic methods have improved the survival of patients, BC is still one of the main causes of death from cancer [5, 6]. Studies have estimated that in 2020, more than 685,000 deaths from BC in women were recorded, and BC was the cause of 1 out of every 6 (16%) cancer deaths [6–8].

Mansour Bahardoust and Benyamin Kazemi are equal first authors.

✉ Adnan Tizmaghz
adnan_ti@yahoo.com

1 Department of Epidemiology, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2 Breast Cancer Research Center, Iran University of Medical Sciences, Tehran, Iran

3 School of Medicine, Iran University of Medical Sciences, Tehran, Iran

4 Firoozabadi Clinical Research Development Unit (FACRDU), University of Medical Sciences(IUMS) , Tehran, Iran

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The 5-year survival of breast cancer patients is estimated between 80 and 90% based on various studies [9]. The overall survival (OS) and recurrence-free survival (RFS) rates have improved with the improvement of BC management in recent years [10]. Treatment depends on various factors, including local treatment approaches (such as surgery and radiation therapy) and systemic treatment. Surgical treatment is considered the first line of BC treatment, especially in early BC [10, 11].

The survival of patients after surgery depends on various factors, including demographic characteristics, tumor characteristics (such as tumor stage, metastasis to other organs, pathology, and the number of involved lymph nodes) [5, 12–15]. Therefore, determining the effect of factors that influence patient survival can help predict survival and, consequently, inform better decisions about planning treatment interventions to prevent economic costs [16, 17].

In addition to the role of the number of positive lymph nodes (PLNs) removed, the relationship between the number of negative lymph nodes (NLNs) and patient survival has been reported in recent studies [18–20]. Eliminating a greater number of NLNs could reduce the risk of hidden lesions, potentially improving the prognosis. Therefore, the quantity of NLNs removed may serve as a measure of how appropriate the axillary lymph node dissection is [18]. Resection of high numbers of NLNs compared to low during BC surgery, as in other cancers [21, 22], may be associated with improved postoperative OS and RFS []. Although most studies have reported that a high number of NLNs can be associated with improved patient survival, the effect size has been reported differently across several studies, which may be due to the small sample size of the original studies [23–25].

Therefore, considering the importance of the topic, this meta-analysis was conducted to investigate the association between the number of NLNs removed and overall survival and survival rate in BC patients after surgery.

Methods

Literature search

The aim was to identify observational studies that assessed the association of removing a high number of NLNs compared to a low number on OS and RFS after surgery in patients who are candidates for axillary lymph node dissection. We conducted this systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [26].

Based on the PICO formula (population, intervention, comparator, and outcome), the research question was defined by a team of epidemiologists, oncologists, and oncologist-surgeons, and then the search strategy was determined. Based on mesh terms, we searched the PubMed, Embase, Scopus, Google Scholar, and Web of Science databases, as well as study references, to find related articles from the beginning of 2000 to October 2024. Two independent researchers performed the search.

The general search strategy was defined as follows:

(Breast cancer " OR " Breast Neoplasms" OR " Breast Tumors" OR ‘‘ Breast Tumor" OR " Cancer of Breast" OR " Breast Malignant Neoplasms" OR " Breast Malignant" OR" Breast Malignant Tumor" OR " Mammary Cancer " OR " Human Mammary Neoplasms " OR ‘‘ Breast Carcinoma" OR " Human Mammary Carcinomas " OR " Triple Negative Breast Neoplasms " OR " ER-Negative PR-Negative HER2-Negative Breast Cancer" OR" Triple-Negative Breast Cancers") and (" Negative Lymph Nodes " OR ‘‘ Lymph Nodes" OR " Node, Lymph “) and (" Lumpectomy " OR ‘‘ surgery " OR " surgical resection" OR " resection " OR ‘‘ Mastectomy " OR ‘‘ Lymphadenectomy OR ‘‘ breast conserving surgery" OR" Simple Mastectomies" OR ‘‘ Total Mastectomy’ ’OR" Mammectomies" OR ‘‘ Breast Cancer Lymphedemas" OR" Lymph Node Excision" OR ‘‘ Lymph Node dissection") AND (“ Survival Rate " OR " Survival " OR " Overall Survival " OR " Cumulative Survival Rate " OR" Mean Survival Time “).

Eligibility criteria

The inclusion criteria for this meta-analysis included observational studies (cross-sectional, case-control, or cohort) that investigated the resection of a high number of NLNs versus a low number of NLNs on OS or RFS rates. Studies examining the association between the number of NLNs removed and OS and RFS in BC patients who are candidates for axillary lymph node dissection were included. Studies published from the beginning of 2000 to October 2024, as well as those with a follow-up of at least six months, were also included. Studies that examined the association between NLN count, OS, and RFS in patients who underwent sentinel lymph node biopsy, as well as experimental studies, systematic reviews and meta-analyses, laboratory studies, letters to the editor, and case reports of studies published in non-English languages, were identified as exclusion criteria for this meta-analysis.

