Risk Factors for Lymphedema After Breast Surgery: a Prospective Cohort Study in the Era of Sentinel Lymph Node Biopsy

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Abstract

Introduction: We aimed to investigate the incidence of lymphedema after breast cancer treatment, to analyze the risk factors involved, and to improve existing protocols for the prevention of lymphedema.

Patients and methods: This was a prospective cohort study of 232 patients undergoing surgery for breast cancer at our institution between September 2013 and February 2018. Sentinel lymph node biopsy (SLNB) or axillary lymphadenectomy (ALND) were mandatory in this cohort. Lymphedema was diagnosed by circumferential measurements and truncated cone calculations. Patients and tumor characteristics, as well as local and systemic therapies, were analyzed as possible risk factors for lymphedema.

Results: In total, 201 patients met the inclusion criteria and had a median follow-up of 31 months (range, 1–54 months). Most cases of lymphedema cases appeared in the first 2 years. 13.9% developed lymphedema: 31% after ALND and 4.6% after SLNB ($p < 0.01$), and 46.7% after mastectomy and 11.3% after breast-conserving surgery ($p < 0.01$). The lymphedema rate increased when axillary radiotherapy (RT) was added to radical surgery: 4.3% for SLNB alone, 6.7% for SLNB + RT, 17.6% for ALND alone, and 35.2% for ALND + RT ($p < 0.01$). In the multivariate analysis, the only risk factors associated with the development of lymphedema were ALND and mastectomy, which had hazard ratios (95% confidence intervals) of 7.28 (2.92–18.16) and 3.9 (1.60–9.49), respectively.

Conclusions: The main risk factors for lymphedema were the most radical surgeries (ALND and mastectomy), while the risk associated with these appeared to be worsened by the addition of axillary radiotherapy. A follow-up protocol in patients with ALND for at least two years, where these risk factors are recognized, is necessary to guarantee a comprehensive control of lymphedema that provides early detection and treatment.

Keywords: Breast cancer, Lymphedema, Sentinel lymph node biopsy, Axillary lymphadenectomy Mastectomy.

Introduction

Lymphedema is a direct consequence of damage to the lymphatic drainage system following the removal of lymph nodes in surgery for breast cancer. Research has shown that body mass index (BMI), the type of breast and axillary surgery, and the use of radiotherapy (RT) or chemotherapy with taxanes, among others, are risk factors for its development.[1–5] Damage to the lymphatic system from axillary lymphadenectomy (ALND) is greater to that from sentinel lymph node biopsy (SLNB), but both procedures are associated with developing lymphedema.[6,7] Therefore, novel surgical therapies have been developed to avoid this morbidity.

Since the standardization of the SLNB in patients with breast cancer and no clinical lymph-node involvement (cN0) in 1990–2000,[8] the trend has been to decrease the number of ALND procedures in favor of SLNB, even in some node-positive cases.[9] The latest St. Gallen Consensus, including work by other authors,[10] recommend avoiding ALND in women with 1 or 2 sentinel-positive lymph nodes after breast-conserving surgery when adjuvant RT and systemic therapy are given, irrespective of the tumor biology.[11] Due to the increase in SLNB surgeries in preference to ALND, we have observed a decrease in the overall rate of lymphedema occurrence and an increase in the number of patients with lymphedema secondary to breast cancer treatment after SLNB. This led us to consider whether our follow-up protocol for lymphedema prevention, which is lasts for 2 years after ALND, should be extended to patients with SLNB, or at least when the number of SLNBs is high (>3 SLNB).

The aim of this study was to investigate the incidence of arm lymphedema in our rehabilitation unit prospectively to 3 years after breast cancer surgery, and to determine the risk factors for its appearance. This information may help to improve the early detection and prevention of lymphedema.

Methods

A prospective longitudinal observational cohort study was performed of 232 patients with breast cancer. All patient underwent surgery at the multidisciplinary breast cancer unit of the Bellvitge University Hospital, Catalan Institute of Oncology, Barcelona, Spain, between September 2013 and February 2018. Axillary surgery was mandatory, either SLNB or ALND. Patients were enrolled in a pre-surgery visit in the Bellvitge University Hospital Rehabilitation Department and follow-up was at 1, 6, 12, 18, 24, and 36 months to assess the appearance and evolution of lymphedema. The inclusion criteria were as follows: age >18 years; male or female; unilateral primary breast cancer with a pathological diagnosis of breast carcinoma or carcinoma in situ; axillary surgery (SLNB or ALND); and conservative breast surgery or mastectomy without reconstruction. Patients with stage

IV breast cancer, no axillary surgery, mastectomy with immediate reconstruction, bilateral breast cancer, or a personal history of breast cancer or shoulder pathology were excluded.

Diagnosis of lymphedema related to breast cancer and cohorts

Lymphedema was diagnosed by circumferential measurements of the perimeters of both upper limbs, using an inextensible tape at pre-established points. The ulnar styloid, olecranon, and two points each on the forearm and middle arm served as anatomical landmarks.[12] The volumes of the affected and unaffected upper extremities were then obtained using perimeter measurements and the truncated cone formula.[13] The excess volume was recorded as the difference between the affected and unaffected limbs in milliliters. Lymphedema was considered present when the excess volume in the affected limb was at least 10% greater than that in the healthy limb,[3,14] and classified into three categories by severity: mild (excess volume <20%), moderate (20%–40%), and severe (>40%).[15] To analyze potential risk factors, patients were grouped into those with and without lymphedema.

