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A Comparative Study for Lymphedema Following Formal Axillary Lymph Node Dissection versus Lymphnode Sentinel Biopsy for Breast Cancer

Mohamed khalaf[1]; Wagih Fawzy[2]; Sherif Morad[1]; Alaa Mohamed Abd Elsalam Khedr[1]

[1]General Surgery Department, Faculty of medicine, Ain Shams University, Cairo, Egypt
[2]Vascular Surgery Department, Faculty of medicine, Ain Shams University, Cairo, Egypt
Alaakhdr00@gmail.com

Abstract: Background: Breast cancer treatment related lymphedema (BCRL) is associated with significant morbidities. To reduce the rate of BCRL, surgeons have changed the clinical practice in the surgical treatment of breast cancer, by performing sentinel lymph node biopsy (SLNB) instead of performing axillary lymph node dissection (ALND). **Objective:** The aim of this study is to compare and describe occurrence of lymphedema after complete axillary dissection versus sentinel lympnode biopsy in management of breast cancer. **Methods:** The present study is a prospective comparative study. It was conducted in the period from July, 2017 through June, 2018. The present study sought to compare using SLNB versus ALND in breast cancer patients in respect to occurrence of lymphedema. The study recruited 20 women indicated for modified radical mastectomy. They were equally and randomly allocated to one of the treatment groups: group I patients were subjected to ALND while group II patients were subjected to SLNB. Postoperatively, all patients were followed for lymphedema and related symptoms up to 6 months. **Results:** Comparison between the studied groups at baseline regarding age, BMI and pathological data revealed no statistically significant differences. In addition, there were no statistically significant differences between the studied groups regarding the preoperative arm circumference. Matching of the basic data assures that the study outcome would be probably attributed to the different surgical interventions. In the current study, comparison between the studied groups regarding the postoperative arm circumference higher arm circumference in GI patients which was short of statistical significance. However, the percent of arm circumference increase was significantly higher in GI patients. These differences were reflected in the significantly higher rate of lymphedema in GI patients as compared to GII patients (40.0 % versus 0.0 %, p=0.025). **Conclusions:** SLNB is associated with significantly lower rate of lymphedema.

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1. Introduction

Breast cancer survivors are at lifetime risk for developing lymphedema, a common side-effect that occurs in up to 40% of breast cancer patients undergoing radiation and surgical resection of axillary lymph nodes. Second only to breast cancer recurrence, lymphedema is the most dreaded outcome of breast cancer treatment ***(Armer et al., 2009)***.

Lymphedema is a chronic lymphatic condition that consists of interstitial accumulation of protein-rich fluid and subsequent inflammation, adipose tissue hypertrophy and fibrosis, resulting in swelling, disfigurement, heightened risk of infection, and decreased mobility and function ***(Finnane et al., 2015)***.

Breast cancer-related lymphoedema (BCRL) as a disabling complication has a long term impact on quality of life ***(Goker et al., 2013)***.

Risk factors contributing to the development of BCRL include higher stage of breast cancer, higher number of axillary lymph node removed, postoperative complications, hypertension, high body mass index, chemotherapy and radiotherapy ***(DiSipio et al., 2013; Goker et al., 2013; Hidding et al., 2014; Zhu et al., 2014)*** and certain genes ***(Miaskowski 2013)***.

The incidence of BCRL was about four times higher in women who had an axillary lymph node dissection than that in those who had sentinel-node biopsy ***(DiSipio et al., 2013)***.

Exercise such as strength training has been associated with lower risk of BCRL ***(Park, 2008; Swenson, 2009)***.

BCRL can affect the arm, hand, fingers, wrist, elbow, shoulder, neck, breast, chest or any combination of these areas. Arm BCRL is the most widely studied and is classified according to the excess volume of the affected arm compared to the unaffected arm. A common arm classification is mild (< 20% excess volume), moderate (20% to 40% excess volume) and severe (> 40% excess volume) ***(Partsch et al., 2010)***.

In addition to the excess fluid build up, BCRL is associated with feelings of discomfort and heaviness, creates considerable disability, pain, functional limitation, heaviness, numbness, disfigurement, physio-psychological distress (anxiety or depression), an elevated risk of recurrent infection, it also negative effect on quality of life ***(Chan et al., 2010; Cheifetz et al., 2010; Fu et al., 2013; Zhu et al., 2014)***.

Early detection and treatment of BCRL can both reduce lymphatic swelling and maintain that reduction over time ***(Hayes, 2012)***.

Management of BCRL remains a major challenge for patients and health care professionals ***(Fu, 2014)***.

There were several treatment strategies that aim to reduce swelling, prevent progression, reduce risk for infection, and alleviate associated symptoms (***Fu, 2014; Finnane et al., 2015).***

These strategies include complete decongestive therapy ***(Lasinski et al., 2012)***, low level laser therapy, complex physical therapy, manual lymphatic drainage (MLD), pneumatic pumps, oral pharmaceuticals, compression bandaging and garments, limb exercise and limb elevation ***(Kwan et al., 2011)***, massage ***(Pan et al., 2014)***, surgery ***(Leung et al., 2015)***.

