Chirurgia (2024) 119: 676-686
No. 6, November - December

http://dx.doi.org/10.21614/chirurgia.3006

Axillary Lymph Node Dissection versus Loco-regional Radiotherapy in Management of the Axilla in Node-Negative Locally Advanced Breast Cancer Post Neoadjuvant Chemotherapy

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Received: 11.07.2024
Accepted: 15.09.2024

Rezumat

Disecția ganglionilor limfatici axilari versus radioterapia loco-regională în managementul axilei în cancerul de sân avansat local, ycN0

Introducere: managementul axilar în cancerul de sân a evoluat semnificativ în ultimele decenii, conducând la o reducere generală a intervențiilor chirurgicale. Practicile actuale au suferit modificări notabile, urmărind reducerea morbidității în timp ce mențin rezultatele oncologice şi stadializarea precisă pentru pacienții nou diagnosticați cu cancer de sân. Aceste progrese au fost facilitate de eficiența îmbunătățită a terapiilor adjuvante. *Obiectiv:* Compararea rezultatelor disecției ganglionilor limfatici axilari (ALND) şi ale radioterapiei axilare loco-regionale (ART) în privința limfedemului şi a recurenței bolii la cazurile de cancer de sân local avansat (LABC) cu downstaging al statusului axilar după chimioterapia neoadjuvantă (NACT).
Material şi Metode: şaizeci de pacienți cu LABC cu status inițial cN1-2 au prezentat downstaging axilar la cN0 după NACT. Aceştia au fost randomizați în două grupuri. În primul grup (grupul de control) s-a practicat ALND, în timp ce al doilea grup (grupul de studiu) a beneficiat de biopsie a ganglionului santinelă (SLNB) şi ART postoperatorie. Pacienții cu SLNB neconcludent sau SLNB pozitiv au fost excluşi. Toți pacienții au fost urmăriți pentru recurența loco-regională şi limfedem pe o perioadă de cel puțin un an.

Rezultate: nu s-au identificat diferențe statistic semnificative între cele două grupuri în ceea ce priveşte recurența loco-regională. Rata de limfedem al brațului a fost însă mai mare în grupul de control. Limfedemul a fost prezent la 46,7% dintre pacienții la care s-a efectuat ALND, comparativ cu 13,4% în grupul de studiu (pacienți cu SLNB şi radioterapie).
Concluzie: radioterapia axilară după SNLB nu a prezentat diferențe în ceea ce priveşte recurența axilară comparativ cu ALND. Cu toate acestea, rezultatele noastre au fost favorabile radioterapiei în ceea ce priveşte limfedemul. Cu cercetări continue care vizează reducerea intervențiilor chirurgicale axilare, acest studiu ar putea reprezenta o inițiativă pentru o nouă strategie în LABC.

Cuvinte cheie: cancer de sân avansat local, disecția ganglionilor limfatici axilari, radioterapie axilară, limfedem, terapie neoadjuvantă

Abstract
Background: the evolution of axillary management in breast cancer has witnessed significant changes in recent decades, leading to an overall reduction in surgical interventions. There have been notable shifts in practice, aiming to minimize morbidity while maintaining oncologic outcomes and accurate staging for newly diagnosed breast cancer patients. These advancements have been facilitated by the improved efficacy of adjuvant therapies. Objective: To compare the outcomes of axillary lymph node dissection (ALND) and loco-regional axillary radiotherapy (ART) on lymphedema and disease recurrence in locally advanced breast cancer (LABC) cases that have shown a downstaging of their axillary status after neoadjuvant chemotherapy (NACT).
Material and Methods: sixty patients with LABC with an initial cN1-2 disease showed a downstaging of their axillary status to cN0 after NACT. They were randomized into two groups. The first group (the control group) underwent ALND, while the second group (the study group) had a sentinel lymph node biopsy (SLNB) and post-operative ART. Patients with failed SLNB or positive SLNB were excluded. All patients were followed up for loco-regional recurrence and lymphedema for at least one year.
Results: no statistical significance was found between both groups regarding loco-regional recurrence. There was a higher rate of arm lymphedema in the control group. Lymphedema was found in 46.7% of patients who underwent ALND, compared to 13.4% in the study group (patients with SLNB and radiotherapy).
Conclusion: axillary radiation after SNLB has shown no difference regarding axillary recurrence when compared to ALND. However, our results were in favor of radiation concerning lymphedema. With all the ongoing research aiming at reducing axillary surgery, this study could be an initiative for a new strategy in LABC.