All patients with a ≥10% excess lymphedema volume received treatment at the Bellvitge University Hospital Rehabilitation Department. Treatment consisted of lymphatic drainage, pressotherapy, and a multilayer bandage during the first phase, before moving to compression garments in the maintenance phase. Although treatment can improve lymphedema to different degrees, it never cures the chronic pathology.[13,16]

Recorded variables

Patient age, BMI, histological type, surrogate subtype, clinical stage at diagnosis (T and N), breast and axillary surgery type, number and level of lymph nodes dissected, adjuvant therapies, and shoulder range of motion (ROM) limitation were assessed. Immunohistological staining of the tumor samples by receptor status was classified into five surrogate subtypes according St Gallen 2019:[11] Luminal A-like, Luminal B-like, Luminal B Her2-positive, Her2-positive, and Triple Negative. ROM was measured with a goniometer and compared with the contralateral arm's mobility. A difference of 10º was chosen as the cut-off point to diagnose ROM limitation, as done in previous studies.[17]

Local and systemic treatment

We planned surgery for 4 weeks after a breast cancer diagnosis or the last chemotherapy course. Breast-conserving surgery was offered if optimal margins were guaranteed with a good aesthetic result. SLNB was only performed in clinically N0 cases, while ALND was performed in cases with >2 positive sentinel lymph nodes (according to the ACOSOGZ0011 and AMAROS criteria[10,18]) or N-positive (N+) disease at diagnosis.

Neoadjuvant chemotherapy included anthracyclines followed by taxanes for 6 months, with anti-

HER2 therapy added as appropriate. Lymphadenectomy was performed when SLNB was positive after neoadjuvant chemotherapy and for all N+ tumors. All patients who underwent breast-conserving surgery received radiotherapy. A boost to the tumor bed was administered by brachytherapy or external-beam RT in young patients or in those at high risk of locoregional recurrence.[10,11] RT to the chest wall after mastectomy was administered according to local guidelines for N+ cases, those with affected surgical margins, or those with large tumors (≥T3). Nodal RT was given if >3 lymph nodes were affected. Risk factors were considered to determine the need for nodal irradiation when 1–3 lymph nodes were involved.

Statistical analysis

Categorical variables are presented as numbers and percentages of cases, while continuous variables are presented as means and standard deviations (if normally distributed). Differences between groups were analyzed by chi-square or Fisher exact tests for categorical variables and by Student t-tests for continuous variables. Axillary surgery combined with axillary radiotherapy and breast surgery was also analyzed to better assess the impact of this association. A Cox regression multivariate analysis was performed to determine the impact of each risk factor on the development of lymphedema, and hazard ratios (HRs) with 95% confidence intervals (95%CIs) were calculated. Statistical significance was arbitrarily set at the 5% level and statistical analyses were performed using IBM SPSS Version 23.0 (IBM Corp., Armonk, NY, USA).

Ethical approval

The institutional ethics committee of the Bellvitge University Hospital (PR004/13) approved the present study. All procedures were performed in accordance with the ethical standards of the institutional ethics committee and national research standards, as well as those of the 1964 Declaration of Helsinki and its later amendments, or comparable ethical standards. Prior to inclusion, patients taking part in the study signed a written informed consent form.

Results

Participants

Informed consent was provided by 232 patients with breast cancer from September 2013 to February 2018, but only 201 (71 ALND and 130 SLNB) were included in the final sample (Figure 1). The patient and tumor characteristics for the overall sample are shown in Table 1.

Lymphedema incidence, grade, and severity

After a median follow-up of 35 months (Q1-Q3, 20-36 months), 28 of the 201 patients developed upper limb lymphedema: 22 after ALND (31%) and 6 after SLNB (4.6%). Thus, 13.9% of patients in our sample developed lymphedema during the first 3 years of follow-up (Figure 2), with most (24 of 28) doing so within the first 2 years. This equated to 86% of lymphedema cases starting during the first 2 years after surgical treatment of breast cancer. Lymphedema severity was mild in all cases after SLNB, but after ALND, it was mild in 18 cases (81.9%) and moderate in 4 cases (18.1%). All cases became stable over time with the use of compression garments.

Univariate analyses of the risk factors

The results of the univariate analyses of the risk factors for lymphedema are summarized in Table 2.

Mastectomy significantly increased the risk of developing lymphedema compared with breast-conserving surgery (HR 5.68; 95%CI, 2.40–13.39). However, 7 out of 15 mastectomies (46.7%) were performed for locally advanced tumors (T3 or T4) compared with just 12 out of 186 breast-conserving surgeries (6.5%). Mastectomies were performed in a significantly higher percentage of advanced tumors compared with conservative surgeries ($p < 0.0001$).

Regarding the type of axillary surgery, ALND also significantly increased the risk of lymphedema compared to SLNB (HR 8.55; 95%CI, 3.41–21.47). We observed more lymphedema cases when ALND included level III nodes rather than only levels I and II, though the differences were not statistically significant. Removing high numbers of lymph nodes in SLNB (>3) was not correlated with an increased risk of lymphedema.