The number of NLNs was calculated by subtracting the number of positive lymph nodes from the total number of lymph nodes removed, as defined in various studies. Sensitivity analysis was used to determine the best cutoff for the number of NLNs removed. The results of the sensitivity analysis showed that 10 NLNs had the highest sensitivity and accuracy (AUC: 0.92, 95% 0.86, 0.99).

Screening

After an initial search of all databases by two independent researchers, 1,741 primary studies were identified. Duplicate articles between databases, case reports, letters to the editor, and experimental studies (854) were subsequently removed using EndNote version 22 software. Two independent researchers evaluated the remaining articles based on their titles, research questions, and abstracts. Ultimately, 71 studies were selected for this meta-analysis following a comprehensive evaluation of the full texts of the articles. Finally, fourteen cohort studies were included in this meta-analysis. (Fig. 1).

Data extraction

First, a committee of epidemiologists, oncologists, and oncology surgeons designed the checklist of required variables. The Excel software was used, based on the designed checklist, to extract the desired variables from the primary studies. The desired variables were determined based on a literature review. Two independent researchers extracted the variables in separate files. Then, the third researcher reviewed two files, and the final file was prepared for analysis. A third researcher resolved any differences and disagreements for a variable between the two researchers.

The variables of this systematic review included the first author, the year and city of the study, the study design, the total number of patients studied, the number of patients with BC by study group (high number of NLNs removed and low number), five-year survival separately groups, RFS by groups, median follow-up period, median age, progesterone receptors (PR)+, estrogen receptors (ER)+, human epidermal growth factor receptor 2 (HER2)+, tumor characteristics (tumor classification based on TNM), type of surgical procedure, effect size (hazard ratio (OR) and 95% confidence interval (CI))).

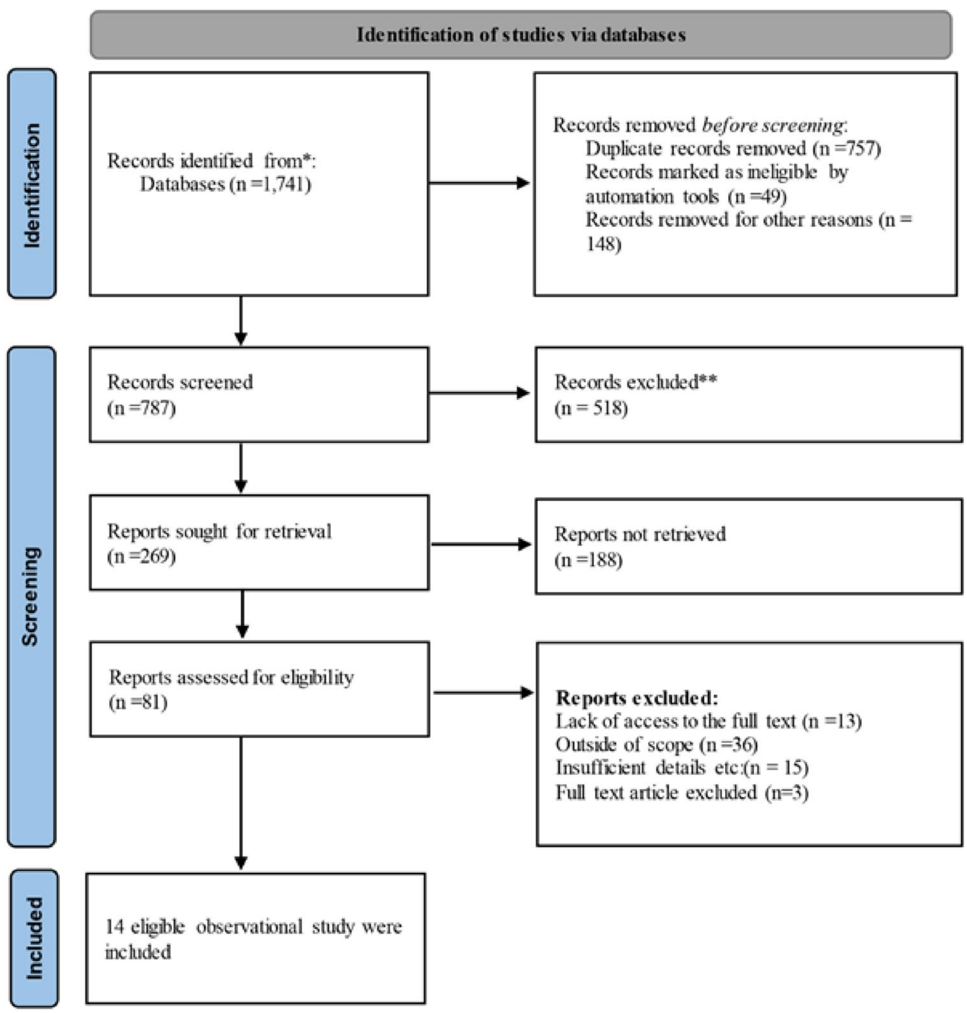

Fig. 1 Flowchart page of studies based on PRISMA 2020

Quality assessment

The Newcastle-Ottawa Quality Assessment Form for Cohort Studies checklist [27] was used to evaluate the quality of cohort studies. This checklist assesses the quality of studies in three key areas: selection, comparability, and result/introduction. Based on the evaluation, points are assigned to each section.

