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Article

Total Sealing Technique: A Novel Surgical Approach that Significantly Reduces the Incidence of Upper Extremity Lymphedema Following Axillary Dissection in Patients with Breast Cancer

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Simple Summary: Breast cancer-related lymphedema (BCRL), characterized by lymphatic fluid accumulation in the upper extremities following breast cancer treatment, significantly affects the quality of life of survivors of breast cancer. In a previous study, we introduced a novel surgical procedure, the Total Sealing Technique (TST), which utilizes a bipolar vessel sealing system (LigaSure™ Exact Dissector) to reduce lymphatic leakage during axillary lymph node dissection (ALND) for breast cancer. After observing that patients who underwent this procedure had fewer cases of BCRL, we evaluated its incidence. A comparative analysis of 36 patients who underwent conventional electrocautery (CONV) and 35 who underwent TST revealed that TST significantly reduced the incidence of BCRL. Once the surgeon becomes accustomed to it, TST becomes a simple surgical procedure that provides reliable outcomes regardless of the surgeon, timing, or location, suggesting that it has the potential to transform axillary dissection in breast cancer surgery.

Abstract: Background/Objectives: In a previous study, we reported a novel surgical procedure called the Total Sealing Technique (TST), which uses a bipolar vessel-sealing system to reduce lymphatic leakage during axillary dissection for breast cancer. Follow-up observations showed a lower incidence of breast cancer-related lymphedema (BCRL) in patients in the TST group. Therefore, in this current study, we aim to investigate and compare the incidence of BCRL between two groups (TST and conventional electrocautery (CONV)) and discuss why the incidence of BCRL was significantly lower in the TST group than in the CONV group. **Methods:** We conducted a comparative analysis of 36 patients who underwent total mastectomy with axillary lymph node dissection (ALND) using the CONV procedure during the first three years, and 35 patients who underwent the same procedure using TST during the subsequent three years. We evaluated the incidence of BCRL and its association with the risk factors in both groups. **Results:** The incidence of BCRL was 2.9% in the TST group and 22.2% in the CONV groups, respectively ($p = 0.028$). In the TST group, no significant association was found between the incidence of BCRL and known risk factors. However, in the CONV group, the incidence of BCRL was significantly higher in younger patients and in those who received neoadjuvant or postoperative chemotherapy, a taxane-containing regimen, or > 600 mL of drainage. **Conclusions:** TST with LigaSure™ Exact Dissector significantly reduces BCRL incidence, suggesting that it may become an important surgical procedure for axillary dissection in breast cancer in the future.

Keywords: breast cancer-related lymphedema; axillary lymph node dissection; Total Sealing Technique; bipolar vessel sealing system; LigaSure™ Exact Dissector

1. Introduction

The primary goal in treating patients with breast cancer who have positive axillary lymph nodes is to achieve optimal tumor control while minimizing side effects that include breast cancer-related lymphedema (BCRL). However, despite notable efforts to reduce axillary surgery, BCRL remains a common complication of locoregional treatment [1], significantly affecting both individuals and the healthcare system. Additionally, lymphedema has no known cure, and its management is costly, therefore placing an unfair financial burden on patients. In 2020, Naoum et al. conducted a prospective study of 1,815 patients and reported that the risk of BCRL correlated with the extent of axillary surgery. The authors classified patients according to the extent of axillary surgery with or without regional lymph node radiation (RLNR): SLNB alone, SLNB plus RLNR, axillary lymph node dissection (ALND) alone, and ALND plus RLNR and found a five-year cumulative BCRL incidences of 8.0%, 10.7%, 24.9%, and 30.1%, respectively [2]. Notably, recent data show that more than one in four patients who undergo axillary dissection develop BCRL. In response to this challenge, various nonsurgical and surgical strategies have been developed to prevent and treat BCRL effectively [3]. Axillary Reverse Mapping (ARM), a surgical approach used to prevent lymphedema, was introduced by Klimberg in 2008 and is an improved lymph node mapping technique that identifies the SLN while preserving upper extremity function to minimize the risk of lymphedema [4,5]. ARM was designed to reduce the risk of lymphedema by identifying and preserving lymphatic drainage pathways of the arm in patients undergoing ALND or Sentinel Lymph Node Biopsy (SLNB) [6]. Immediate lymphatic Reconstruction (ILR) is a surgical technique designed to restore the lymphatic drainage of surgical extremities. ILR has been increasingly discussed in the literature; however, it requires further investigations for more supporting evidence [7]. In practice, performing these complex procedures in patients with breast cancer requiring axillary dissection is quite challenging. Most importantly, there is an urgent need for the development of a simple surgical procedure that provides consistent results regardless of when, where, or who performs the procedure to reduce the risk of BCRL. In this study, we aim to evaluate whether TST using a vessel sealing device (LigaSure™ Exact Dissector (LGSED)) improves BCRL incidence compared with conventional axillary dissection performed using a monopolar electrocautery scalpel.

