

BRIEF COMMUNICATION

LYMPHEDEMA DEVELOPMENT FOLLOWING BREAST CANCER SURGERY WITH FULL AXILLARY RESECTION

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ABSTRACT

Several studies have investigated the influence of disease related, treatment related, and patient related risk factors on the development of postmastectomy edema (PME). The aim of the present study was to determine which factors present a higher risk of developing PME after breast surgery with full axillary resection (level I, II and III). To accomplish this aim, we investigated 245 women who underwent unilateral breast cancer surgery in the Academic Hospital of the Vrije Universiteit, Brussels. Information concerning treatment and disease related factors were collected from the patient's medical records and factors related to clinical condition were obtained by a personal interview. Arm circumference was taken at 15 cm proximal and 10 cm distal to the olecranon. PME was defined as 2.5 cm difference between the arms. Height and weight of the patient were also measured. Statistical analysis was performed by calculating the Odds Ratio and the 95% Confidence Interval. We found the following factors posed an increased risk of developing PME: axillary/supraclavicular radiotherapy, pathological status of the lymph nodes, overweight (BMI > 25 kg/m²), trauma to the arm, menopause and surgery on the dominant side.

Approximately 30% of patients develop postmastectomy edema (PME) as a conse-

quence of breast surgery for cancer (1). Although seldom life threatening, swelling of the arm is a very serious complication accompanied by a loss of range of motion, inflammation and tissue fibrosis, which can result in an aesthetic handicap for the patient (2,3). The main cause of PME is the interruption of the lymphatic system due to lymph node resection. In addition, other factors can contribute to the development of PME. These can be grouped into 3 categories: treatment related, disease related and patient related factors (4). Several studies have focussed on this issue, and different outcomes have been reported (1-14). The aim of our study was to determine which factors are associated with a higher risk of the development of swelling of the arm after breast surgery in our specific patient population.

We investigated women who underwent unilateral breast surgery with total axillary resection (Level I, II and III) in the Academic Hospital of the Vrije Universiteit, Brussels. All patients volunteered freely (oral informed consent was obtained), and our study had the approval of the Ethics Committee of the Vrije Universiteit, Brussels. The following treatment related factors were investigated: adjuvant radiotherapy (chest radiotherapy or breast radiotherapy or axillary/supraclavicular radiotherapy in combination with chest or breast radiotherapy); radiotherapy dose (46 or 50 Gy); number of resected lymph nodes; types of surgery; and chemotherapy. The

following disease related factors were studied: side of surgery; tumor stage (T); pathological nodal status (N); number of metastatic lymph nodes; and tumor localization. Information on these factors was collected from the patient's medical record. The following factors related to clinical condition were obtained by personal interview: age; operation on dominant side; trauma to the arm; menopause status; and smoking. A circumferential measurement was obtained at 15 cm proximal and 10 cm distal to the olecranon using a tape. A difference of at least 2.5 cm between the arms was used for our determination of edema.

Statistical analysis was performed with SPSS 12.0 for Windows. We computed the Odds Ratios (OR) between risk conditions and non-risk conditions and their 95% Confidence Interval (CI) in a 2x2 table. Odds ratios with a lower 95% CI border >1 are considered to indicate a significantly increased risk of developing PME.

Two hundred forty five patients were included in our study. The average age was 59 years (range 27-85 years), with a mean body weight of 68.4 kg (range 44-105.4 kg) and an average body length of 1.61 m (range 1.45-1.8 m). The average BMI was 26.3 kg/m² (range 17.7-38.14 kg/m²). One hundred and forty-seven patients (60.0%) had undergone a modified radical mastectomy (Madden) and ninety-eight patients (40.0%) had undergone a lumpectomy. Both also underwent total axillary resection (Level I, II and III). One hundred forty three patients (99%) had adjuvant radiotherapy (chest wall (n= 98), chest wall and axillary/supraclavicular (n=55), breast (n= 75), breast and axillary/supraclavicular (n=23))

Fifty-nine patients (24%) presented a swelling of the arm of more than 2.5 cm between the treated and non-treated side. Patients who received axillary/supraclavicular radiotherapy in combination with chest or breast radiotherapy had a higher risk of developing PME (OR=2.53; 95% CI, 1.38-4.64). A logical explanation is that the main evacuation route (axillary lymph vessels) had been damaged by surgery, and the cephalic

lymph vessels (Mascagni pathway) have taken over to form the main drainage pathway. When, however, these vessels are destroyed by post-radiotherapy fibrosis, active drainage routes have been further impeded resulting in inadequate lymphatic drainage of the arm. This finding is supported by most studies (3,5- 9), although Pezner et al (10) found no relationship between axillary radiotherapy and the presence of PME. As they had few patients who received axillary radiotherapy in combination with complete axillary surgery, no conclusions could be made. Patients with metastatic lymph nodes had a higher risk of the appearance of PME (OR=2.60; 95% CI, 1.43-4.75). This is confirmed by studies of Werner et al (6), Kissin et al (7) and Suneson et al (8) but in contradiction to the results of Larson et al (11) and Hoe et al (12). As in our hospital, these patients receive supplementary radiotherapy in the axillary/supraclavicular region and this makes it difficult to consider metastatic lymph nodes as an independent factor.

Contrary to other studies (3,7,13), in which no relation between arm dominance and swelling of the arm was determined, we found an increased risk for PME in patients who had been operated upon the dominant side (OR= 1.97; 95% CI, 1.09-3.55). The dominant arm is more frequently used for daily activities and excessive use of the arm may likely cause an increase of net capillary filtration, which can precipitate swelling of the arm. Our results indicate that trauma to the arm increases the risk of PME (OR= 7.23; 95% CI, 1.45-20.58). Simple burns or puncture wounds may produce further lymphatic destruction and increase lymph load, which promotes accumulation of edema fluids (15). Overweight (BMI≥25) is a major risk factor for swelling of the arm (OR= 2.45; 95% CI, 1.34-4.47). Segerström et al (3), Werner et al (6), and Edwards (13) also found this association, whereas other authors (9-11) did not. The pathophysiological mechanism behind the association between BMI and edema is not clear (2). It is possible that fat accumulation will overload the already

perturbed lymphatic system or interfere with lymph drainage, which would facilitate swelling of the arm. Our results indicate that women in menopause have a higher risk of swelling of the arm (OR= 3.15; 95% CI, 1.07-9.28). The only studies (7,14) that investigated this factor found no significant correlation. Hormonal changes due to menopause may have an influence on the development of PME. Another possibility is that women during menopause tend to gain weight, with an increase of BMI (16), which can result in a higher risk of PME. The following factors show no significant association with swelling of the arm in our study: radiotherapy dose; radiotherapy to the chest wall and to the breast; number of resected lymph nodes; kind of surgery; chemotherapy; side of surgery; tumor stage; number of pathological lymph nodes; tumor localization; age; and smoking.

In conclusion: we found additional provoking factors (such as menopause and surgery on the dominant side) that should be taken into account in further studies, and we were able to confirm factors (like axillary/supraclavicular radiotherapy, arm injury and positive lymph nodes) about which a consensus exists in the literature.

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