Aim of the study

The aim of this study is to compare and describe occurrence of lymphedema after complete axillary dissection versus sentinel lympnode biopsy in management of breast cancer.

2. Patients and Methods

The present study is a prospective comparative study. It was conducted in the period from July, 2017 through June, 2018. The study protocol was approved by the local ethical committee and all patients gave informed consent to participate in the study.

Patients

Selection of patients

The study included 20 patients. They were selected to participate in the present study on the basis of the following criteria:

Inclusion criteria:

Female breast cancer patients, aged 20 – 50 years, and subjected to modified radical mastectomy for stage 1,11 breast cancer.

Exclusion criteria: Recurrent cases, congenital lymphatic disease, and vascular disease of the upper limb.

Patients groups and randomization

The20 patients were equally and randomly allocated to one of the treatment groups: group I patients were subjected to ALND while group II patients were subjected to SLNB. Postoperatively, all patients were followed for lymphedema and related symptoms up to 6 months.

Methods

All patients included in the study were subjected to the following:

A. Thorough clinical and laboratory assessment

- Careful history taking.
- Thorough clinical examination.
- Radiological assessment.
- Pathological assessment.

B. Study intervention

All patients were subjected to modified radical mastectomy. In addition, patients with subjected to ALND or SLNB.

- **SLNB**

A combined mapping technique was used, with an intradermal injection of technetium-labeled sulfur colloid and an intraparenchymal injection of isosulfan blue dye. All radioactively ‘‘hot,’’ blue, and clinically suspicious LNs were removed ***(Cody et al., 1999).***

C. Outcome intervention

Pre and 6 months postoperatively, upper midarm circumference was measured in all patients using a non-stretchable tape. Lymphedema was defined as an increase in the measured circumferences postoperatively by ≥ 2 cm ***(Armer et al., 2004).***

Statistical analysis

Data obtained from the present study were computed using SPSS versions. Continuous data were expressed in the form of mean ± SD while categorical data were expressed in the form of count and percent. Comparison of continuous data were performed utilizing student t test, while categorical data were done using Chi-square test. P value less than 0.05 was considered statistically significant.

3. Results

Table (1) shows no statistically significant differences between the studied groups regarding age, BMI and pathological data.

Table (1): Comparison between the studied groups regarding the basic data

		GI (ALND) n=10	GII (SLNB) n=10	P value
Age		48.3 ± 1.5	46.9 ± 2.1	0.11
BMI		28.7 ± 2.3	27.3 ± 1.9	0.18
Pathology	**IDC**	8 (80.0 %)	7 (70.0 %)	0.61
	ILC	2 (20.0 %)	3 (30.0 %)	
Grade	**I**	4 (40.0 %)	6 (60.0 %)	0.37
	II	6 (60.0 %)	4 (40.0 %)	

Table (2) shows no statistically significant differences between the studied groups regarding the preoperative arm circumferences.

Table (2): Comparison between the studied groups regarding preoperative arm circumference

		GI (ALND) n=10	GII (SLNB) n=10	P value
Preoperative arm circumference	**Range**	29.0 -35.0	30.0 – 35.0	0.65
	Mean ± SD	32.0 ± 1.9	32.4 ± 1.9	

Table (3) shows no statistically significant differences between the studied groups regarding the postoperative arm circumferences. Table (4) shows significantly higher arm circumference increase in GI patients when compared to GII patients.

Table (3): Comparison between the studied groups regarding postoperative arm circumferences

		GI (ALND) n=10	GII (SLNB) n=10	P value
Postoperative arm circumference	**Range**	31.0 – 48.0	30.0 – 36.0	0.11
	Mean ± SD	36.0 ± 6.3	32.9 ± 2.0	

Table (4): Comparison between the studied groups regarding in percent of increase in arm

		GI (ALND) n=10	GII (SLNB) n=10	P value
Arm circumference increase (%)	**Range**	0.0 – 41.2	0.0- 6.9	0.031*
	Mean ± SD	14.3 ± 14.8	2.2 ± 2.3	

Table (5) shows significantly higher frequency of lymphedema in GI patients when compared with GII patients.

Table (5): Comparison between the studies groups regarding the prevalence of lymphedema

		GI (ALND) n=10	GII (SLNB) n=10	P value
Lymphedema	**+ve**	4 (40.0 %)	-	0.025*
	-ve	6 (60.0 %)	10 (100.0 %)	

4. Discussion

The present study sought to compare using SLNB versus ALND in breast cancer patients in respect to occurrence of lymphedema. The study recruited 20 women indicated for modified radical mastectomy. They were equally and randomly allocated to one of the treatment groups: group I patients were subjected to ALND while group II patients were subjected to SLNB. Postoperatively, all patients were followed for lymphedema and related symptoms up to 6 months.