RT and chemotherapy both affected the risk of lymphedema. Patients who received axillary RT to levels I–III and supraclavicular nodes presented a greater risk of developing lymphedema (HR 5.8; 95%CI, 2.55–13.27) than those who did not receive RT. The use of neoadjuvant chemotherapy was also associated with a slightly higher risk of developing lymphedema, independently of whether this included taxanes. Regarding adjuvant chemotherapy, no significant differences were found between groups, although it should be noted that all patients with lymphedema who we treated in the adjuvant setting received taxanes.

When we analyzed the increased risk of suffering from lymphedema by grouping axillary surgical technique and RT (Table 3), the risk increased progressively with the aggressiveness of axillary treatment. Compared with patients who underwent SLNB alone, patients who underwent SLNB plus axillary RT, ALND without axillary RT, and ALND plus axillary RT had 1.5-times, 4.3-times, and 10.9-times higher risks of suffering from lymphedema, respectively. Most SLNB cases received no adjuvant axillary radiotherapy (115/120), while most ALND cases received adjuvant radiotherapy

(54/71), exponentially increasing the risk of lymphedema in this group.

Limited shoulder ROM, another comorbidity related to breast cancer treatment, appeared principally during the first month after surgery and was associated with a significantly increased risk of lymphedema (HR 2.3; 95%CI, 1.00–5.26).

Multivariate analysis of risk factors

The risk factors significantly associated with the development of lymphedema in the multivariate analysis were mastectomy and ALND. These represented the most aggressive surgical options in both the breast and axilla. Overall, patients undergoing lymphadenectomy had a 7-times greater risk of developing lymphedema than those undergoing SLNB, especially when also undergoing mastectomy (Table 4).

Discussion

In this prospective study, the cumulative incidence of lymphedema secondary to breast cancer was 13.8% after a median follow-up of 35 months. ALND was the most important risk factor associated with its development (31% following ALND and 4.6% following SLNB; $p < 0.01$), especially when mastectomy was performed concurrently (70% following mastectomy plus ALND).

The percentage of lymphedema observed in our study is comparable with that observed in the literature.[3,19] Although the reported incidence varies from <5% to >50% overall, the incidence varies less in prospective studies from 8.4% to 21.4%. This variability may be influenced by the different definitions of lymphedema and by the methods used for measurement. Most diagnoses are made when there is a difference of ≥2 cm at any point of the circumference around the upper limb compared to the contralateral one, but this is not an absolute value. In our study, we used the definition that lymphedema is present when there is a volume excess >10%, which shows a good correlation with symptoms and is the absolute value referenced most often in a prominent meta-analysis.[19] In our experience, most cases of lymphoedema appeared during the first 2 years of follow-up, beyond which the risk reduced but did not disappear; again, these results are consistent with those reported by other authors.[3,5,20,21] The 2-year period when most cases of lymphedema appeared is extremely useful for deciding when to delimit the follow-up period in a multidisciplinary unit such as ours. Indeed, our current protocol for preventing lymphedema appears appropriate, with no need to adjust the follow-up period.

Regarding the severity of lymphedema, all patients with SLNB and most with ALND developed mild

lymphedema (volume excess of <20%), whereas only four developed moderate lymphedema after ALND (volume excess 20%–40%). These results were maintained from the measurement at the first visit to that at the last visit after 3 years, being similar to reports described by other authors.[20,22–24] This likely reflects our early detection during follow-up, the advanced and specialized treatment with multilayer bandages, and the use of effective maintenance treatment with compression garments.

Limited shoulder ROM appears mainly during the first postoperative month, as described by others.[3,25–27] In our opinion, limited shoulder ROM appears during the first month because it corresponds to a period during which the patient experiences post-surgery pain and surgeons may recommend care to avoid suture dehiscence. If the arm is kept immobilized, it will be understandable that patients experience limited shoulder mobility when they start to use it after 2–3 weeks. However, the relationship between shoulder ROM limitations and lymphedema has not been analyzed in other studies. We have observed an increase in lymphedema in this cohort, probably because muscle normally helps to drain the lymph vessels through its pumping action during normal use. Given that this is less active during the first postoperative month, we believe that limited arm mobility could promote the appearance of lymphedema. Although the small number of cases in our multivariate analysis was insufficient to confirm this hypothesis, it is consistent with advice to move the arm after surgery to avoid the appearance of lymphedema.[28]

In the multivariate analysis, it was the type of breast and axillary surgery that most significantly influenced the development of lymphedema. Our results show that ALND was associated with an increased risk of lymphedema, confirming the results of previous studies.[19,29–32] Interestingly, and contrary to the belief of many surgeons and the perception of some rehabilitation physicians, we did not find significant differences in the risk of developing lymphedema by the number of SLNBs. To date, very few studies have sought to differentiate the risk of developing lymphedema by the number of lymph nodes removed during SLNB, but those that do exist support the current work.[20,33–36] There is a fine balance between preventing lymphedema and causing undue worry, and thanks to research, we cannot advocate changing the status quo. Thus, lymphedema prevention follow-up should remain for patients undergoing ALND, but this need not be extended to patients undergoing SLNB. Mastectomy was also associated with a higher risk of lymphedema in these analyses, albeit only when ALND was also performed. This may be because mastectomy allows for more radical lymphadenectomy compared with conservative surgery or because mastectomy is chosen over breast-conserving surgery for more advanced or larger tumors. Several other authors have also reported this association.[1,4,19,37–39]

