

# Lymphoedema after mastectomy for breast cancer: Importance of supportive care

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**Background.** Lymphoedema resulting from axillary lymph node dissection remains a challenging complication after modified radical mastectomy.

**Objective.** To examine the effects of supportive therapy such as rehabilitation and medical and physical treatment on the development of lymphoedema, in an attempt to establish non-surgical ways to help prevent or reduce it.

**Methods.** Patients ( $N=5\ 064$ ) who underwent breast cancer surgery in the Department of General Surgery, Ankara Oncology Research and Training Hospital, Turkey, between 1995 and 2010 were included. Data were collected by retrospectively examining all the patients' files and the pre- and postoperative breast cancer follow-up forms.

**Results.** Of the patients in the study, 19.9% developed lymphoedema. It was significantly less common in patients who participated in physiotherapy than in those who did not, and it was more common in patients with a body mass index (BMI, kg/m<sup>2</sup>) between 30 and 34.9 than in those with lower BMIs. Postoperative axillary radiotherapy did not affect the occurrence of lymphoedema.

**Conclusion.** It is clear that the most successful method to reduce the impact of lymphoedema is to prevent it. We believe that educating patients about the risk factors for developing lymphoedema and referring them to postoperative physical therapy and rehabilitation clinics are the most important ways to avoid this distressing condition.

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Lymphoedema is the substantial effusion of protein into the interstitial areas resulting from a failure in lymph drainage. Symptoms of this chronic condition may include swelling, fibrosis, restricted joint mobility and pain. In addition, the presence of protein in the interstitial area increases the risk of infection.<sup>[1]</sup>

The prevalence of secondary lymphoedema in breast cancer patients has been reported to be between 6% and 80%.<sup>[1]</sup> Although surgery and axillary radiotherapy are considered to be primary contributing factors, the true cause is multifactorial and has not been established with certainty.<sup>[2]</sup> The problem is easy to detect, causing a decrease in quality of life due to pain, a heavy sensation in the limbs, decreased mobility and repeated tissue infections.<sup>[3-5]</sup> We examined the effects of supportive therapy such as rehabilitation and adjuvant medical and physical treatment on the development of lymphoedema, to determine whether there are non-surgical ways to help prevent it.

## Methods

Patients ( $N=5\ 064$ ) with stage II and III disease who underwent breast cancer surgery in the Department of General Surgery, Ankara Oncology Research and Training Hospital, Turkey, between 1995 and 2010 were included in the study. Data were collected by retrospectively examining all the patients' files and the pre- and postoperative breast cancer follow-up forms. Patients who

sustained upper limb trauma during the pre- and postoperative period, were known to have vascular disease or to have had a serious thromboembolic event, had undergone neoadjuvant chemotherapy or radiotherapy, or had uncontrolled diabetes mellitus, cardiovascular disease that caused sufficient perfusion deficiency to delay recovery or a history of serious infection or surgery in the involved arm were excluded from the study.

The patients were operated on by different surgeons, with between 8 and 36 years' experience. All underwent the same operation, i.e. modified radical mastectomy with level I-II-III axillary dissection. As part of the mastectomy, which included Cooper's ligaments, a Stewart transverse incision was made. The axillary dissection was completed by dissecting under the pectoralis minor muscle. Preoperatively all patients were instructed to reduce the risk of lymphoedema in the arm on the side that had been operated on by preventive measures such as avoiding needle punctures, withdrawal of blood and blood pressure readings on that side. During the postoperative period, pressure dressings on the axillary fossa and flap region were used during the first 5 days. If there was concern regarding wound healing, the patient was referred to the appropriate department to discuss possible delay in adjuvant treatment (chemotherapy and radiotherapy). Venous cannulation was not performed on the involved arm during the first 2 postoperative years.