Key words: locally advanced breast cancer, axillary lymph node dissection, axillary radiation, lymphedema, neoadjuvant therapy

Key Message

With all the ongoing research aiming at reducing axillary surgery, this study could be an initiative for a new strategy in LABC for patient who have shown down-staging of their axillary status after NACT. Radiotherapy can show better results in the long term with regards lymphedema.

Introduction

Breast carcinomas are a heterogeneous group of diseases that can be classified based on histology, biomarkers, and molecular profiles. These classifications provide crucial information regarding treatment options (1). Clinical staging is determined by gathering information pre-operatively, combining clinical examination, imaging, and pathological examination. Pathological staging is based on pathological examination of the primary tumor and/ or regional lymph nodes after surgery and, if applicable, data regarding core biopsies obtained during surgery at metastatic sites. Evolving knowledge of breast cancer biology and increased validation of various biomarkers for the prediction of treatment benefits suggest that several biomarkers should be documented on the initial diagnosis. These biomarkers include histological grade, hormone receptor status (estrogen receptor, ER, and progesterone receptor, PR), human epidermal growth factor receptor-2 (HER2), and markers of proliferation (such as Ki-67 or a mitotic count) (2).

Locally advanced breast cancer (LABC) is a subset of breast cancers characterized by highly advanced tumors without distant metastases. According to recent guidelines from the U.S. National Comprehensive Cancer Network (NCCN), LABC falls under AJCC stage III breast cancer. This classification includes breast cancers meeting any of the following criteria in the absence of distant metastasis: tumors larger than 5 cm with regional lymph node involvement (N1-3); tumors of any size with direct extension to the chest wall or skin, including ulcers or satellite nodules, regardless of regional lymph node involvement; or the presence of regional lymph node involvement, such as clinically fixed or matted axillary lymph nodes, or any infraclavicular, supraclavicular, or internal mammary lymph node involvement, irrespective of tumor stage (3).

Locally advanced breast cancer (LABC) is further categorized as "operable" or "inoperable" based on the likelihood of achieving negative margins on histopathological examination following an initial surgical intervention that could lead to a long-term reduction in loco-regional recurrence. While the sequence of chemotherapy relative to surgery (preoperative versus postoperative) does not impact overall survival (4), neoadjuvant chemotherapy (NACT) is indicated for inoperable LABC to enhance the possibility of achieving R0 resection. LABCs constitute a highly diverse group; nonetheless, employing consistent terminology for LABC is crucial for oncologists and researchers to exchange information regarding their patients and to assess and compare outcomes across different studies (5).

The management of locally advanced breast cancer (LABC) has undergone significant evolution, necessitating a multimodal approach that integrates radiotherapy, surgery, and systemic treatments (6,7). In cases in which neoadjuvant chemotherapy (NACT) is administered, decisions regarding radiotherapy and treatment fields should be guided by the highest stage determined prior to therapy initiation and tumor characteristics (8). One benefit of neoadjuvant chemotherapy (NACT) is the enhancement of long-term prognosis. Patients who attain a complete pathological response (pCR) in the breast and axilla experience improved loco-regional control and survival outcomes, with nodal pCR serving as a significant prognostic indicator (9). In instances of biopsy-proven axillary nodal metastases, levels I and II axillary lymph node dissection (ALND) (medial and posterior to pectoralis minor, respectively) remain the gold standard in LABC management. While its impact on overall survival may be limited, ALND plays a crucial role in staging, providing prognostic information, and ensuring regional control. Furthermore, radiation therapy typically targets centrally located axillary lymph nodes (high level II and level III) as moderate doses are effective in sterilizing lymph nodes measuring 1 cm or smaller (10).

Lymphedema is the most serious and difficult complication to treat. However, lymphedema is not the only ALND-related complication. The literature primarily reports lymphedema, paresthesia, pain, and range-

of-motion restriction as complications of ALND. Lymphedema incidence and prevalence widely vary due to different measurement methods and intervals between ALND and lymphedema measurements (11).

