THE RISK OF LYMPHEDEMA AFTER BREAST CANCER SURGICAL TREATMENT

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(Abstract): The aim of this study is to emphasize the importance of knowing the predisposing factors of the occurrence of homolateral upper limb lymphedema after breast cancer surgery. Material and methods: The study included 1104 patients with breast cancer, who were hospitalized in the IIIrd Surgical Clinic, Iasi, between 2000 and 2010, for surgical treatment followed by oncological adjuvant therapy. The surgical intervention was conservative in 228 cases and modified radical mastectomy – Madden type – in 876 patients. Periodic clinical follow-ups were done every 3 months during the first postoperative year, every 6 months during the second year and annually thereafter. Results: Early lymphedema occurring in the first 14 postoperative days or between day 14 and day 21 was found in 8 patients. Late lymphedema, occurring up to 12 months or more after surgery, was diagnosed in 41 patients. Medium and severe lymphedema occurred at 42 patients. We evaluated the pre-existing risk factors, the risk factors related to the type of surgery and those related to the cancer staging. Conclusions: It’s ideal to identify predisposing factors of developing lymphedema related to breast cancer surgery before applying any type of treatment. There are therapeutic methods (general, drug therapy, physiotherapy) and methods related to the surgical act that influences the prophylaxis of lymphedema or have an amazing effect on already occurred lymphedema. Keywords: UPPER LIMB LYMPHEDEMA, BREAST CANCER, AXILLAR ADENOPATHY

Multiple statistics consider that lymphedema secondary to surgical treatment of breast cancer has an incidence ranging from 3 to 87% (1). This difference between statistics can be explained by different criteria, the presence of some difficulties in the measurement methodology, the duration of the follow-up of the patients and, not least, through a series of individual particularities of the patients. The risk of developing lymphedema in women treated for breast cancer in The United States of America is expected in more than 2.5 million patients (2). Lymphedema may also occur after conservative surgery of the breast cancer associated with the biopsy of the sentinel lymph node, the percentage reaching up to 23% (3), but with an average of 6%, as 15 studies on 4241 patients show (4,5). The occurrence of lymphedema has multiple consequences: on the upper limb functional status and breast status (for
lymphedema occurring after conservative surgery), the quality of life, the work integration, the relationship with family members (related to lifestyle changes, the self perception in terms of personal independence, the patient considering that she has an invalidity in what her aesthetic appearance is concerned) the risk of erysipelas, sometimes with a relapsing character and not least with important financial consequences (long term medication and therapeutic methods, often expensive). Of course, the studies have a follow-up period ranging from 3 months to 20 years, without a basic value (9). The aim of this study is to find, at a lot of patients treated for breast cancer, the risk factors of the occurrence and progression of lymphedema. Another objective is to analyze the value of preventive methods for upper limb lymphedema in relation to the surgical treatment sequence for breast cancer.

**MATERIAL AND METHODS**

The study included 1104 patients with breast cancer aged between 26 and 93 years who were hospitalized and operated by the same surgical team between 2000 and 2010. 178 patients were in stage I and II and 926 patients in stage III and IV. The surgical treatment was conservative - quadrantanectomy with axillary lymphadenectomy in 228 patients and modified radical mastectomy (Madden operation) was performed on 876 patients. All the patients were treated with fractionated heparin and micronized flavonoids (Detralex) or procanidolic oligomers, flavan derivatives (Endotelon), starting with the first day after the surgery for a period of 7 to 21 days. All patients had elastic compression of the chest and arm for 14 postoperative days. The patients began the adjuvant chemotherapy between for 21-30 days after surgery and the radiotherapy - when indicated - up to thirty days after the last infusion of chemotherapy. Our study only took into consideration the lymphedemas from the II\textsuperscript{nd} and III\textsuperscript{rd} degree (42 patients) according to the International Society of Lymphology (9).