Patients were asked to attend for follow-up once a month for the first 3 postoperative years, once every 6 months for next 4

years, and then once a year. The minimum follow-up period was 13 months and the maximum 12 years, with a mean of 64 months (not all patients attended as regularly as they had been instructed to). Preoperative measurements of the circumference of each patient's arms, forearms and elbows were made, and a difference of >5% between the arms postoperatively was considered to indicate lymphoedema. No distinction was made between mild, moderate or severe lymphoedema.

In patients who received adjuvant radiotherapy, this included treatment of the axillary area. Cyclophosphamide, adriablastine, 5-fluorouracil and docetaxel were used for first-line adjuvant chemotherapy. None of the drugs used is reported to have isolated lymphoedema as a side-effect.

All patients were referred to physiotherapy and the rehabilitation clinic postoperatively. They were taught self-drainage massage techniques to use daily, and flexibility and strength exercises. Patients were also informed about the symptoms of lymphoedema, personal hygiene measures and general protective measures. This information was detailed and was reinforced in a booklet that was given to the patient to keep. Patients who continued to visit the physiotherapy department for therapy and did their exercises regularly were included in the 'physiotherapy' group, while those who lived in areas where there was no opportunity to receive physiotherapy and rehabilitation, or who did not do the exercises regularly, were included in the 'no physiotherapy' group.

The patients' age, employment status (employed/unemployed), baseline body mass index (BMI, kg/m<sup>2</sup>) (<17.9, 18 - 24.9, 25 - 25.9, or 30 - 34.9), and history of adjuvant chemotherapy, adjuvant radiotherapy and physiotherapy were evaluated, recorded and compared. Because of the synchronised level of axillary dissection (level I-II-III), the number of axillary lymph nodes (mean 16.8 v. 14.9) and positive lymph nodes (mean 8.3 v. 9.2) were similar between all groups, and this information was not included in the study criteria.

The following statistics were used to summarise the data: numbers and percentages for categorical data/averages, standard deviations, lowest and highest values for normally distributed numerical data/medians, interquartile ranges, and highest and lowest values for abnormally distributed numerical data. The  $\chi^2$  test or Mantel-Haenszel test was used for comparing categorical variance, and the Mann-Whitney *U* test for comparisons between subgroups. The effects of patient age, employment status, baseline BMI and history of adjuvant chemotherapy, adjuvant radiotherapy and physiotherapy were evaluated, with the significance level set as  $p < 0.05$ . The analyses were done using NCSS 2007 version 07.1.14 software.

## Results

Of the patients in the study, 19.9% developed lymphoedema (Table 1), after a mean of 29 months. The median ages of the patients with and without lymphoedema were 51 years (interquartile range (IQR) 34 - 75), and 50 years (IQR 71 - 31), respectively; the difference was statistically significant ( $p < 0.001$ ).

Lymphoedema was significantly more common in unemployed patients than in those who were employed ( $p < 0.001$ ). Patients who worked outside the home ( $n = 1\ 023$ ) accounted for only 20.2% of the total group, and most of them (63.7%) were in the physiotherapy group (Table 2).

Lymphoedema was also more common in patients with a BMI between 30 and 34.9 than in other patients. Multivariate analysis showed that a patient with a BMI of 25 - 29.9 was 1.445 times more likely to develop lymphoedema than a patient with a BMI of <17.9 ( $p < 0.001$ ), and a patient with a BMI of 30 - 34.9 was 6.643 times more likely to develop it than a patient with a BMI of <17.9 ( $p < 0.001$ ).

Lymphoedema was more likely to occur in patients who received postoperative chemotherapy than in those who did not ( $p < 0.001$ ). This finding was most striking at the 6-month follow-up visit. In most of these patients no difference was detected between the measurements of the two arms, so the lymphoedema was considered to be generalised. We did not find that postoperative axillary radiotherapy affected the occurrence of lymphoedema ( $p = 0.217$ ).

Lymphoedema was significantly less common in patients who participated in a physiotherapy programme than in those who did not ( $p < 0.001$ ) (Table 3).