SLNB

With a better selection of patients for NACT and improved effectiveness of targeted therapy, ALND could potentially be avoided in a large number of initially node-positive patients if SLNBs were shown to be accurate at identifying those who have achieved an axillary pCR (12). This was established in the American College of Surgeons Oncology Group ACOSOG Z1071 trial, which was designed to determine the false negative results (FNR) of SLNB after chemotherapy in women initially presenting with cN1-2 disease (13). Current NCCN guidance states that SLNB is an accepted option for patients who show downstaging of their previously positive axilla and show downstaging after NACT. However, a FNR > 10% is expected. The NCCN requires marking the site of the biopsied nodes using a dual tracer and removing more than two SLNs to decrease FNRs. It has been concluded that the dissection of more than three LNs reduced FNR even if a single tracer was used. An FNR between 4.9% and 9.1% was found when more than three LNs were dissected (14).

Radiotherapy

The ACOSOG Z0011 trial tested the omission of complete ALND in clinically lymph node-negative and SNB-positive patients. This trial showed no significant differences between the groups. Radiation in this trial was restricted to tangential breast treatment. However, when the treatment fields were analyzed, most patients received substantial doses to the axillary lymph nodes, which might have contributed to the favorable outcome (15,16).

Advanced treatment planning and delivery approaches allow for improved dose homogeneity, the exclusion of critical normal tissues, and the reduction of the risks of radiation-related toxicity. The MA20 trial showed only a 1.2% incidence of radiation pneumonitis (0.2% with breast irradiation alone, without regional ART) and an 8.4% risk of lymphedema (a risk that was 4.5% with breast irradiation alone). Pneumonitis typically resolves spontaneously or after a course of corticosteroids. Dose-dependent cardiac toxicity has been shown in historical trials in which mean heart doses were substantially higher than those delivered in modern practice; observational studies suggest a very low risk of cardiac sequelae from regimens administered in contemporary practice with appropriate care to reduce cardiac exposure. A brachial plexus injury has been reported from treatment to the supraclavicular region. Perhaps the most dreaded consequence of therapeutic radiotherapy is secondary malignancies. The risk of soft tissue sarcoma is approximately 0.2% at 15 years, and the risk of lung cancer is also increased by radiotherapy (17).

Material and Methods

This prospective randomized study was conducted between February 2019 and August 2021. The protocol was reviewed and approved by the institutional research and ethics committee. Patients with clinically node-positive breast cancer, managed by the breast cancer multidisciplinary team and planned for NACT, were screened.

Patients were considered eligible for inclusion in the current study if they fulfilled the following criteria: female patients, aged 18-70, with pathologically proven breast cancer, initially node-positive cN1/2, who were downstaged to node-negative (cN0) after NACT. Exclusion criteria included pregnancy, inflammatory breast cancer, distant metastasis, and post-neoadjuvant node-positive patients.

Methodology

One hundred patients were evaluated for the study *(Fig. 1)*. Thirty were excluded before randomization. Seventy patients were randomized into two groups. Four patients had failed intra-

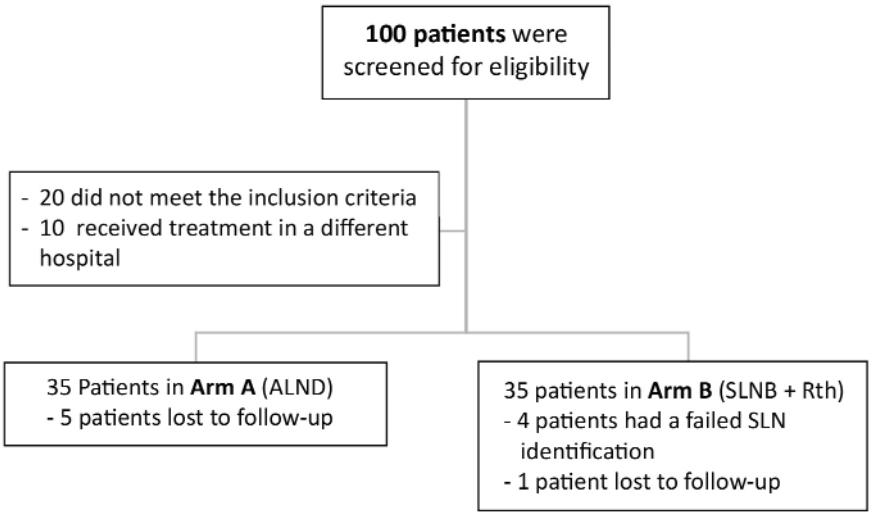

Figure 1. Consort diagram of patients included in the study.

operative identification of SLNB and were excluded and underwent ALND. Six patients were lost to follow-up.