Statistical analysis

The pooled OS and RFS were estimated with the meta-prop command for the groups (harvested NLNs). Pooled estimation of the effect of harvesting a high number of NLNs compared to a low number on OS and RFS was used using the hazard ratio (HR) in the 95% confidence interval (95% CI). The data were analyzed using the random effects method. Cochran's Q and I2 tests were used to check heterogeneity between studies. Egger's test evaluated the publication bias of the studies. Due to the publication bias in studies on RFS, the trim-and-fill method was used to address potential publication bias and its impact. Funnel plots were used to illustrate the publication bias in the studies. Heterogeneity between studies was controlled by meta-regression based on study quality and surgical method. Subgroup analysis was performed based on the surgical method for both outcomes. To estimate the effect size and weight of each study on the overall result, a sensitivity analysis was performed. Data were analyzed with STATA version 17 statistical software.

Results

Fourteen retrospective cohort studies [23–25, 28–37], including 36,576 BC patients, were included in this meta-analysis. The mean age of the patients in this study was 51.4 ± 6.2 years. The mean follow-up of patients after surgery was 5.8 years. Mastectomy was the most common surgical procedure. Most of the studies were conducted in China. The majority of studies were of good or moderate quality.

The overall 5-year OS and RFS rates after surgery were 84.2% and 69.3% respectively. The OS rate was higher in patients with a high number of NLNs removed than in those with a low number of NLNs removed (88.1% vs. 74.6%). The RFS rate was 74.5% and 63.4% in patients with a high number of NLNs removed and a low number of NLNs removed, respectively.

The characteristics of the studies included in this meta-analysis are reported separately in Table 1.

Table 1 The characteristics of the studies included in this meta-analysis

Author	Country	Sample size	NO. ≥10 VS. <10	5-OS Rate ≥10 VS. <10	5-RFS Rate ≥10 VS. <10	Mean follow-up (Year)	Mean Age	Pathology(Well/ Moderate/pool differentiated)	T stage>I	Metastasis	Systemic treatment	ER+	PR+	HER2+	Quality of studies
RL Camp(2000)(39)	USA	101	23/77	84.7/96.3	NA/NA	4.9	59.1	NA	128	79	NA	226	237	NA	Poor
PG Moorman(2001)(25)	USA	911	255/656	85/83	NA/NA	7	58.1	NA	911	NA	911	694	306	NA	Moderate
L Weir(2002)(31)	Canada	2278	NA	82/77	NA/NA	7.5	59.9	295/1028/772	1984	527	810	1226	1125	NA	Good
JK Salama(2005)(35)	USA	1094	851/247	91/82	89/77	4.6	57.2	165/433/213	NA	NA	261	NA	NA	NA	Good
I Blancas(2006)(34)	Spain	1668	851/817	87/74	79/69	5.1	57.1	263/431/167	598	806	1496	719	647	54	Good
SG Wu(2014)(38)	China	605	128/477	79/62	68/42.1	4.5	NA	NA	134	284	NA	320	376	229	Moderate
SG Wu(2015)(32)	China	2515	897/1618	88/78	79/61	5.35	49.8	1319/802/394	1844	NA	NA	1439	1589	804	Moderate
SG Wu(2016)(33)	China	2455	NA	NA/NA	87.5/69.5	5	46.2	1263/769/423	1642	1421	NA	1292	421	666	Good
F Xin(2016)(28)	China	275	103/172	75/48	71/41	4.2	51.3	145/58/72	143	250	258	275	275	275	Moderate
H Wang(2017)(36)	China	16,686	4342/12,344	80.7/66.6	84.3/71.3	8.11	49.5	994/5820/8509	14,024	9346	NA	11,361	9346	NA	Good
J Yang(2017)(26)	USA	929	725/204	95/77	NA/NA	5.6	60.1	318/223/388	NA	NA	NA	544	644	232	Moderate
QX Wang(2018)(37)	China	394	187/207	NA/NA	NA/NA	4.8	52	NA	202	159	NA	NA	NA	NA	Moderate
X Wang (2019)(27)	China	435	NA	87/82	78.2/34.8	NA	53.5	5/354/32	417	42	NA	249	201	57	Moderate
H Wu(2020)(40)	China	6230	3375/2855	NA/NA	91.8/78.2	8.1	58	3495/1665/1070	5552	2225	3657	NA	NA	NA	Moderate