2. Materials and Methods

2.1. Patients

A previous study was conducted on a consecutive series of 71 patients who underwent total mastectomy and ALND at Nara Medical University between December 1st, 2015, and November 30th, 2021. The patients were divided into two groups according to the surgical procedure: The conventional electrocautery (CONV) and the TST group. Several factors were compared between both groups, including intraoperative blood loss, operative time, total drainage volume, mean number of days to drain removal, postoperative hospital stay, mean time from surgery to induction of postoperative chemotherapy, and postoperative complications [8]. During the follow-up period, most patients who underwent TST did not develop BCRL. However, there was no comparison of the level of incidence of BCRL between both groups in the previous study. Therefore, in this current study, we performed a comparative analysis of the incidence of BCRL between these two groups. Additionally, we investigated the relationship between BCRL and various factors that may influence its incidence, including age, body mass index (BMI), postoperative radiotherapy, neoadjuvant and/or postoperative chemotherapy, use of a taxane-containing regimen, number of dissected lymph nodes, total drainage volume, duration of drainage, and incidence of seroma in each group. In both groups, age, BMI, number of dissected lymph nodes, total drainage volume, and drainage duration were stratified based on median values. Subsequently, all patients were followed up until December 31st, 2024, with a median follow-up period of 74.6 months (range: 39.1-110.3 months). Specifically, the median follow-up period was 95.6 months (range: 74.4-110.3 months) and 61.6 months (range: 39.1-70.1 months). in the CONV and TST groups, respectively.

2.2. Surgical Technique and Axillary Drain Management

Following the procedure outlined in the previous study, total mastectomy was performed using an electrocautery scalpel to create skin flaps extending 2-3 cm below the subclavian bone on the cephalic side and beyond the inferior breast margin on the caudal side in both groups. Subsequently, ALND was performed through the same wound as the mastectomy in both groups. In the TST group, all tissues dissected with the LGSED were sealed with the LGSED prior to resection, as demonstrated in the video from the previous study [8], thereby eliminating the need for instrument exchange, sutures, or electrocautery during ALND. This procedure was termed "Ikeda's TST." Nevertheless, it is important to note that these dissected and sealed tissues from the sealing process contain micro-vessels and micro-lymphatics. Conversely, in the CONV group, electrocautery or suture ligation was used for hemostasis during total mastectomy and ALND. There are multiple lymphatic pathways from the breasts to the axillary lymph nodes, with a substantial amount of lymphatic fluid draining into the anterior axillary region [9] [10]. In order to prevent lymphatic leakage from the micro-lymphatic vessels during total mastectomy, the breast margin near the axilla was resected after sealing with LGSED using the same procedure as ALND in the TST group. During ALND, level I and II lymph nodes were dissected through the mastectomy incision, using a unique technique for sealing micro-lymphatic vessels. Concurrently, the remaining side was double-sealed and resected. At the end of the ALND procedure, a closed suction drain was placed in the axilla and the anterior chest, and the wound was sutured in the subdermal layer using an absorbable monofilament suture (4-0 PDS®). In all cases, ALND was performed after total mastectomy, and the duration of surgery was documented from skin incision to completion of the procedure. There were no planned restrictions on the arm movement. The axillary drain was removed if the daily output was < 50 mL over 24 hours. Patients were generally discharged from the hospital the day following drain removal. However, discharge was delayed in cases of uncontrolled drainage. Regardless of total drainage volume output, drain removal was scheduled within 14 days to avoid the risk of retrograde infection. Nurses monitored the drainage volume daily and recorded complications. Following discharge, the patients returned for follow-up every one to two weeks for at least 30 days to document any complications.

2.3. Lymphedema Education

All patients who underwent ALND were educated on lymphedema following discharge, by a certified breast care nurse in an outpatient setting. This education included the causes, symptoms, diagnoses, treatment options, and prevention of lymphedema. Prevention strategies emphasize avoiding heavy lifting and infection, exercising regularly, and using compression garments.