An association between axillary RT and lymphedema has been described in the literature.[40–42] In a

systematic review of eight studies, Lee et al.[3] reported a combined odds ratio of 1.46 for the development of lymphedema in patients treated with RT. In a meta-analysis, Di Sipio et al. also confirmed axillary RT to be a risk factor.[19] However, we found a higher risk of lymphedema for patients with axillary RT in the univariate analysis, but that this significance was lost in the multivariate analysis. The added risk of axillary surgery could have affected this result, and although axillary RT may increase the risk of developing lymphedema, the fundamental risk factor is the type of axillary surgery. It must be emphasized that there were too few cases with ALND and without RT to analyze their effects independently. Therefore, we must rely on analyzing axillary surgery plus RT together, which showed that the risk of suffering from lymphedema increased progressively with the aggressiveness of axillary surgery and the addition of axillary RT, similar to the results Naoum.[43]

RT treatment to the breast did not significantly alter the risk of lymphedema in the current study. This is consistent with other studies that have shown that breast irradiation does not increase the risk of upper limb lymphedema.[19,44,45] However, most patients in our population received adjuvant breast RT (197 of 201), meaning that this variable does lacks statistical power for independent analysis.

Neoadjuvant chemotherapy, regardless of whether it included taxanes, increased the risk of developing lymphedema in the univariate analysis, but not in the multivariate one. In the literature, chemotherapy with taxanes has been associated with the development of lymphedema due to its anti-lymphangiogenic effect, inhibiting the lymphatic regeneration process that normally prevents lymphedema, and thereby increasing the volume of extracellular fluid.[2,46,47]

Although no significant differences were found between groups based on whether they used adjuvant chemotherapy, we should point out that all patients developing lymphedema received adjuvant chemotherapy that included taxanes. Findings on this topic in the scientific literature are heterogeneous, with some studies finding no relationship with the development of lymphedema.[1,19,24,42,48,49] It may be that lymphedema develops only with more advanced tumors.

BMI was not a risk factor for lymphedema in the present study, but a clear association with a worsening of lymphedema has already been established in both the literature and clinical practice. Although other studies have failed to show a significant relationship between BMI and the risk of lymphedema,[35] most, including a meta-analysis,[19,40,41,44] conclude that obesity is a risk factor for its development. It is thought that lymphatic flow is impaired in obesity because the muscle pump is less active.[19]

Few mastectomies were performed in the current work, undoubtedly because we did not include patients with immediate reconstruction who typically have more advanced tumors. The decision to exclude these patients was because breast reconstruction is associated with an increased risk of

shoulder pathology and comorbidities that could bias the effect of axillary surgery, which was the focus of our study.

Despite limitations, such as the loss of patients over time and the small subgroups that precluded evaluation of taxanes and RT, the present study has several strengths. It was a prospective, single-center study that had a large sample size (n = 201) and used reliable and valid methods to assess lymphedema. Moreover, it had a long follow-up time of 35 months (Q1-Q3 20-36 months); given that the peak incidence of arm lymphedema is before the 24 months after surgery, we believe that our follow-up period was long enough.

Conclusion

The findings of this study show that, although the incidence of lymphedema after SLNB is not negligible, our existing follow-up protocol for lymphedema can only be recommended after ALND, especially when mastectomy was also performed. The prevalence of lymphedema during the first 3 years after breast cancer treatment was 31% when ALND was performed, but this decreased to 4.6% when SLNB was performed instead. ALND was the most important risk factor for the development of lymphedema, especially when performed concurrently with mastectomy. Surprisingly, however, the number of sentinel nodes removed was not a risk factor. We recommend close monitoring during the first 2 years in these cases, which is when most cases of lymphedema will arise. This approach should allow for the early detection and treatment of lymphedema, ultimately reducing its severity and impact on the quality of life of patients. More studies are needed to confirm our findings and suspicions.