Comparison between the studied groups at baseline regarding age, BMI and pathological data revealed no statistically significant differences. In addition, there were no statistically significant differences between the studied groups regarding the preoperative arm circumference. Matching of the basic data assures that the study outcome would be probably attributed to the different surgical interventions.

In the current study, comparison between the studied groups regarding the postoperative arm circumference higher arm circumference in GI patients

which was short of statistical significance. However, the percent of arm circumference increase was significantly higher in GI patients. These differences were reflected in the significantly higher rate of lymphedema in GI patients as compared to GII patients (40.0 % versus 0.0 %, p=0.025).

The prevalence of lymphedema in the present study (40.0 %) is in line with results reported by the Indian study of ***Pillai et al., (2010)***. In their work on 231 patients, overall incidence of lymphedema was 41.1%. Also, in the study of ***Soran et al., (2016)*** lymphedema was present in 36.1% (n = 65) of 180 patients with ALND.

The 0.0 % of lymphedema in women subjected to SLNB in the present study is in agreement with the study of ***Ozcinar et al., (2012)*** who aimed to determine the rate of mid-term and late time period lymphedema in breast cancer patients with different loco-regional treatments, and factors associated with lymphedema. In their study, patients with SLNB had no postoperative lymphedema.

In contrast to the 0 % of lymphedema in women subjected to SLNB in the present study, the prevalence was 5.0 in the study of ***Goldberg et al., (2010)***. They found no significant association between the number of excised lymph nodes and the reported postoperative lymphedema. They suggested that other factors, such as the global disruption of the lymphatic channels during axillary lymph node dissection, play a larger role in development of lymphedema than does the number of LNs removed.

Interestingly, the systematic review of ***Gebruers et al., (2015)*** that assessed the incidence/prevalence and time path of lymphedema in patients with sentinel node-negative breast cancer found that the overall incidence of lymphedema in patients with sentinel node-negative breast cancer ranged from 0% to 63.4%.

The significantly higher rate of lymphedema in GI patients as compared to GII patients in the present study is in agreement with the study of ***McLaughlin et al., (2008)*** who compared SLN biopsy (SLNB) alone or SLNB followed by axillary lymph node dissection (SLNB/ALND) in women with breast cancer. The study found that when compared to SLNB/ALND, SLNB-alone results in a significantly lower rate of patient-perceived arm swelling postoperatively, and is perceived by fewer women than are measured to have it.

In another study conducted on older women, the prevalence of lymphedema was 7.0 % in patients subjected to SLNB in comparison to 21.0 % in patients subjected to ALND ***(Yen et al., 2009).***

Moreover, the study of ***Norman et al. (2010)*** who aimed to identify the risk factors for lymphedema in women subjected to breast cancer treatment found that with standard multivariable analyses, ALND and chemotherapy increased lymphedema risk whereas radiation therapy and SLNB did not.

Also, the study of ***Miller et al. (2012)***, the authors sought to determine the risk of lymphedema after mastectomy with and without nodal evaluation. Of 234 mastectomies performed, 15.8 % (37/234) had no axillary surgery, 63.7 % (149/234) had SLNB, and 20.5 % (48/234) had axillary lymph node dissection (ALND). The study found that mastectomy with ALND was associated with a significantly greater mean weight-adjusted arm volume change compared to mastectomy with SLNB and without axillary surgery.

In another study, ***Wetzig et al. (2017)*** aimed to determine whether the benefits of sentinel-node-based management (SNBM) over routine axillary clearance (RAC) persisted to 5 years. The study found that significant predictors for lymphedema development determine whether the benefits of sentinel-node-based management (SNBM) over routine axillary clearance (RAC) persisted to 5 years.

Even after 10 years, the combination of axillary dissection and number of lymph nodes dissected was the main factor related to lymphedema ***(Vieira et al., 2016).***

Most recently, the studies of ***Bhatt et al., (2018)*** and ***McDuff et al., (2019)*** found significantly higher rates of lymphedema in women subjected to ALND in comparison to those subjected to SLNB.

On the other hand, ***McLaughlin et al., (2013)*** prospectively enrolled 120 women undergoing sentinel node biopsy (SLNB) or axillary node dissection (ALND) for breast cancer and assessed lymphedema by upper extremity volume preoperatively and at 6 and 12 months postoperatively. At 6 months, lymphedema was similar between ALND and SLNB patients but was higher in ALND women at 12 months.

Moreover, the study of ***Boughey et al., (2014)*** on 124 women found that lymphedema did not occur more often after axillary lymph node dissection versus sentinel lymph node biopsy and was not associated with total number of nodes removed.

The study of ***Boneti et al. (2008)*** provided an explanation of situations where there is a relatively high rate of lymphedema in patients subjected SLNB. They noted that those patients had disrupted lymphatics due to the proximity of sentinel LN to the course of lymphatics.

Conclusion

SLNB is associated with significantly lower rate of lymphedema.

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