

The Vascularized Omentum Lymph Node Transfer - A Key Point in the Lymphedema Management

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Abbreviations:

BCRL: Breast Cancer Related

Lymphedema;

VOLNT: Vascularized Omentum

Lymph Node Transfer;

VLNT: Vascularized Lymph Node

Transfer;

LN: Lymph Nodes;

ICG: Indocyanine Green;

LVA: Lymphovenous anastomosis;

BMI: Body mass index;

EKG: Electrocardiogram.

Rezumat

Transferul liber vascularizat de ganglioni limfatici din oment – un punct cheie în managementul limfedemului

Introducere: Pe măsură ce un număr tot mai mare de femei înving cancerul de sân în întreaga lume, limfedemul asociat cancerului de sân a câștigat mai multă atenție recent. Transferul liber vascularizat de oment reprezintă un instrument util pentru cazurile avansate și recurente. Scopul lucrării este de a analiza avantajele și dezavantajele acestei metode.

Materiale și metode: Acest studiu retrospectiv a fost realizat pe un lot de 17 pacienți cunoscuți cu cancer de sân care au beneficiat de transfer liber vascularizat de oment. Datele au fost înregistrate între ianuarie 2022 și ianuarie 2023. În studiu au fost incluși pacienți diagnosticați cu limfedem secundar stadiul II sau III, cu rezultat insuficient în urma efectuării anastomozelor limfovenoase anterioare.

Rezultate: Cel mai frecvent afectat a fost membrul superior stâng (59%), unde edemul a fost identificat în principal la nivelul antebrățului (75%). Cu toate acestea, mai mult de jumătate dintre subiecți au avut anterior anastomoze limfovenoase. Corelația dintre stadiul limfedemului și reducerea postoperatorie a volumului membrului afectat a fost de -0,26, panta ajungând la -0,33, cu o valoare intercept de 2,64. Monitorizarea postoperatorie a arătat o reducere a volumului membrelor superioare și o îmbunătățire a calității vieții pacienților.

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Concluzii: Experiența chirurgilor face ca acest lambou versatil să aducă speranță supraviețuitorilor cancerului de sân afectați de limfedem.

Cuvinte cheie: limfedem, bypass limfovenos, transferul vascularizat de ganglioni limfatici, lambou de oment, microchirurgie

Abstract

Background: As an increased number of women beat breast cancer worldwide, the breast cancer related lymphedema has gained more attention recently. The vascularized omentum lymph node transfer has been approached as an useful tool for advanced and recurrent cases. The purpose of the paper is to emphasize the advantages and disadvantages of this method.

Materials and Methods: This retrospective study consists of 17 patients known with breast cancer related lymphedema who received vascularized omentum lymph node transfer. Data was recorded between January 2022 and January 2023. Patients diagnosed with secondary lymphedema stage II or III, unresponsive to previous microsurgical lymphovenous bypass were included.

Results: The most prevalent affected site was the left upper limb (59%), where edema was mainly identified in the forearm (75%). Nevertheless, more than half of the subjects have previously received lymphaticovenous anastomosis. The correlation between the stage of lymphedema and the postoperative reduction of the volume of the affected limb was -0.26 , the slope to reached -0.33 , with an intercept value of 2.64 . The follow-up period showed reduced upper limb volume and an improved quality of life.

Conclusion: Through an experienced hand, this versatile flap brings hope to breast cancer survivors with lymphedema.

Key words: lymphedema, lymphovenous bypass, vascularized lymph node transfer, omentum flap, microsurgery

Introduction

Lymphedema is a chronic condition (1) affecting around 250 million people worldwide (2). It consists of accumulation of fluid in the interstitial space (3), leading in time to complications, such as adipose tissue hypertrophy, fibrosis (4), numerous episodes of cellulitis, lymphangitis, reduced extremity range of motion (5), low self-esteem, and altered perception of body image (6).