2.4. Breast Cancer-Related Lymphedema Screening and Definition

BCRL measurements were performed according to the Japanese Lymphedema Society Guidelines [11] [12]. The following preoperative measurements were taken from both upper extremities to establish baseline values and assess left-right differences: 1. Palmar diameter along the line connecting the metacarpophalangeal joints of the second through fifth fingers; 2. Circumference of the wrist; 3. The circumference 5 cm distal to the cubital fossa; 4. The circumference 10 cm proximal to the cubital fossa. To assess the incidence of BCRL, all patients who underwent axillary dissection were subsequently assessed at the above-mentioned upper extremity sites during their outpatient visits every three to 12 months. Assessment of BCRL was conducted as follows: pre-treatment circumference was measured, and post-treatment comparative observations were made on the same side and area. BCRL was diagnosed when a difference of 2 cm or more was observed between the affected and non-affected side [12] [13].

2.5. Statistical Analysis

Categorical variables were compared using the chi-square test or Fisher's exact test. Fisher's exact test was used when the observed data contained zero values to ensure statistical validity, as the expected frequencies in some cells were less than five. Continuous variables were analyzed using the student's t-test. Statistical significance was set at $p < 0.05$, and the JMP software package (SAS, Tokyo, Japan) was used to perform all statistical analyses.

3. Results

The patients’ baseline characteristics are presented in Table 1. The following factors were compared between the CONV and TST groups: age, BMI, postoperative radiation therapy, neoadjuvant chemotherapy, postoperative chemotherapy, taxane-containing regimen, total number of removed lymph nodes, and stage. The TST group included significantly more patients with advanced disease stages than in the CONV group; however, no significant differences were observed between both groups regarding other factors.

3.1. Incidence of BCRL

As shown in Table 2, the incidence of BCRL was significantly lower in the TST group than in the CONV group (2.9% vs. 22.2%; p = 0.028).

3.2. Relationship Between BCRL and Various Factors

In the TST group, there was no significant relationship between the occurrence of BCRL and factors including age, BMI, postoperative radiotherapy, neoadjuvant and/or postoperative chemotherapy, taxane-containing regimen, total number of removed lymph nodes, total drainage volume, duration of drainage, or incidence of seroma (Table 3).

Conversely, a significant relationship was observed between BCRL incidence and age, neoadjuvant and/or postoperative chemotherapy, taxane regimen, and total drainage volume for the CONV group (Table 4).

Table 1. Clinicopathologic characteristics of the study population.

	Total Sealing Technique (TST)	Conventional method (CONV)	P
Number of patients	35	36	
Age	60 .6 ± 14.1	66.2 ± 13.0	0.114
BMI (kg/m2)	24.4 ± 4.4	23.2 ± 4.1	0.337
Radiotherapy	14 (40.0%)	15 (41.7%)	> 0.999
Neoadjuvant chemotherapy	18 (51.4%)	11 (30.6%)	0.074
Postoperative chemotherapy	10 (28.6%)	14 (38.9%)	0.454
Taxane containing regimen	26 (74.2%)	21(58.3%)	0.211
Total number of removed lymph nodes	17.3 (14.5 - 20.1)	15.3 (13.7 - 16.9)	0.119
Stage			0.015*
0	0	2	
IA	1	4	
IIA	10	10	
IIB	5	9	
IIIA	6	7	
IIIB	3	2	
IIIC	5	1	
IV	5	1	

* p-value < 0.05 was significant.

Table 2. Comparison of lymphedema incidence between TST group and CONV group.

	Total Sealing Technique (TST)	Conventional method (CONV)	P
Number of patients	35	36	

Lymphedema			
(+)	1	8	
(-)	34	28	
Lymphedema incidence rate (%)	2.9	22.2	0.028*

* p-value < 0.05 was significant.

Table 3. Correlation between BCRL incidence and risk factors in the TST group.

	TST group		P
	BCRL(+) (n = 1)	BCRL(-) (n = 34)	
Age, years			> 0.999
< 63	0	17	
≥ 63	1	17	
BMI category (kg/m2)			> 0.999
< 25	1	22	
≥ 25	0	12	
Radiotherapy received			> 0.999
Yes	0	14	
No	1	20	
Neoadjuvant or Postoperative chemotherapy received			
Yes	1	27	> 0.999
No	0	7	
Taxane containing regimen			> 0.999
Yes	1	25	
No	0	9	
Total lymph nodes removed			> 0.999
< 19	0	17	
≥ 19	1	17	
Postoperative drainage volume, ml			> 0.999
< 270	0	17	
≥ 270	1	17	
Duration of drainage, days			> 0.999
< 5	0	17	
≥ 5	1	17	
Seroma			0.286
Yes	1	9	
No	0	25	

Fischer’s exact test indicated no significant difference between the two groups (p > 0.999), reflecting complete independence in the variable distribution.

Table 4. Correlation between BCRL incidence and risk factors in the conventional group.