## Discussion

Breast cancer is the most common cancer in women today. Each year, 35 - 44 new cases are diagnosed per 100 000 women, and the rate is increasing.<sup>[3]</sup> Lymphoedema continues to be one of the main and most feared complications of breast cancer treatment,<sup>[3]</sup> occurring in an estimated 25% of patients who undergo treatment, although rates varying from 6% to 70% have been reported.<sup>[3,4]</sup> In our study, 19.9% of the patients developed lymphoedema.

**Table 1. Lymphoedema rates after modified radical mastectomy**

No lymphoedema, <i>n</i> (%)	4 056 (80.1)
Lymphoedema, <i>n</i> (%)	1 008 (19.9)
Total, <i>n</i> (%)	5 064 (100.0)

**Table 2. Relationship between lymphoedema and employment**

	No lymphoedema	Lymphoedema	Total
Employed, <i>n</i> (%)	852 (83.3)	171 (16.7)	1 023 (100.0)
Unemployed, <i>n</i> (%)	3 204 (79.3)	837 (20.7)	4 041 (100.0)
Total, <i>n</i> (%)	4 056 (80.1)	1 008 (19.9)	5 064 (100.0)

Employment v. lymphoedema  $p = 0.004$  ( $\chi^2$  test).

**Table 3. Effect of physical therapy and rehabilitation on development of lymphoedema**

Physical therapy and rehabilitation	No lymphoedema	Lymphoedema	Total
Yes, <i>n</i> (%)	1 704 (89.6)	198 (10.4)	1 902 (100.0)
No, <i>n</i> (%)	2 352 (74.4)	810 (25.6)	3 162 (100.0)
Total, <i>n</i> (%)	4 056 (80.1)	1 008 (19.9)	5 064 (100.0)

Physical therapy and rehabilitation v. lymphoedema  $p < 0.001$  ( $\chi^2$  test).

Lymphoedema can be defined as the accumulation of lymph in the interstitial spaces, principally in the subcutaneous fatty tissues. It is caused by a defect in the lymphatic system and is marked by an abnormal increase in tissue proteins, oedema, chronic inflammation and fibrosis.<sup>[2-3]</sup> Three stages have been described. Stage I presents with pitting and is considered reversible; some women have no increased arm girth or heaviness at this stage and no signs of pitting oedema. As the oedema progresses, it becomes brawny, fibrotic, non-pitting and irreversible (stage II). In advanced lymphoedema (stage III), which rarely occurs after treatment of breast cancer, cartilaginous hardening occurs, with papillomatous outgrowths and hyperkeratosis of the skin.<sup>[3]</sup>

Some of the main problems associated with lymphoedema are pain, inability to recognise the location of tactile sensations, a heavy sensation in the limbs, decreased mobility, psychosocial stress, isolation and repeated tissue infections.<sup>[3,4]</sup> The effect on the patient's quality of life should be taken seriously. Lymphoedema causes considerable psychosocial stress, and patients lose confidence when in a social environment because they are concerned about how their affected arm is perceived.<sup>[5]</sup> Major current problems with regard to lymphoedema are lack of a standard guideline, standard reporting system or realistic estimate of incidence, and even lack of a clear aetiological definition.<sup>[4]</sup> For these reasons, in addition to determining that lymphoedema is present and classifying it as mild, moderate or severe, self-reporting techniques described by Ahmed *et al.*<sup>[6]</sup> are used to evaluate it.

Lymphoedema has been a problem since radical mastectomies were first performed.<sup>[7]</sup> Although some have maintained that there is no difference between modified radical mastectomy and breast-conserving therapy in terms of its development,<sup>[8]</sup> we only included patients who underwent modified radical mastectomy in our study. Because lymphoedema and its associated pain and reduction in mobility can decrease quality of life,<sup>[9]</sup> we aimed to draw attention to the risk factors and evaluate the use of physiotherapy and rehabilitation for treatment and prevention.