All the patients were supervised by the same surgical team; the clinical periodic evaluations were performed every 3 months during the first year after surgery, every 6 months during the second year and annually thereafter. Every 6 months we performed an ultrasound examination (bilateral axillary region, bilateral supraclavicular region, bilateral breast region in case of conservative surgery and breast and pectoral region in case of Madden operation). The clinical evaluation also focused on the measurement of the forearm and of the arm circumferences.

**RESULTS**

From 42 cases of severe and medium lymphedema, in 8 cases (19.04%), we found that an early lymphedema appeared in day 14 after the surgery and between 14 and 21 postoperative days. The late lymphedema that appeared after day 21 after surgery can be divided into 2 categories: lymphedema occurring during the first postoperative 12 months (9 cases) and lymphedema occurring later than 12 postoperative months (25 cases) (tab. I, fig. 1).

Regarding the impact on the patient’s clinical condition, we found pain, a feeling of weight in the upper limb and decreased motility of the upper limb (48% of cases). 3 patients with important and persistent lymphedema presented almost a total motor deficit of the affected upper limb. We also evaluated the impact of that lymphedema
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of the upper limb had on the state of mind of these patients. Therefore 21 patients had obsessive-phobic concerns related to the absence of the breast, the already installed lymphedema and concerns regarding the fear of recurrence of the disease. 4 of these 21 patients developed depression and were guided to see a psychiatrist.

TABLE I
Risk factors for medium and severe lymphedema after breast surgery related to patient’s status

<table>
<thead>
<tr>
<th>Severe/medium lymphedema (42 cases)</th>
<th>Age ≤ 45 years</th>
<th>Age &gt; 45 years</th>
<th>BMI normo-ponderal</th>
<th>BMI I-II obesity</th>
<th>BMI morbid obesity</th>
<th>Same dominant arm</th>
<th>Trauma/burns on same arm</th>
<th>Smoking</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>8</td>
<td>36</td>
<td>2</td>
<td>38</td>
<td>2</td>
<td>41</td>
<td>6</td>
<td>13</td>
</tr>
</tbody>
</table>

**Fig. 1.** Risk factors for medium and severe lymphedema after breast surgery related to the extension of the cancer and surgical treatment

**DISCUSSION**

The current study refers to 42 cases of medium and severe lymphedema, with the following objectives: the assessment of the incidence of postoperative lymphedema in the studied group, the assessment of the risk factors for lymphedema, determining the occurrence interval of postoperative lymphedema, monitoring the degree and the evolution of the lymphedema under different therapeutic methods and estimation of the duration of patient surveillance.
It would be ideal to identify predisposing factors of developing lymphedema before applying any therapeutic methods in order to inform the patient on this possible complication and to apply more precise prevention methods before surgery.

Elder women seem to be more prone to lymphedema – as the majority of the studies show (6, 7, 8) as we also found in our research. We concluded that the extent of mastectomy has no great influence on the occurrence of the lymphedema as other studies also observed (10). Moreover, the results of some studies highlighted that the lymphedema was present in 37% of the cases when axillary lymphadenectomy was performed, 8% of the cases with dissection of the lower third of the axillary lymph nodes and 5% related to the biopsy of an axillary lymph node (10). Other studies observed that women who underwent sentinel lymph node biopsy followed by radiotherapy, had an increased risk of developing lymphedema when chemotherapy regimens were based on anthracyclines (11).

Higher body weight with a BMI over 25 kg/m² and thorough lymph node dissection were associated with a higher incidence of lymphedema, a fact that is also found in literature.