Association between a high versus a low number of NLN removed and the OS

A pooled estimate of 14 studies showed that, adjusted for demographic and tumour characteristics, a high number of NLN removed compared to a low number of NLN removed was significantly associated with an improved 5-year survival rate (HR: 0.82, 95% confidence interval (CI): 0.74, 0.90, I2 = 93.8). Fig 2: Subgroup analysis showed that the effect size was different based on the type of surgery (0.89 for mastectomy and 0.71 for breast conserving surgery). (Fig. 3)

Association between high versus low number of NLN removed and the RFS

A pooled estimate of 9 studies showed that, adjusted for demographic and tumour characteristics, the 5-year RFS rate was better in patients with a high number of removed NLNs than in patients with a low number of removed NLNs (HR:0.76, CI: 0.765, 0.86), I2 = 86.3—Figure 4. Subgroup analysis showed that the effect size was smaller for patients who underwent mastectomy. (Fig. 5)

Sensitivity analysis and meta-regression

Sensitivity analysis was performed based on the results of each study, and the effect of each study on OS and RFS was determined (Supplement 1). To identify factors that contributed to the heterogeneity of this meta-analysis, meta-regression results showed that study sample size, study quality, NLN classification, mean age, Pathology status, Tumor characteristics and biology (T stage, number of lymph nodes involved, presence of metastases, and tumor stage), PR+, ER + receipt of adjuvant therapy (chemotherapy or radiotherapy after surgery), and type of surgery (breast conserving surgery or lumpectomy versus mastectomy) were significantly associated with effect size (OS) ($p < 0.05$). (Table 2)

Publication bias

There was no significant effect of publication bias on OS rate estimates. (Egger test: −1.65, p: 0.097, 95%CI: −4.5, 1.23, P: 0.25)(Fig. 6A). Our examination revealed that biased publication influences the emergence of negative results for RFS, resulting in an imbalance in the funnel plot. Additionally, we identified evidence of publication bias using Egger's test (Egger's test t = −3.09, $P = 0.024$, 95% CI: −4.8 to −1.38) (Fig. 6B). Since we observed significant publication bias, we applied the Trim & Fill method to address the influence of censored studies on our combined estimate. After our evaluation, it became apparent that four studies were censored due to publication bias. When we adjusted for the impact of unpublished papers on the overall estimate, it became clear that the pooled effect would decrease to 0.86.