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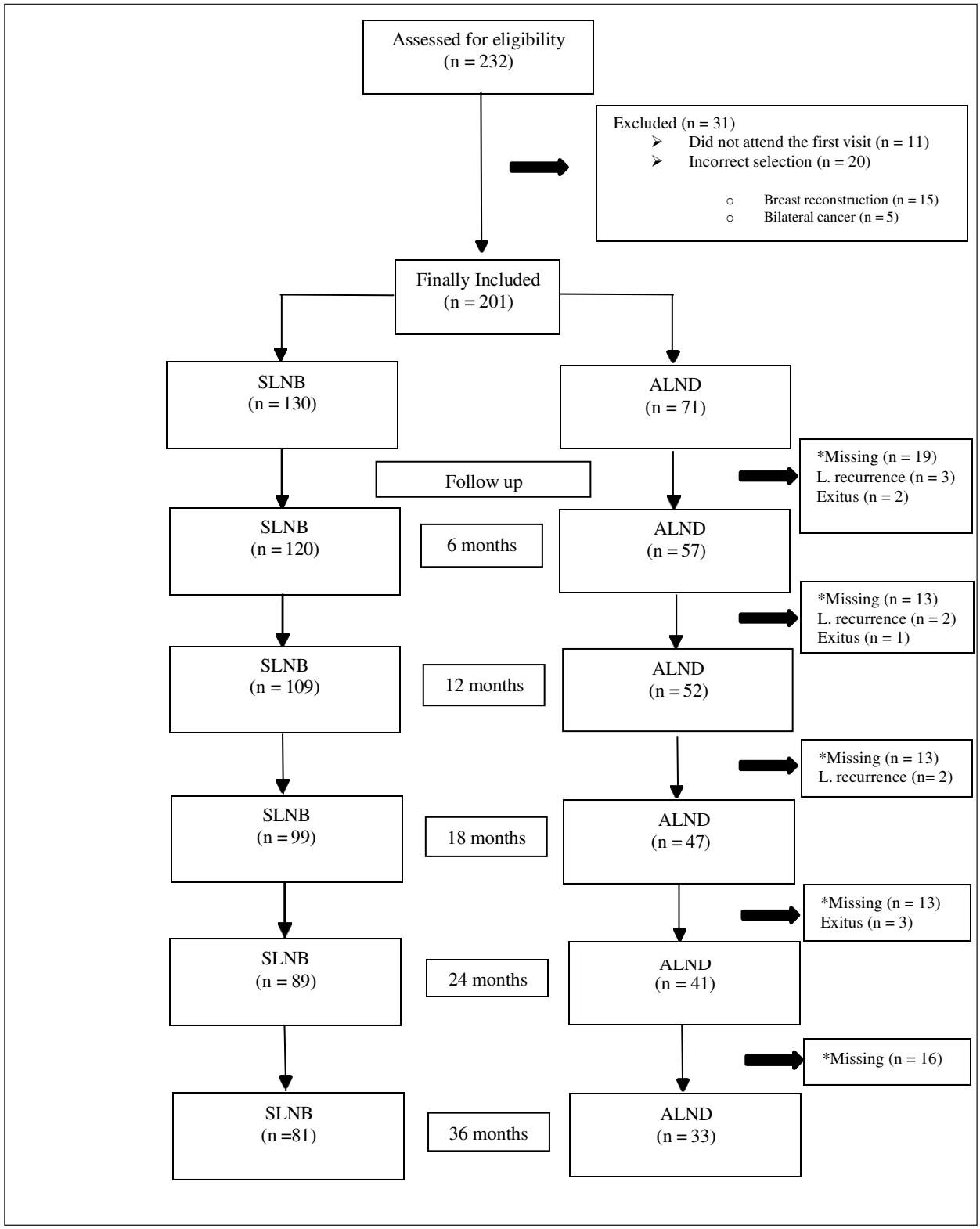

Figure 1. Flow chart of study participation

Abbreviations: SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection; L= Local.

* The missing patients continued follow-up by the Oncology Service, although they did not come for follow-up by the Rehabilitation Service.

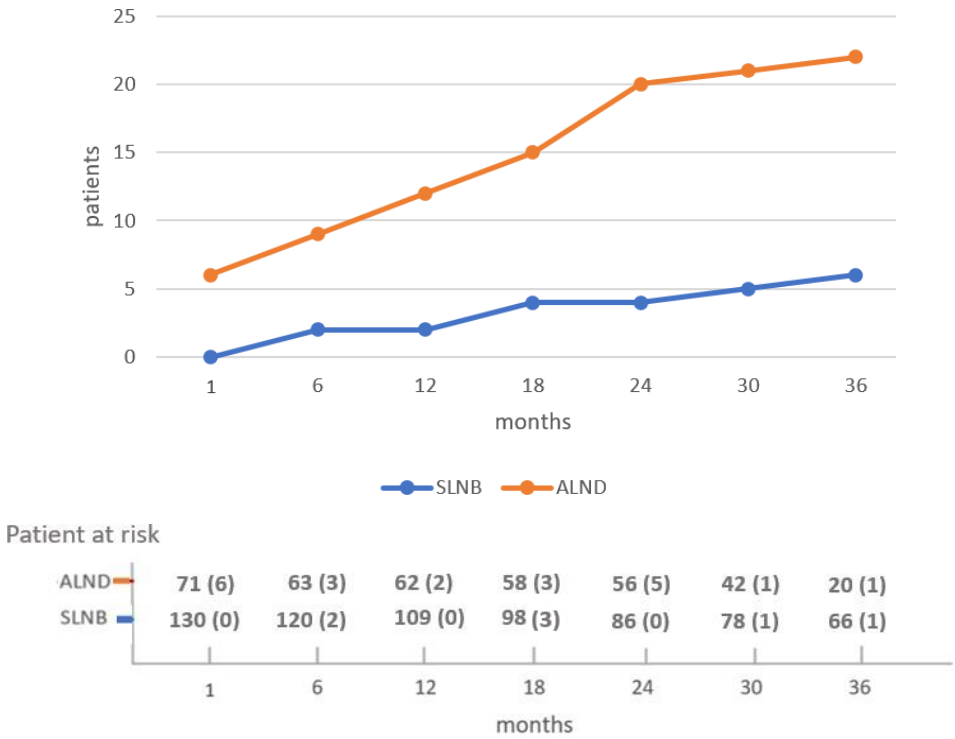

Figure 2. Lymphedema incidence by axillary surgery type.

Abbreviations: SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection.