In the studied group we found that the excision of the axillary lymph node relapse or the redissection of the lymph nodes (in cases of incomplete axillary dissection on a previous surgical intervention) and the dissection of an encapsulated lymphatic collection adjacent to the axillary vein were associated with a medium lymphedema. We also found that the dissection of the fatty tissue around the axillary vein was associated with a higher risk of lymphedema of the homolateral upper limb. This may be due to the removal of some derivative lymphatic pathways traveling close to the vein; there is also, in these cases, a venous stasis and a fibrous tissue organized around the axillary vein, causing its stranguation. Postoperative axillary vein thrombosis that occurred especially after the dissection of the lymph nodes adherent to the vein and preoperative vein thrombosis due to the presence of tumor thrombus are other factors responsible for stasis and edema; in these cases, lymphedema is associated to venous edema. As an argument, we noticed that in those cases when the axillary vein was occluded (by the tumor thrombus or by the lymph nodes), when we managed to spare the substernal venous package as a derivative pathway, through the intercostals veins, we had no lymphedema, in comparison with those situations in which the substernal veins were resected together with the axillary ganglionar block.

There are studies showing that postoperative lymphedema is related to the lymph node tumor invasion. On our patients we found that when the lymph node dissection was complete, without residual tumor and with the spearing of the fatty tissue around the axillary vein, the incidence of postoperative lymphedema was 0 and that’s because the tumoral invaded lymph nodes did not serve for lymph drainage anymore and there already were derivative pathways. In those cases when we had residual tumor, we usually had postoperative lymphedema.

There is still a controversy regarding the prevalence of lymphedema in the dominant upper limb (13, 14). For our study this element is only relevant in the case of patients declaring the occurrence of lymphedema after physical effort. The occurrence
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of lymphedema is related to lymph node invasion (12). On the analyzed casuistry we noticed that when in cases when the ganglionic tumor invasion was important, when the lymphadenectomy was Ro and when a ganglionic fatty tissue around the axillary vein could be kept, then there was no lymphedema. In the cases where there has remained a ganglionic tumor tissue around the axillary vein as well as at those with detailed dissection around the axillary vein, the lymphedema appeared. The explanation is: in the first case the tumor invaded nodules were not useful at the drainage of the lymph, which found other derivative paths; in the second case the edema that appeared had an important venous component by wrapping the axillary vein with the tumor remains that continued growing. The prophylactic administration of micronized flavonoids and derivatives of flavani for a period of 14 to 21 days starting with the first day after surgery together with the administration of fractionated heparins decreased the incidence of lymphedema. Meanwhile, in patients who developed postoperative lymphedema, we prolonged the administration of this medication associated with elastic compression of the upper limb, gymnastics and maintaining of the upper limb in an elevated position turned severe edema into mild edema. Another factor that led to severe lymphedema remission was the decreasing of the body mass. We also paid attention to the nutrition of the patients by recommending a diet that does not significantly increase the lymphatic flow; the patients are advised to consume foods containing medium chain triglycerides. Another prophylactic method related to the surgical act is to identify the main lymphatic pathways from the upper limb by preoperative infiltration of methylene blue in the forearm, this being able to protect the main lymphatic collectors that transport the lymph from the upper limb to the thoracic duct.

Surgery for lymphedema had no significant long time results. Excisions of subcutaneous fat had been practiced, but postoperative infections and poor cosmetic results were discouraging. Partial excision of subcutaneous fat and "burying" a skin flap – without epidermis – under the arm muscle aponeurosis was tried by some of us, but without favorable results. More recently, liposuction has been practiced through several small incisions, with relative good results in 12 months of patient surveillance (15). Lympho-venous anastomoses showed good results in 50-77% of patients (16). The results seem to improve when lympho-venous anastomosis was associated with excision of subcutaneous tissue.

CONCLUSIONS

Our study shows that preoperative detection of risk factors for upper limb lymphedema in breast cancer would allow the early and intensive application of targeted therapeutic methods. On the other hand, avoiding aggressive and excessive dissection around axillary vein and maintaining the body fat surrounding axillary vein would limit collateral damage to the lymphatic system and diminish the risk of lymphedema.

Our paper show a relevant factor: micronized flavonoids associated with methods of physical therapy from an early stage provide a good prophylaxis for lymphedema occurring after breast cancer surgery. Patients should avoid extensive physical effort of homolateral upper limb and should
be thought the methods that can sometimes prevent recurrent erysipelas in the upper limb, thus avoiding severe lymphedema installation.

REFERENCES