All patients had the usual work-up for LABC in the form of a chest, abdomen, and pelvis CT. Immuno-histochemical studies were performed for ER, PR, HER2/neu receptors, and Ki67 proliferation index (PI).

All study subjects received NACT, consisting of sequential anthracycline/taxane-based chemo-therapy administered for 6-8 cycles with regular clinical and radiological assessment of response.

In HER2-positive cases, Trastuzumab target therapy was added.

Before initiation of NACT, a surgical plan is decided based on tumour and breast sizes, multifocality, multicentricity, intra-ductal extension, and the presence and extent of suspicious micro-calcifications. The surgical decision was then revalidated by the MDT after NACT within the context of tumour response to treatment in addition to the previously mentioned factors.

As for the axilla, patients enrolled in this study were randomized into two groups, i.e., Group A, where patients underwent ALND, and Group B, where patients underwent SLNB followed by ART.

Surgical Technique

Selected eligible patients were randomized through a closed envelope technique (chosen randomly by an assigned nurse) into two groups:

Group A (Control Group): underwent ALND according to the protocol of the department.

Patients were positioned supine with arms extended at ≤ 90 degrees abducted from the chest wall to avoid overstretching of the brachial plexus. The incision would vary depending on the surgery being performed. For patients undergoing ALND concurrently with BCS, a curvilinear incision is made approximately 1 to 2 cm below the edge of the axillary hairline following the natural skin folds, extending from the anterior to the posterior axillary fold. For patients under-going a standard, modified radical mastectomy without reconstruction, ALND was performed through the mastectomy incision once the breast had been removed. For patients undergoing oncoplastic breast surgery, ALND was performed from the same skin incision if feasible.

Post-operative Radiotherapy

All patients received whole breast hypo-fractionation (40 Gy in 15 fractions), usually administered through tangentially oriented beams that encompass the entire breast, while reducing exposure to the heart and lungs by targeting nodal fields at levels 3 and 4.

Group B (study group): underwent SLNB by the following technique.

Injection of 3-5 ccs of either 1% methylene blue or patent blue was administered either peri-tumorally or sub-areolarly. After a 15-minute interval, a small incision was made in the axilla, positioned 2 cm below the hairline. Subsequently, the axillary fascia was opened, and approximately 3 lymph nodes were retrieved (*Fig. 2*). All lymph nodes exhibiting blue staining, enlargement, or proximity to bluish lymphatic streaks were excised, and the incision was closed without drainage. The excised lymph nodes were then promptly sent to the frozen section unit of the operating room for determination of SLN positivity or negativity.

PPatients with a positive SLNB or failed SLN detection were excluded from the study and underwent ALND. Patients with a negative SLNB were given post-operative radiotherapy as the control group. However, the dedicated axillary field was defined by the radiation oncologist as aiming at a higher tangential field (reaching the sternoclavicular joint), including levels 1-4, to cover the whole axilla.

After one year, axillary ultrasound and axillary examination were done to detect any recurrence. The arm circumference was also measured and compared to the contralateral side to detect lymphedema.

Follow-up

Patients were followed up every three months for one year. Our primary objective was to detect loco-regional recurrence through clinical and radiological assessment. The secondary objective was lymphedema detection by a method in which both arms were measured by a circumferential tape 10 cm above and below the olecranon process. A difference of $\geq$ 2 cm at either level between the two arms is generally accepted for diagnosing lymphedema.

Lymphedema was classified according to arm circumference at the last follow-up as mild, moderate, and severe. An increased arm circumference between 2 cm and 4 cm without limitation in movement was considered mild. A circumference between more than 4 cm and less than 7 cm was considered moderate. The presence of a limited arm movement with an increased arm circumference or an increased arm circumference greater than 8 cm was considered severe.