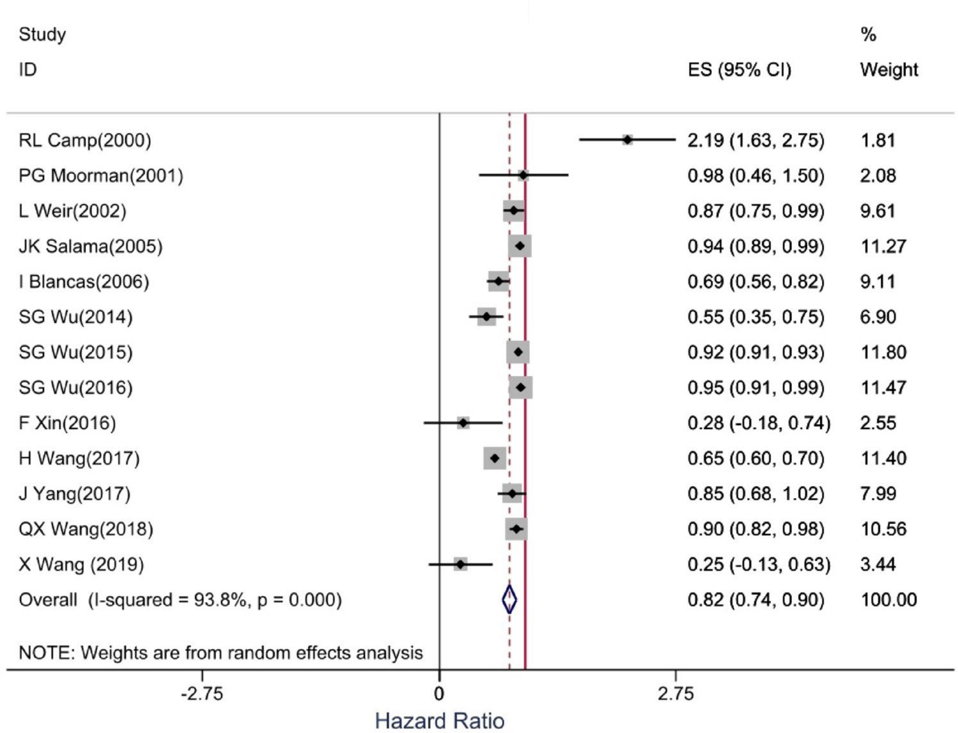

Fig. 2 Association between high versus low numbers of NLN removed and the OS

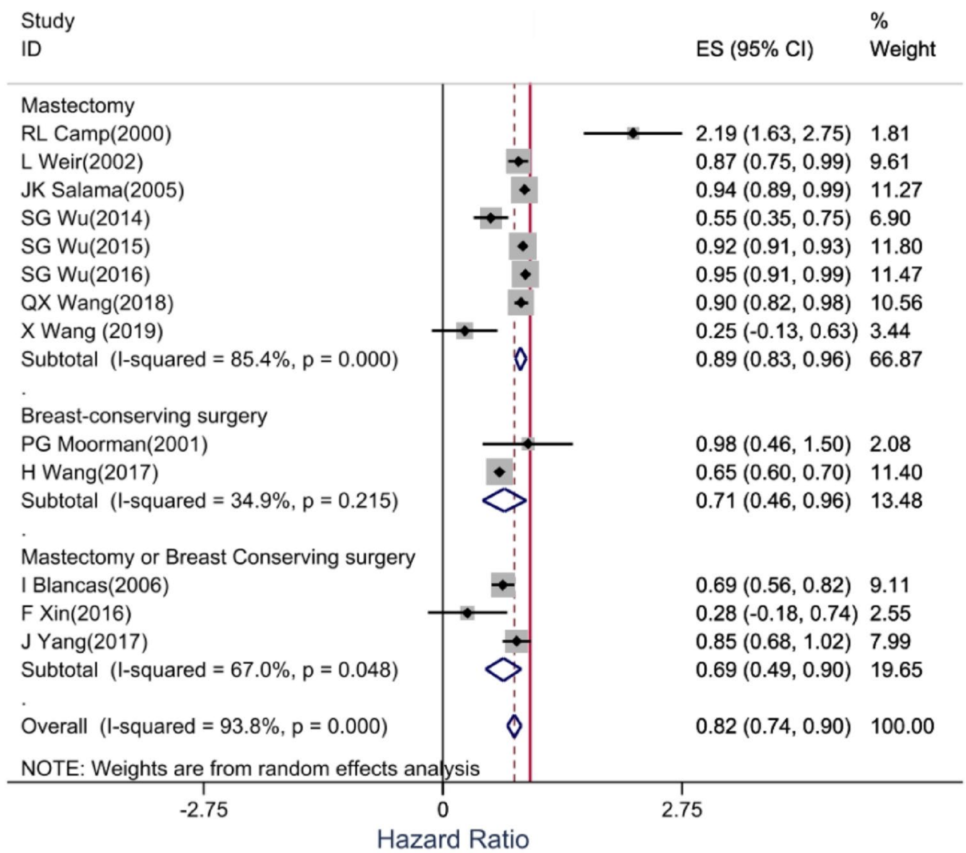

Fig. 3 Association between high versus low number of NLN removed and the OS based on surgery type