Table 1: Patient Characteristics (n = 201)		
Variable	**N**	**n (%)**
Age	201	
Mean, years (SD)		56.6 (10.1)
Gender	201	
Female		199 (99%)
Male		2 (1%)
BMI (kg/m^2)	197	
<25		44 (22.3%)
≥25		153 (77.7%)
Histologic type	201	
DCI		164 (81.6%)
LCI		13 (6.5%)
In situ carcinoma		6 (2.9%)
Others		18 (9%)
Surrogate subtypes	195	
Luminal-A like		57 (29.3%)
Luminal-B like		75 (38.4%)
Luminal-B like Her2		32 (16.4%)
Her-2 positive		10 (5.2%)
Triple negative		21 (10.7%)
T Stage	201	
is		6 (3%)
1		111 (55.2%)
2		65 (32.3%)
3		14 (7%)
4		5 (2.5%)
N Stage	201	
0		101 (65.7%)
1		77 (22.8%)
2		19 (9.5%)
3		4 (2%)
Breast surgery type	201	
Breast conserving		186 (92.5%)
Mastectomy		15 (7.5%)
Axillar surgery type	201	

SLNB		130 (64.7%)
ALND		71 (35.3%)
Neoadjuvant CT	201	
No		153 (76.1%)
Yes		48 (23.9%)
Adjuvant CT	201	
No		128 (63.7%)
Yes		73 (36.3%)
Axillar RT	201	
No		129 (64.2%)
Supraclavicular		3 (1.5%)
I–III and Supraclavicular		69 (34.3%)

Abbreviations: ALND = axillary lymph node dissection; BMI = body mass index; CT = chemotherapy; DCI = Ductal Carcinoma invasive; Is = in situ; LCI = Lobular Carcinoma invasive; N = node involvement; RT = radiotherapy; SD = standard deviation; SLNB = sentinel lymph node biopsy; T = tumor size.

Table 2. Results of univariate analyses of risk for lymphedema

Variable	No Lymphedema (n=173)	Lymphedema (n=28)	HR [IC95%]	P
Age (SD)				
	57 (9)	55 (11)	0.99 [0.96-1.02]	0.53
BMI (kg/m^2)				
<25	38(86.4%)	6(13.6%)	Ref	
≥25	131(85.6%)	22(14.4%)	1.12 [0.45-2.76]	0.8
Histologic type				
DCI	142(86.6%)	22(13.4%)	Ref	
LCI	4(66.7%)	2(33.3%)	2.55 [0.59-10.88]	0.2
In situ carcinoma	11(84.6%)	2(15.4%)	1.31 [0.31-5.57]	0.71
Others	16(88.9%)	2(11.1%)	0.88 [0.21-3.73]	0.86
Surrogate subtypes				
Luminal-A like	48(84.2%)	9(15.8%)	Ref	
Luminal-B like	66(88%)	9(12%)	0.64 [0.25-1.61]	0.34
Luminal-B like Her2	28(87.5%)	4(12.5%)	0.84 [0.26-2.71]	0.83
Her-2 positive	8(80%)	2(20%)	1.66 [0.36-7.7]	0.51
Triple negative	19(90.5%)	2(9.5%)	0.55 [0.12-2.55]	0.44
T Stage				
Is-1-2	159 (87.4%)	23 (12.6%)	Ref	
3-4	14 (73.7%)	5 (26.3%)	2.63 [1-8.93]	0.05
N Stage				
0	95(94.1%)	6 (5.9%)	Ref	
1-3	78 (78%)	22 (22%)	7.19 [3.04-17.02]	<0.001
Breast surgery type				
Conserving	165 (88.7%)	21 (11.3%)	Ref.	—
Mastectomy	8 (53.3%)	7 (46.7%)	5.68 [2.40–13.39]	**<0.01**
Axillary surgery type				
SLNB	**124 (95.4%)**	**6 (4.6%)**		
<3	*85 (95.5%)*	*4 (4.5%)*	*Ref.*	—
≥3	*39 (95.1%)*	*2 (4.9%)*	*1.05 [0.19–5.76]*	*0.96*
ALND	**49 (69%)**	**22 (31%)**	8.55 [3.41–21.47]	**<0.01**
I–II	*38 (71.7%)*	*15 (28.3%)*	*Ref.*	—
III	*11 (61.1%)*	*7 (38.9%)*	*8.56 [3.41–21.48]*	*0.60*

ROM limitation at 1 month				
No	127 (87%)	19 (13%)	Ref	
Yes	25 (75.8%)	8 (24.2%)	2.30 [1–5.26]	**<0.05**
Breast RT				
No	4 (100%)	0 (0%)	Ref.	—
Yes	169 (85.8%)	28 (14.2%)	NA	0.42
Axillary RT				
No	124 (93.9%)	8 (6.1%)	Ref.	—
Yes	49 (71%)	20 (29%)	5.82 [2.55–13.27]	**<0.01**
Neoadjuvant CT				
No	133 (86.9%)	20 (13.1%)	Ref.	—
Yes	40 (76.9%)	8 (23.1%)	2.67 [1.26–5.64]	**0.01**
Taxanes	*31 (83.8%)*	*6 (16.2%)*	*1.25 [0.5–3.11]*	*0.64*
Others	*9 (81.8%)*	*2 (18.2%)*	*1.92 [0.45–8.27]*	*0.38*
Adjuvant CT				
No	111 (86.7%)	17 (13.3%)	Ref.	—
Yes	62 (84.9%)	11 (15.1%)	*2.50 [0.14–0.08]*	0.27
Taxanes	*51 (82.3%)*	*11 (17.7%)*	*1.24 [0.58–2.65]*	*0.58*
Others	*11 (100%)*	*0 (0%)*	*NA*	*0.98*

Abbreviations: ALND = axillary lymph node dissection; CT = chemotherapy; HR = hazard ratio; Is = in situ; N = node involvement; NA = Not applicable; ROM = range shoulder of motion, RT = radiotherapy; SLNB = sentinel lymph node biopsy; T = tumor size; Tis = tumor in situ.