Figure 2. Sentinel Lymph Node Biopsy

Statistical Analysis

Data were coded and entered using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). The data were summarized using means, standard deviations, medians, minimums, and maximums for quantitative data, and frequencies (counts) and relative frequencies (percentages) for categorical data. Quantitative variables were compared using the non-parametric Mann-Whitney test (Chan, 2003a). Categorical data were compared using the Chi-square ($\chi^2\chi^2$) test. An exact test was used when the expected frequency was less than 5 (Chan, 2003b). P-values less than 0.05 were considered statistically significant.

Results

Sixty patients were included. Patients were randomly selected in either group A or group B. Patients in group A underwent ALND, while those in group B underwent SLNB and radiotherapy, and the identification rate of SLNB was 88.5%.

The median age of patients was 49 (range w SD), with 77.8% of patients above 40. The median age was 48 in group A and 49 in group B (*Table 1*). When the TNM staging between both groups was compared, no statistical difference was noted, similar to biological markers (*Table 2*).

Table 1. Demographics and tumor details

		Count	%
Clinical T	T1	6	10.0%
	T2	36	60.0%
	T3	11	18.3%
	T4b	6	10.0%
	T4c	1	1.7%
Clinical N	N1	55	91.7%
	N2	5	8.3%
Menopausal state	Pre	37	61.7%
	Post	23	38.3%
Biological Type	Luminal A hormone receptor +ve	22	36.7%
	Luminal B1	10	16.7%
	Luminal B2	12	20.0%
	Her 2 enriched	6	10.0%
	Tripple -ve	10	16.7%
Surgery	BCS	44	73.3
	Mastectomy	16	26.7

Type of Surgery

In group A, 20 patients underwent BCS + ALND, and 10 underwent MRM. In group B, 24 patients underwent BCS + SLNB, and six underwent simple mastectomy + SLNB.

Recurrence

Nodal Recurrence

In group A, only one patient had an axillary recurrence during follow-up. No clinical or radiological axillary recurrence was noted in any patient in either group.

Systemic Recurrence

Three patients in group A showed distant metastasis (liver secondaries) during their follow-up. No statistical significance was concluded compared to group B (P value 0.237).

Local/mass Recurrence

Two patients in group A had local recurrence, yet no statistical significance was found (p value 0.492) (*Table 3*).

Lymphedema

In group A, the incidence of lymphedema was 46.7% (14 patients), of which 16.7% were mild (five patients), 20% were moderate (six patients), and 10% were severe (three patients). A total of 13.4% of patients in group B showed lymphedema (four patients). No patients had severe lymphedema; mild and moderate lymphedema were seen equally in group B (6.7% each).

The lower incidence of lymphedema in group B compared to group A was found to be statistically significant, with a p value of 0.035 (*Table 4, Fig. 3*).

Discussion

The goals of axillary surgery for breast cancer

Table 2. TNM staging in both groups and biological markers

		ARM				P value
		A		B		
		Count	%	Count	%	
Clinical T	T1	4	13.3%	2	6.7%	0.280
	T2	14	46.7%	22	73.3%	
	T3	7	23.3%	4	13.3%	
	T4b	4	13.3%	2	6.7%	
	T4c	1	3.3%	0	0.0%	
Clinical N	N1	27	90.0%	28	93.3%	1
	N2	3	10.0%	2	6.7%	
ER	Weak	1	3.3%	0	0.0%	0.754
	Moderate	7	23.3%	10	33.3%	
	Strong	14	46.7%	12	40.0%	
	Negative	8	26.7%	8	26.7%	
PR	Weak	1	3.3%	0	0.0%	1
	Moderate	7	23.3%	8	26.7%	
	Strong	14	46.7%	14	46.7%	
	Negative	8	26.7%	8	26.7%	
Her2neu	Positive	6	20.0%	10	33.3%	0.243
	Negative	24	80.0%	20	66.7%	
Ki67	Low	17	56.7%	16	53.3%	0.795
	High	13	43.3%	14	46.7%	