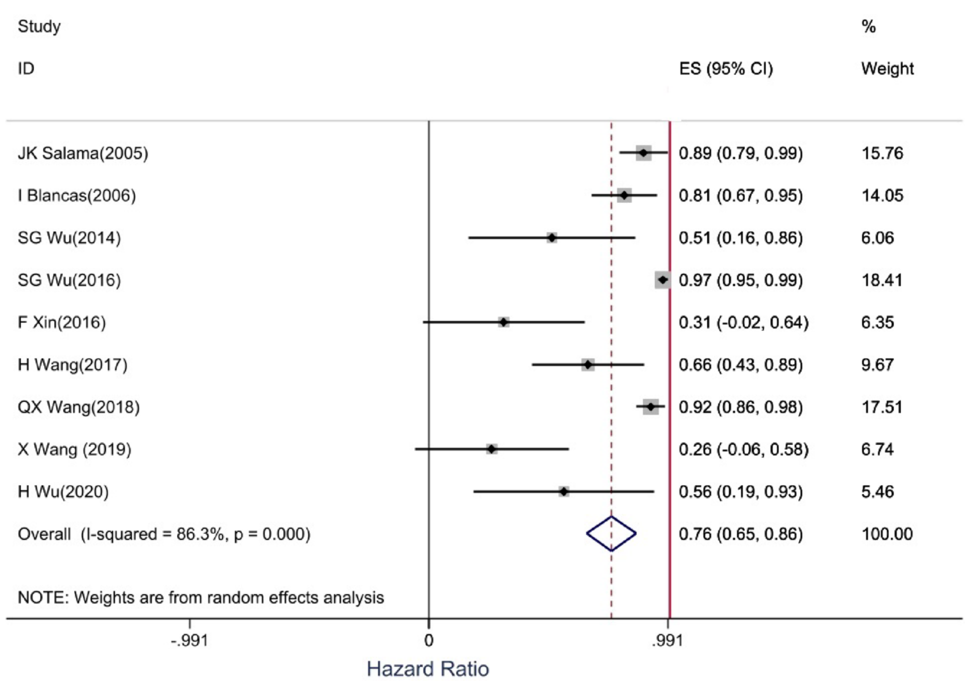

Fig. 4 Association between high versus low number of NLN removed and the RFS

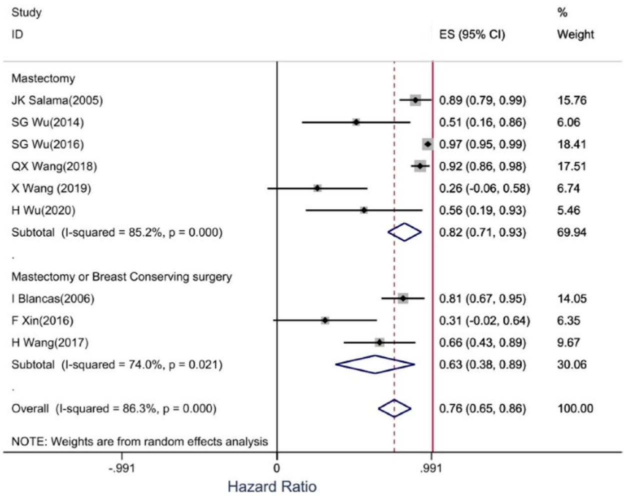

Fig. 5 Association between high versus low number of NLN removed and the RFS based on surgery type

Table 2 Meta-regression model of the effect of variables on effect size

Variable	β	se	*P*
NLN classification	0.28	0.12	0.001
Sample size	0.51	0.11	0.009
Mean Age	−0.25	0.1	0.029
Pathology status (Well vs. poor/moderate)	0.78	0.22	0.001
Number of lymph nodes involved	−0.14	0.06	0.014
PR+	0.41	0.16	0.009
ER+	0.33	0.22	0.006
presence of metastases	−0.68	0.28	0.001
T stage (>T2)	−0.57	0.19	0.006
Tumor stage	−0.21	0.11	0.008
Receipt of adjuvant therapy	0.51	0.16	0.001
Type of surgery (lumpectomy versus mastectomy)	−0.32	0.21	0.025

Discussion

In this meta-analysis, we evaluated the association of removing a high number of NLNs compared with a low number of NLNs with postoperative OS and RFS in 36,576 patients with postoperative BC in 15 retrospective studies.

Results interpretation

The results of this meta-analysis showed that removal of a high number of NLNs compared with a low number of NLNs may be associated with improved OS and postoperative RFS rates in BC patients who underwent axillary lymph node dissection.

The 5-year survival rate, adjusted for individual characteristics and tumour characteristics, in patients with a high number of removed NLNs was 13.5% and 11.1% higher, respectively, than in patients with a low number of removed NLNs.

The pooled results showed that a high number of NLNs removed had a positive effect on OS and RFS improvement. The effect of a high number of removed NLNs on OS and RFS was different based on the type of surgical procedure, and the protective effect of a high number of removed NLNs was less in patients who underwent mastectomy, which can be justified due to the poor prognosis in patients undergoing mastectomy. The majority of studies included in this meta-analysis were of high quality or methodological rigour.

There was heterogeneity between studies, which could be attributed to differences in the characteristics of the study populations, the type of surgery, and the characteristics of tumour biology and pathology. Meta-regression analysis revealed that study sample size, study quality, NLN classification, ER+, PR+, characteristics of the study populations (mean age), pathology status, tumour characteristics and biology, receipt of adjuvant therapy, and type of surgery were significantly associated with the outcome effect size and heterogeneity between studies. The surgical procedure of mastectomy versus lumpectomy, receipt of adjuvant

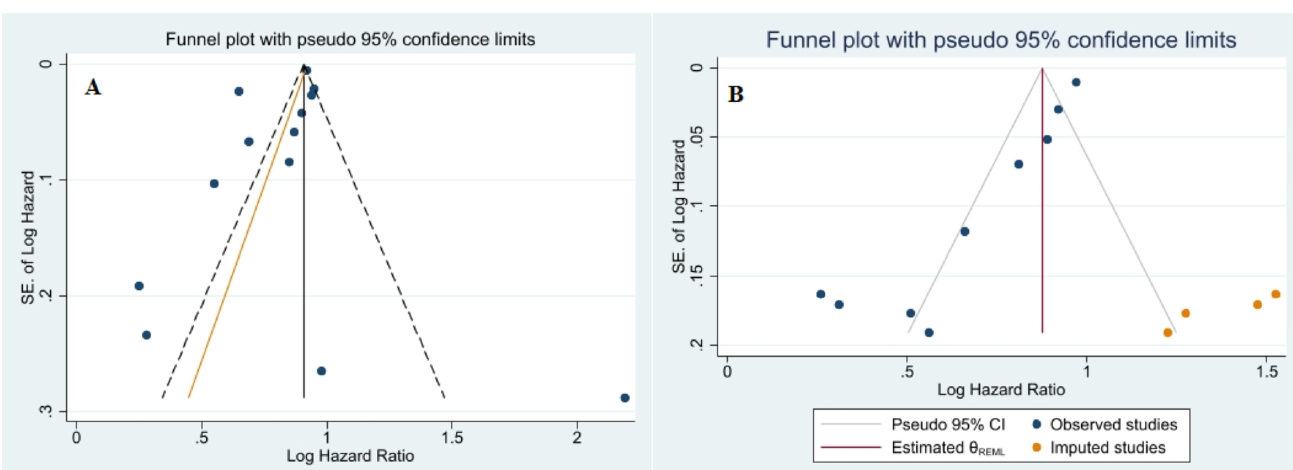

Fig. 6 Bias publication assessment in the funnel plot based on outcomes; (**A**): OS, and (**B**): RFS