Table 3. Lymphedema risk based on combined interaction factors

Variable	No Lymphedema (n=173)	Lymphedema (n=28)	HR [IC95%]	P
Axillar surgery and axillary RT				
SLNB without axillary RT	110 (95.7%)	5 (4.3%)	Ref	–
SLNB with axillary RT	14 (93.3%)	1 (6.7%)	1.51 [0.18–12.98]	0.71
ALND without axillary RT	14 (82.4%)	3 (17.6%)	4.33 [1.02–18.39]	0.05
ALND with axillary RT	35 (64.8%)	19 (35.2%)	10.92 [4.02–29.66]	**<0.01**
Axillar and breast surgery type combined				
BC + SLNB	119 (95.2%)	6 (4.8%)	Ref.	—
Mastectomy + SLNB	5 (100%)	0 (0%)	NA	0.98
BC + ALND	46 (75.4%)	15 (24.6%)	5.93 [2.29–15.341]	**<0.001**
Mastectomy + ALND	3 (30%)	7 (70%)	29.51 [9.76–89.23]	**<0.001**

Abbreviations: ALND = axillary lymph node dissection; BC = breast conserving; RT = radiotherapy; SLNB = sentinel lymph node biopsy.

Table 4. Results of multivariate analyses of risk factors for lymphedema

Variable	No Lymphedema (n=173)	Lymphedema (n=28)	HR [IC95%]	P
Axillar surgery type				
SLNB	124 (95.4%)	6 (4.6%)	Ref.	—
ALND	49 (69%)	22 (31%)	7.28 [2.92–18.16]	**<0.01**
Breast surgery type				
Breast conserving	165 (88.7%)	21 (11.3%)	Ref.	—
Mastectomy	8 (53.3%)	7 (46.7%)	3.9 [1.60–9.49]	**<0.01**

Abbreviations: ALND = axillary lymph node dissection; SLNB = sentinel lymph node biopsy; NA = Not applicable.