Table 3. Recurrence rates and lymphedema

		ARM				P value
		A		B		
		Count	%	Count	%	
Nodal Recurrence	Yes	1	3.3%	0	0.0%	1
	None	29	96.7%	30	100.0%	
Systemic Recurrence	Yes	3	10.0%	0	0.0%	0.237
	None	27	90.0%	30	100.0%	
Local Recurrence	Yes → Mastectomy	2	6.7%	0	0.0%	0.492
	None	28	93.3%	30	100.0%	

Table 4. Lymphedema in both arms

		ARM				P value
		A		B		
		Count	%	Count	%	
Lymphedema	Mild	5	16.7%	2	6.7%	0.035
	Moderate	6	20.0%	2	6.7%	
	Severe	3	10.0%	0	0.0%	
	None	16	53.3%	26	86.7%	

are to control regional lymph node disease, guide systemic treatment, and improve survival rates. Over the last three decades, modifications in systemic and radiation therapy have significantly reduced regional lymph node recurrence rates (18).

Presently, axillary lymph node dissection (ALND) following neoadjuvant chemotherapy (NACT) is recommended for patients with confirmed node-positive disease at the time of diagnosis. However, in certain cases, the metastases in the axillary lymph nodes might

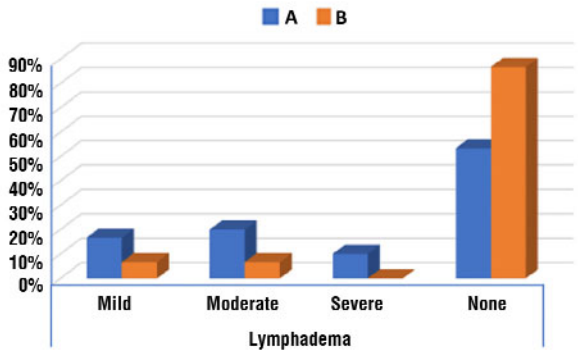

Figure 3. Lymphedema in both groups.

have been eliminated by the chemotherapy, allowing some patients to avoid ALND. Even among patients initially diagnosed with nodal disease, sparing them the morbidity associated with axillary dissection would be advantageous (19). Historically, all patients clinically diagnosed with node-positive disease underwent ALND after NACT, regardless of their response to treatment. However, current evidence indicates that a complete pathological response can occur in the axilla in 12-65% of patients, with approximately 50% of triple-negative cancers, and 65% of HER2-positive cancers showing no residual disease on ALND following neoadjuvant chemotherapy (20).

Our study used radiotherapy to manage the axilla in patients who showed a down-staging in their nodal status from positive to negative after NACT, given that the SLNB was negative. The aim was to compare ALND and radiotherapy regarding recurrence and lymphedema. Sixty patients were involved in our study; 30 underwent ALND, and 30 had post-operative radiotherapy. Regarding loco-regional recurrence, the ALND group had a 10% recurrence rate compared to none in the axillary radiotherapy group, with a median follow-up of 1.41 years.

The higher-than-usual recurrence rate in the ALND group was found in three patients; of these, one was HER2/neu-enriched, and her treatment was delayed because of a shortage of Herceptin at the beginning of the COVID-19 crisis – the drug is not produced locally. The other two patients showed positive SLNBs despite having a negative axilla by clinical and ultrasound examination. However, the data were not considered significant because of the small sample size and the higher incidence of unusual events.

In the AMAROS study, ALND was compared to axillary radiotherapy in early breast cancer with clinically non-palpable ALNs that showed a positive SLNB. Five-year axillary recurrence was found to be 0.4% in the ALND group and 1.2% in the axillary radiotherapy group. The authors concluded that the primary outcome was underpowered and inconclusive, given the lower-than-expected event rate (21).

The OTOASOR trial was another study comparing ALND to regional nodal irradiation in stages I and II of breast cancer. It demonstrated an 8-year axillary recurrence rate of 2.0% in the ALND group and 1.7% in the ART group, with a mean follow-up of 8.1 years (22).