therapy including postoperative chemotherapy and radiotherapy, PR+, ER+, and pathology with good versus poor resection, may be associated with improved patient survival. H Wang et al. [33] investigated the relationship between the number of NLNs and the prognosis of PMRT in BC patients, showing that cancer-specific survival (CSS) and OS were significantly better in patients with NLNs > 5. They demonstrated that the number of NLNs could serve as a prognostic indicator in patients undergoing PMRT, based on various clinical variables. They also demonstrated that, regardless of the number of NLNs, PMRT significantly improved CSS and OS in patients, indicating the role of multiple factors, including patient characteristics, biological characteristics, tumour stage, and adherence to standard treatment protocols after surgery, in improving the survival of BC patients.

More than eight studies were conducted in China, and the remaining studies were conducted in developed countries, indicating the existence of appropriate cancer registration and follow-up systems in developed countries.

Heterogeneity can be attributed to various factors, including tumor characteristics, study population characteristics, racial distribution, socioeconomic characteristics, and geographic variation. Although meta-regression was performed, not all sources of heterogeneity may have been fully addressed or clearly represented in the original included studies. Therefore, there may still be factors that negatively affect heterogeneity between studies. JM Unger et al. [38] showed that geographic distribution, adjusted for other variables, was significantly associated with the mortality and survival of BC patients. In a review, X Tao et al. [39] showed that the incidence and mortality rates of BC were higher in Asian countries, including China, and in developing countries compared to developed countries. They also showed that BC survival in China was relatively lower compared to some other developed countries. These differences may reflect geographical differences and the availability of early detection and treatment methods for BC in different geographical areas. In another study, K. Sathishkumar et al. [40] demonstrated that the survival of BC patients varied significantly across different geographical regions. In a study by M. Schootman et al. [41], geographic region, poverty, and race were significantly associated with the survival of BC patients. They showed that poverty and black race were associated with reduced survival of BC patients. In a review study, B. Conti et al. [42] showed that socioeconomic inequalities were significantly associated with the survival of BC patients. Survival rates were lower in patients with lower socioeconomic status. In another study, CJ Bradley et al. [43] showed, however, that low socioeconomic status was associated with late-stage breast cancer at diagnosis, type of treatment received, and death. LA Riba et al. [44] demonstrated that socioeconomic inequalities lead to disparities in care provision among BC patients, resulting in differences in BC patient survival.

Comparison with previous studies

To our knowledge, the relationship between the number of NLNs and patient survival in BC has not been investigated in a systematic review study, so we were unable to compare these results with those of other similar studies. However, the role of harvesting a high number of lymph nodes in improving the survival of other cancers has been reported [38–40].

In a meta-analysis, T. Chiyoda et al. [45] demonstrated that performing lymphadenectomy was associated with improved overall survival rates for patients following surgery, regardless of whether they had advanced or early-stage epithelial ovarian cancer. E Visser et al. [46] examined the impact of increasing the quantity of NLNs removed on the OSS and RFS of patients with esophageal cancer across 26 studies. They demonstrated that increasing the number of harvested lymph nodes resulted in a significant improvement in overall survival. Their meta-analysis findings highlighted the advantages of enhancing lymph node effectiveness in terms of both OS and RFS. M Elshaer et al. [47] showed that in patients with pancreatic ductal adenocarcinoma, the ratio of lymph nodes and the number of positive nodes removed during surgery were significantly related to OS after surgery.

In addition to the direct correlation between the increase in the number of NLNs harvested and improved survival in BC patients, the effects of several other variables that we were unable to estimate should also be considered. During our systematic review, the association of several variables, including changing prognostic markers (her2/ERBB2/c-erbB-2 association with improvement in BC in negative lymph nodes), the introduction of new therapies (aromatase inhibitors introduced in the adjuvant setting were associated with improved survival in hormone receptor-positive BC patients), targeting of genetic mutations (BRCA) with newer drugs, and metastatic patterns of tumors have been confirmed to improve patient survival [48]. TNBC/HER2 + tumours show early recurrences, and luminal subtypes exhibit a consistent and long-term risk of recurrence [48]. These findings suggest a significant role for subtype typing in determining the survival outcomes of BC patients, which should be considered comprehensively in their treatment.

Clinical implications

The more lymph nodes are removed during surgery, the better the chances of improving survival and reducing tumour recurrence. The mechanism of the NLN relationship with

BC survival has not yet been fully determined, but various hypotheses have been proposed regarding their relationship. In the majority of cases, tumor recurrence and metastasis after surgery, which are associated with a decrease in patient survival, may be justified by residual PLNs, which are usually difficult to find during surgery, so removing a higher number of NLNs during surgery can reduce metastasis and, as a result, improve OS and RFS [49, 50]. Additionally, a higher number of NLNs leads to a more thorough examination of total lymph nodes, making the N stage a more dependable indicator for assessing survival. The NLN count indicates the lymph node reaction to the tumor, and elevated NLN numbers suggest a lower presence of circulating tumor cells, which independently impact survival [51].