Figures

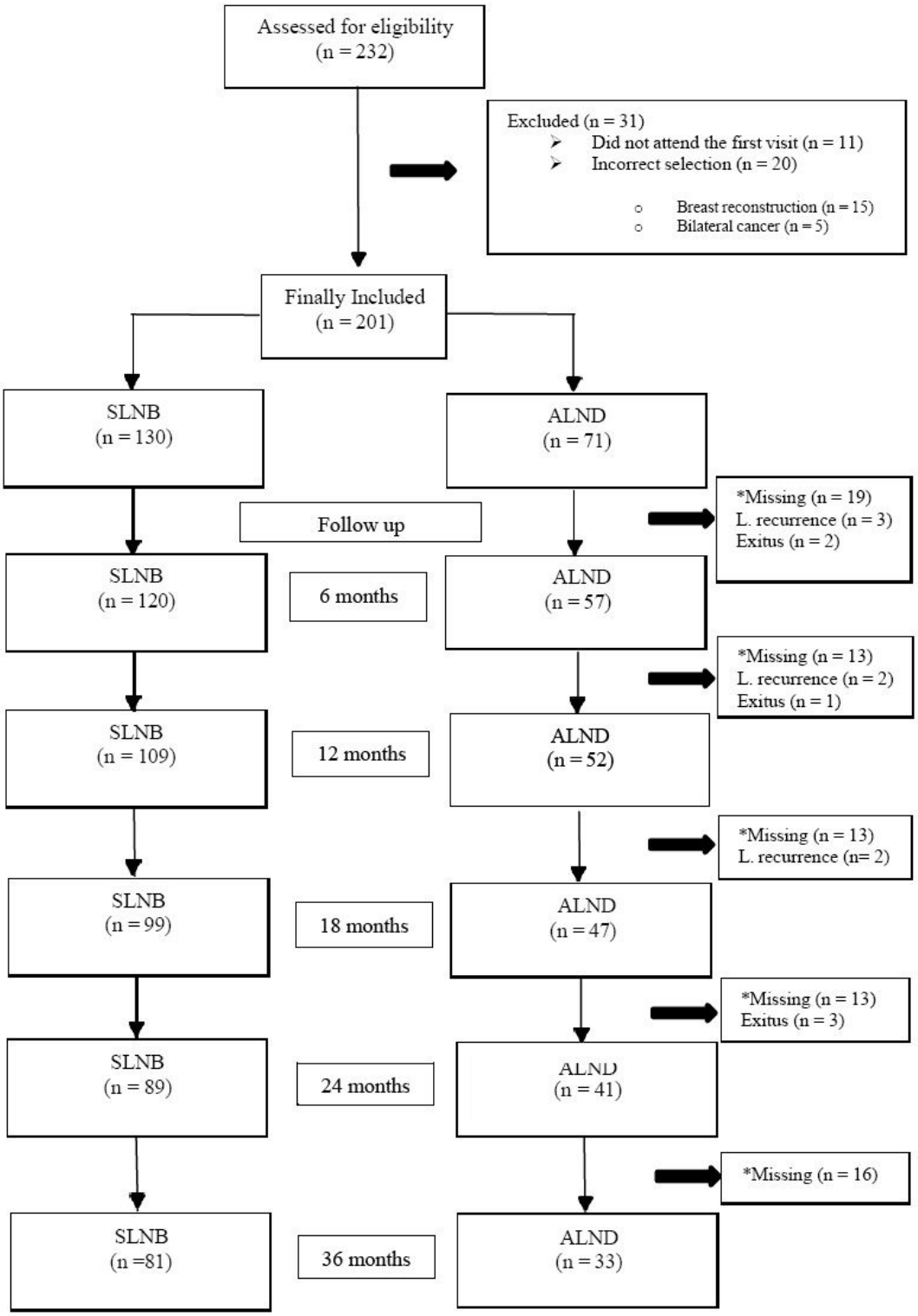

Figure 1

Flow chart of study participation Abbreviations: SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection; L= Local. * The missing patients continued follow-up by the Oncology Service, although they did not come for follow-up by the Rehabilitation Service.

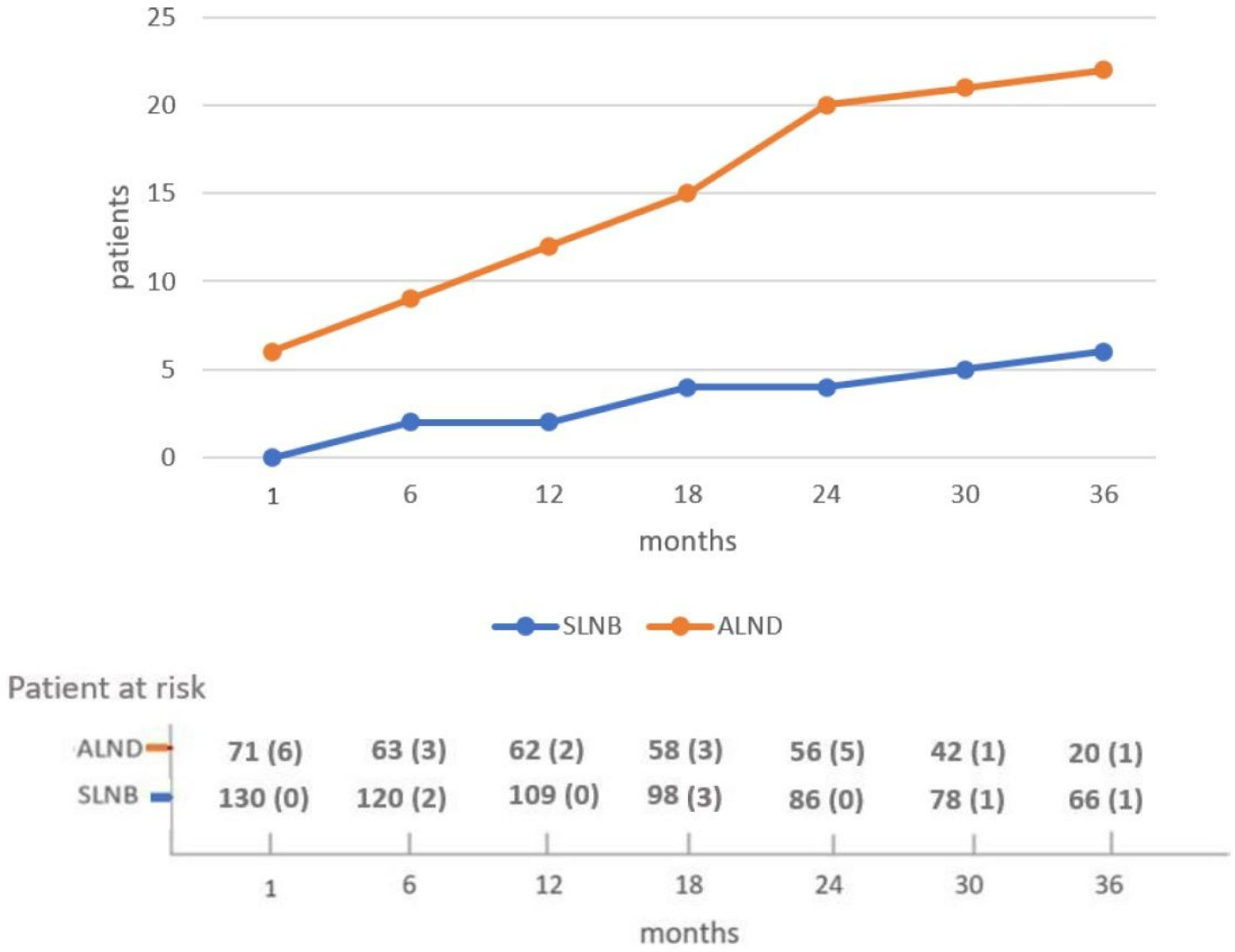

Figure 2

Lymphedema incidence by axillary surgery type. Abbreviations: SLNB = sentinel lymph node biopsy; ALND = axillary lymph node dissection.