Two past randomized control trials, the NSABP-04 trial by Fisher et al. in 2020 and a French trial by Louis-Sylvestre in 2004, compared axillary radiotherapy to ALND without involving SLNB. As no sentinel node biopsy was performed, ALND and axillary radiotherapy were the sole treatments for the axilla. In the NSABP-04 trial, both treatment groups showed a 4% axillary recurrence rate after 25 years (23). The French trial reported better axillary control in the axillary lymph node dissection group (1% vs. 3% in the axillary radiotherapy group; $p = 0.04$) over a 15-year follow-up. Despite initial survival benefits favoring ALND, long-term outcomes revealed no significant difference in disease-free survival or overall survival between the treatment groups (24).

In our study, the secondary outcome was the incidence of lymphedema. ALND showed an incidence of 46.7%, compared to 13.4% in the radiotherapy group (p value = 0.035). The lymphedema in the radiotherapy was mild, and no cases were reported to be moderate or severe.

The AMAROS study measured lymphedema at 1, 3, and 5 years. Lymphedema occurred significantly more often in the ALND group

compared with the ART group at 1 year ($p = 0.001$), 3 years ($p = 0.003$), and 5 years ($p = 0.001$). The incidence of lymphedema after one year in the AMAROS trial was 40% after ALND, compared to 22% in the ART group (21).

In the OTOASOR trial, the rate of lymphoedema was higher in the ALND group (15.3%) than in the (PS12) ART group at one year (4.7%). Combining ALND and radiotherapy in the axillary treatment in the ALND arm further increased morbidity in those 18/57 patients (31.5%) (p value < 0.001) (22).

The MA.20 trial, carried out by the Intergroup/National Cancer Institute of Canada Clinical Trials Group, enrolled women at moderate to high risk of regional recurrence, identified by involved axillary nodes or high-risk node-negative disease. Patients underwent ALND or SLNB if node-negative, followed by whole breast irradiation.

Subsequently, they were randomized to either receive ART or not. After a median follow-up of 9.5 years, those who received ART demonstrated a statistically significant improvement in isolated loco-regional and distant disease-free survival (DFS). This suggests that ART, following positive SLNB and breast-conserving surgery, not only improves loco-regional control, but also diminishes the risk of secondary spread (25).

In our study, the identification rate of SLNB in group B was 88.5%. In a study by Kim et al., the identification rate was found to be around 95.8% (115/120) using a single tracer, either blue dye (isosulfan blue) or a radionucleotide (19).

The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-27 trial stands out as one of the most extensive studies to date concerning sentinel lymph node biopsy (SLNB) after neoadjuvant chemotherapy (NACT), alongside concomitant ALND post-chemotherapy. The trial achieved an identification rate of 84.8% utilizing the blue dye isosulfan blue (26).

The identification rate in our study using a single-agent tracer (1% methylene blue or patent blue) is comparable to the other studies, which have also used a single agent. A negative pre-operative AUS was a must, along with the excision of any blue-stained lymph node, a lymph node near a blue-stained lymphatic streak, or an enlarged lymph node.

No statistical significance was found in our study regarding the clinicopathological data of the tumor, age, or menopausal status. It is important to note that some of the patients involved in our study had their treatment delayed due to the COVID-19 crisis.

Conclusions

Axillary radiotherapy has shown no difference regarding axillary recurrence when compared to ALND in patients who have shown a down-staging of their axillary lymph node status post-NACT. However, regarding lymphedema, a significant statistical difference was found in favor of radiation instead of dissection.

With all ongoing research aiming at the reduction of axillary surgery to spare patients' post-operative morbidities and unnecessary overtreatment, this study could be the initiative for a new treatment strategy in LABC. However, a longer follow-up period and a larger population are needed to implement this study in all patients with LABC and axillary involvement.

Author's Contributions

- Amr Ebrahim (AE): Main investigator, data collection, and background research;
- Omar Lasheen (OL): Manuscript draft and correspondence;
- Emad Khallaf (EK): Supervising professor and background research;
- Mohamed Hassan (MH): Data collection, analysis, and background research;
- Sherif Mokhtar (SK): Data collection, analysis, and background research;
- Shaimaa Lasheen (SL): Helped originate the study idea, data collection, analysis, and background research.

Conflicts of Interests

All authors declare that there is no conflict associated with this publication and that they

did not receive any significant funding that would influence the study.

Ethical Statement

The study obtained approval from the ethical committee of the Department of General Surgery at Cairo University before starting to recruit patients.

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