Age appears to be the most significant risk factor. It has been reported that lymphovenous anastomoses occur more readily in younger patients.<sup>[10]</sup> The body's ability to regenerate slows with ageing, causing inability to cope with lymphoedema. The occurrence of lymphoedema therefore significantly increases with age, as demonstrated in our study.<sup>[10]</sup>

We also found that the risk of lymphoedema increased almost six-fold as weight increased. Being overweight is a risk factor that can be modified and therefore an important parameter.<sup>[11,12]</sup>

We included patients who received adjuvant chemotherapy in our study, but not those who had neoadjuvant chemotherapy. As explained above under 'Results', when arm measurements were found to be increased at the 6-month postoperative check in some patients who received chemotherapy, the oedema was generalised in most cases and the arm on the side of the mastectomy was not larger than the arm on the other side. These findings indicate that adjuvant chemotherapy can therefore be considered a risk factor for developing generalised lymphoedema. We believe that further investigations are required to determine whether chemotherapy poses a significant risk for the development of lymphoedema.

There are differing opinions in the literature regarding the roles of axillary lymph node positivity, axillary dissection and axillary radiotherapy. Some studies classify axillary dissection and radiotherapy as risk factors for lymphoedema.<sup>[13,14]</sup> Clark and Sitzia<sup>[11]</sup> reported that axillary dissection and radiotherapy have no effect on lymphoedema formation; however, they found that 80% of their patients who developed lymphoedema within 3 years had developed it within the first year. Purushotham *et al.*<sup>[2]</sup> found no association between adjuvant treatment and lymphoedema in patients who had undergone the same treatment. Moreover, they found that collateral vessels form earlier and more effectively in patients with axillary node positivity, suggesting that lymphoedema is likely to occur in these patients. In our study, only 19.9% of patients who underwent modified radical mastectomy and full axillary dissection developed lymphoedema, and axillary radiotherapy was not found to be a significant risk factor. We believe that these findings help clarify the relationship between adjuvant radiotherapy and lymphoedema.

We wish to emphasise the importance of postoperative physical treatment and rehabilitation in the prevention of lymphoedema. Mak *et al.*<sup>[10]</sup> found that just walking and being active are effective in preventing postoperative lymphoedema, while Binkley *et al.*<sup>[15]</sup> recently reported that few patients are currently referred for physical therapy after cancer treatment, and of those who are referred, few continue therapy. However, several studies have reported that educating patients about lymphoedema and physical treatment and rehabilitation after surgery are very important.<sup>[13,16,17]</sup> Demonstrating and practising weight-lifting exercises and informing patients about manual drainage with hand techniques are also effective in reducing the risk of developing lymphoedema.<sup>[3,18]</sup> Our patients in the physiotherapy group had a significantly lower incidence of lymphoedema than those in the no physiotherapy group; in addition, patients who were employed had a lower incidence of lymphoedema than those who were unemployed, suggesting that walking, an active

lifestyle and regular participation in physical therapy reduce the risk. At Ankara Oncology Research and Training Hospital, one of the largest oncology hospitals in Turkey, we routinely refer every patient who undergoes mastectomy to the physical therapy and rehabilitation department. We consider this to be the most important step for preventing postoperative lymphoedema, and the findings of the current study support this approach.

Finally, if lymphoedema does develop, it is difficult to treat. Treatment options include liposuction and drugs that stimulate proteolysis, such as 5,6-benzo- $[\alpha]$ pyrone.<sup>[2,19,20]</sup> However, it is clear that the best way to reduce the impact of lymphoedema is to prevent it.<sup>[2,20]</sup> Our findings support our belief that educating patients about the risk factors for developing lymphoedema, and referring them to postoperative physical therapy and rehabilitation clinics, are the most important ways to avoid this distressing condition.

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