	CONV group		P
	BCRL(+) (n = 8)	BCRL(-) (n = 28)	
Age, years			0.041*
< 71	7	11	
≥ 71	1	17	
BMI category (kg/m2)			> 0.999
< 25	5	19	

≥ 25	3	9	
Radiotherapy received			0.236
Yes	5	10	
No	3	18	
Neoadjuvant or Postoperative chemotherapy received			0.033
Yes	8	16	
No	0	12	
Taxane containing regimen			0.011
Yes	8	13	
No	0	15	
Total lymph nodes removed			0.709
< 15	3	13	
≥ 15	5	15	
Postoperative drainage volume, ml			0.003
< 600	0	18	
≥ 600	8	10	
Duration of drainage, days			0.422
< 7	2	12	
≥ 7	6	14	
Seroma			> 0.999
Yes	6	19	
No	2	9	

* p-value < 0.05 was significant.

4. Discussion

Current data suggest that the onset of BCRL is influenced by multiple factors that can be categorized into three groups: disease and treatment-related (including tumor size, ALND surgery, chemotherapy, and radiation therapy), lifestyle (such as physical activity, BMI, and preventive behaviors), and demographic factors (monthly income, marital status, and ethnicity) [14] [15] [1] [16] [17] [18] [19]. Data from this study showed that age, neoadjuvant and/or postoperative chemotherapy, and taxane-containing regimens were risk factors for BCRL occurrence. Notably, cases with a total drainage volume of > 600 ml had a significantly higher incidence of BCRL, recognized as a newly identified factor. A PubMed search yielded one report on the relationship between the amount of fluid drained from the axillary lymph nodes after axillary dissection and lymphedema. In 2017, Kretschmer et al. reported that a high volume of postoperative drainage fluid after complete lymph node dissection for axillary lymph node metastasis of melanoma significantly correlated with lymphedema [20]. However, the underlying mechanism has not yet been elucidated. Some reports indicate that patients with longer drainage periods have a higher risk of developing BCRL [21]. Similarly, Saadet et al. reported that a prolonged duration of axillary drainage is a risk factor for BCRL [22]. There are two possible explanations for this phenomenon. First, a longer drainage duration reflects a higher degree of lymphatic vessel damage, supporting the notion that extensive axillary surgery increases the incidence of BCRL [23]. Second, patients with drainage tubes are at an increased risk of developing BCRL owing to the restricted movement of the affected limb [24]. A cross-sectional study involving 775 patients supports this hypothesis, showing that women who exercise the affected upper extremity have a reduced risk of developing BCRL, potentially due to the "muscle pump" mechanism [19] [25]. A high volume of drainage fluid following ALND for breast cancer may be a predictive factor for BCRL development.

Several approaches have been reported to evaluate the measurement methods for BCRLs, including bioimpedance spectroscopy (BIS), water displacement, circumferential measurement, and infrared techniques. For stage 0 lower extremity lymphedema, which is not associated with extremity volume changes, previous studies recommended BIS [26,27]. However, the evidence remains limited

and inconclusive. Infrared methods have demonstrated high intra-examiner reliability (ICC intra=0.99, 95% CI=0.97-1.00) and validity (SEM:2.1%, SDC:5.6%) for stage I/II upper extremity lymphedema [28] [29]. However, the lack of inter-examiner reliability data and the associated cost and complexity limit their practicality for routine clinical use. In contrast, water displacement has shown high reliability and validity, particularly for the upper extremities (ICC intra=0.99, 95% CI=0.99,0.99/ICC intra=0.99, 95% CI=0.99,0.99/SEM = 0.7%, SDC = 3.6%) [30]. Nonetheless, it is also impractical for daily clinical use. Currently, the most commonly used method in routine practice is circumferential measurement, offering a reliability comparable to that of water displacement (ICC intra=0.99, 95% CI=0.99,0.99/ICC intra=0.99, 95% CI=0.98,0.98) [30]. It also has relatively high validity (SEM, 2.8%; SDC, 6.6%), making it the most practical method for extremity measurement [30]. Clinically significant differences can be determined using circumferential measurement when there is a discrepancy of 2 cm or more between the bilateral upper extremities. As circumference measurement is a novel assessment method for BCRL, some reports suggest that measuring and recording circumference before treatment and then performing comparative observations of the same side and site post-treatment may aid in diagnosis. A difference of 1 cm or more is considered indicative of BCRL [31,32].