Removing more lymph nodes increases the likelihood of eliminating all affected lymph nodes and reduces the chances of missing a positive lymph node during surgery. This, in turn, reduces the misclassification of patients with advanced-stage disease as having an earlier stage of cancer. This process, known as stage migration, may contribute to lower survival rates associated with a low lymph node harvest. This is another interpretation of these findings: removing more lymph nodes leads to higher cure rates [52–57].

The results of this study could have potential implications for clinical practice, which we discuss in detail. (1) Risk stratification and prognostic modification: NLN count may serve as an independent prognostic indicator. For example, among patients with the same number of positive lymph nodes, those with higher NLN counts tend to have better survival outcomes. This could refine postoperative risk stratification and complement pN stage and molecular subtype, particularly in patients with positive lymph nodes. (2) Guiding adjuvant treatment decisions: In cases with limited lymph node involvement (e.g., 1 to 3 positive lymph nodes), a higher number of NLNs may indicate adequate axillary clearance and support the decision to reduce the intensity of regional lymph node radiotherapy or systemic therapy. Conversely, a low NLN count may raise concerns about inadequate staging and necessitate more aggressive adjuvant therapy. (3) Surgical quality index: The number of NLNs may serve as a surrogate marker for surgical accuracy. A low number of NLNs, especially in node-positive disease, may indicate incomplete axillary dissection. In such cases, reassessment of surgical adequacy may be necessary. (4) Adjustment of follow-up strategies: Patients with a low NLN count may benefit from closer surveillance due to the possibility of residual disease or a higher risk of recurrence, whereas patients with a higher NLN count and limited positive lymph nodes may be eligible for less intensive follow-up protocols. (5) Balancing the benefits and risks of surgery: We acknowledge that extensive axillary dissection to obtain a high NLN count must be weighed against known complications such as lymphedema, sensory neuropathy, and shoulder mobility limitation. Therefore, the potential prognostic value of NLNs should not supersede current standards that favour elective axillary surgery when oncologically indicated (e.g., after neoadjuvant therapy or within the framework of Z0011 criteria). In summary, NLN counts may enhance risk prediction, aid in individualized decisions for adjuvant and follow-up treatment, and potentially serve as a quality measure—but always within the context of a balanced, patient-centred surgical approach.

However, extensive lymphadenectomy can also be associated with potential harms, including lymphedema, sensory neuropathy, and shoulder dysfunction, and reduced quality of life, as well as benefits. AJ Forte et al., [58] showed that extensive lymphadenectomy was significantly associated with lymphedema and peripheral neuropathies. Treatment should be tailored to the patient's characteristics (patient-centered) and available and feasible treatment strategies. When it comes to the surgical management of axillary lymph nodes, the current emphasis is not limited to performing axillary lymph node dissection. It should focus on addressing potential harms such as lymphedema, sensory neuropathy, and shoulder dysfunction, and improving quality of life and patient satisfaction by employing more aggressive management approaches, including multimodal systemic therapies and radiotherapy, in addition to surgical treatment.

Limitations

Our study has strengths and weaknesses that should be noted. In this study, we were unable to estimate the association between the number of NLNs removed and outcomes based on several key variables, such as tumor characteristics, socioeconomic characteristics, and race, due to their lack of separate reporting in the original studies. Furthermore, the definition of the high and low NLN groups differed across several studies, although we eventually arrived at a unit classification using sensitivity analysis. Most of the original research was conducted in China and developed countries. Therefore, caution is warranted when applying the results to other countries.

Furthermore, the studies included in this meta-analysis were conducted in different populations and at different times. The definition and classification of BC stages, as well as the standard treatment for patients with BC, have changed over time. Therefore, we were unable to assess and identify the influence of these variables, which may have led to heterogeneity between studies. The most important strength of our study was the evaluation of the relationship between a high number of resected NLNs and a low number of resected NLNs on OS and RFS after surgery in patients with BC, as presented in a meta-analysis.

Conclusion

The results of this meta-analysis showed that a higher number of NLNs removed during surgery in BC patients who are candidates for axillary lymph node dissection appears to be associated with improved OS and RFS. Further prospective validation is needed. However, surgical management can have both limitations and benefits, and treatment should be tailored to the patient's characteristics (patient-centered) and the available and feasible treatment strategies. When it comes to the surgical management of axillary lymph nodes, the current emphasis should extend beyond simply performing axillary lymph node dissection and focus on improving quality of life and patient satisfaction by employing more aggressive management approaches, including multimodality systemic therapies and radiotherapy, alongside surgical treatment.

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Data availability The datasets generated or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

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