The treatment of BCRL in practice after development is challenging. Consequently, many nonsurgical and surgical strategies have been developed for BCRL prevention and treatment. Recently, there has been an increased focus on prophylactic surgical procedures performed during initial axillary surgery to prevent BCRL. Since 2007, ARM has been developed as a novel surgical approach to distinguish the lymphatic drainage pattern of the upper extremity from that of the breast [33] [6]. This procedure aimed to minimize the risk of lymphedema by identifying and preserving the lymphatic drainage pathways of the arm in patients undergoing ALND or SLNB [6]. By injecting a blue or fluorescent dye into the arm, the technetium-labeled lymphatics of the breast can be visually distinguished from those of the arm, allowing their preservation during dissection. A large prospective study of ARM reported that the incidence of lymphedema at 26 months was 0.8% and 6.5% in patients who underwent SLNB and ALND, respectively [34]. In our present study, we found that modifying the surgical procedure by performing ALND with TST resulted in a 2.9% reduction in BCRL incidence, suggesting that this approach provides better results than ALND combined with ARM.

Furthermore, we discuss how TST using an LGSED improves BCRL incidence compared to conventional axillary dissection performed with a monopolar electrocautery scalpel. The primary reason for this difference likely lies in the extent of thermal diffusion into the surrounding tissues. One study described the extent of thermal spread using LigaSure. In the study, laparotomy was performed on eight pigs, and target vessels/organs were sealed with the LigaSure™ (LS1100) system prior to excision. Thermographic data showed that thermal damage was limited to 1.8 mm from the device, with jaw surface temperatures remaining within the range of surgical use (approximately 35°C). Moreover, histological studies confirmed minimal thermal damage [35]. Sutton et al. performed comparative experiments on lateral heat diffusion in porcine muscles using monopolar and bipolar diathermy, the Harmonic Scalpel™, and LigaSure™. The application of monopolar diathermy (10 s at 40 W) resulted in a temperature of 59.2°C in tissue 1 cm from the tip of the instrument. In contrast, both the Harmonic Scalpel™ and the LigaSure™ maintained temperatures below 20°C at equivalent power levels [36]. The thermal spread of electrocautery has been reported to cause thermal damage to surrounding soft tissues at temperatures greater than 43°C [37], meaning that even tissues 1 cm away can suffer significant thermal injury. Additionally, because the electrical conductivity of adipose tissue is approximately three times that of muscle, surrounding tissues are likely to reach higher temperatures during axillary dissection, which primarily involves adipose tissue [38]. Conventional electrocautery ALND often causes thermal damage to the surrounding lymphatic vessels, which should ideally be spared. This damage can lead to inflammation, eventual obstruction of lymphatic vessels, and ultimately, the development of upper extremity lymphedema. In contrast, TST with LGSED allows ALND to be performed without causing excessive thermal damage to the surrounding tissue. Furthermore, by effectively sealing the lymphatic vessels [8], lymphatic leakage is minimized, and the drainage volume is reduced, which likely contributes to the

prevention of BCRL. To the best of our knowledge, this is the first study to suggest that the monopolar electrocautery scalpel may be an important risk factor for the development of BCRL in breast cancer surgery with ALND.

This study has certain limitations, including its single-center design, limited sample size, and lack of randomization. However, these biases were mitigated by selecting consecutive clinical cases. Future research should aim to validate whether TST with LGSED truly reduces the risk of BCRL through multicenter randomized controlled trials (RCTs). In such studies, it is essential to standardize the extent of lymph node dissection and ensure adequate training for the correct use of LGSED.

5. Conclusions

This study demonstrates that TST with LGSED leads to improved surgical outcomes, particularly in terms of reducing BCRL incidence in breast cancer surgery with ALND. We suggest that this technique may become an essential surgical procedure for axillary dissection of breast cancer in the near future.

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Institutional Review Board Statement: This study was conducted in accordance with the guidelines detailed in the Declaration of Helsinki and approved by our institutional review board (approval number 2427, March 11, 2024).

Informed Consent Statement: Informed consent was obtained from all participants enrolled in this study using the opt-out method on our institute's website and at the hospital (as this was a retrospective study that used information from medical charts and computerized records).

Data Availability Statement: The data presented in this study are available upon request from the corresponding author. The data are not publicly available because of ethical approval.

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Conflicts of Interest: The authors declare no conflicts of interest with respect to the research, authorship, or publication of this article.

Abbreviations

The following abbreviations are used in this manuscript:

ALND	Axillary lymph node dissection
BCRL	Breast cancer-related lymphedema
SLNB	Sentinel lymph node biopsy
TST	Total sealing technique
CONV	Conventional electrocautery
RLNR	Regional lymph node radiation
ILR	Immediate lymphatic reconstruction
BMI	Body mass index
LGSED	LigaSure™ Exact Dissector

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