This condition is classified in primary lymphedema where the etiology implies a genetic lymphatic vessels anomaly (7) and secondary one, respectively, in which the modifications occur as a result of a systematic disease, previous surgical procedures (such as modified

radical mastectomy (8), skin cancer (9) or trauma (3,10).

In breast cancer related lymphedema (BCRL) the symptomatology is caused by histological changes of lymphatics vessels, following a mastectomy (11).

In the first world countries, it has been reported that between 5-20% of people who had previous surgery involving lymph node dissection developed lymphedema later (2). Furthermore, it was estimated that 29%-49% of women who have personal history of radical mastectomy with axillary lymph node dissection and consecutive chemoradiotherapy might be diagnosed with lymphedema in the following years (12), while 18% of women with gynecologic cancer surgery involving pelvic

lymphadenectomy develop lower limb lymphedema (13).

Affecting one person of five diagnosed with breast cancer, BCRL has gained more attention in recent years (14). Furthermore, in the United States, from an estimated number of 3.8 million patients who survived breast cancer, approximatively one third of them develop BCRL (1).

Axillary lymph node excision and loco-regional radiotherapy are attributed with the main role for the appearance of BCRL (15). Moreover, the authors of a meta-analysis found a strong association between an increased number of dissected and excised lymph nodes in the axillary region, a high body mass index (BMI), and BCRL. On the other hand, the same team identified a lower level of evidence for adjuvant therapies such as chemotherapy, sedentarism, and BCRL development (16).

BCRL manifests as edema encountered in the upper limb, anterior trunk or the operated breast (17). Symptoms include pain, sensation of heaviness or tightness. Summed up, they lead to an impaired quality of life (18).

Data in literature emphasize the important role of complex decongestive treatment (19). Observational studies have described the role of compressive garments worn for a long term (20), as well as the effectiveness of intermittent pneumatic devices (21). Moreover, the manual lymphatic drainage treatment has been associated in some studies with edema reduction (22).

Accounted as a useful tool, negative pressure wounds therapy has been used for various skin lesions (23). Furthermore, in a study which included 50 patients with secondary lymphedema, the authors described a significant reduction (7%) in limb volume in the group in which they included negative pressure therapy (24).

Various surgical methods have been established for reducing the volume of the affected limb, circumference (13) and improving the quality of life of these patients (25). Almost a quarter of the patients with lymphedema associate cellulitis (4) and hereby recurrent

infections (26). Also, patients who failed previous lymph nodes transfers, with refractory lymphedema and limited donor basins might benefit from the surgical treatment (4).

Among the possible complications, the following were mentioned: intra-abdominal: ileus in 5% of patients, pancreatitis in 2% (34), bowel infarction with consecutive perforation, incisional or internal hernia, internal bleeding (15), intra-abdominal adhesions and bowel obstruction (2).

Materials and Methods

Patients

In this retrospective study the authors included patients treated surgically with vascularized omentum lymph node transfer (VOLNT) for BCRL between January 2022 and January 2023. The inclusion criteria were a confirmed diagnosis of secondary lymphedema stage II or III on lymphoscintigraphy, after modified radical mastectomy, which did not respond to previous lymphovenous anastomosis (LVAs) treatment and body mass index (BMI) < 30. The exclusion criteria were: severe heart failure, chronic renal failure, arteriopathy obliterans, and venous insufficiency.

Ethical Aspects

In order to carry out the research, the approval of the ethics committee of the unit where the study was carried out was obtained. Also, all of the patients included in the study expressed their agreement regarding its development and for the performance of the specifically necessary investigations (set of analyses, lymphography, EKG and radiography).

Study Outcome

The research aims to highlight the effects of performing VOLNT in patients who previously received LVAs for the treatment of secondary lymphedema, under the conditions of

optimizing the results of the primary surgical intervention.

Study Design

The study was structured so that through the comparative analysis of preoperative measurements, after LVAs and after VOLNT, to provide relevant data regarding the efficiency degree of the procedures used, as well as the ability to potentiate the effects of LVAs by associating it with VOLNT.

To evaluate the results, the sizes of the affected upper limbs were comparatively analyzed, both preoperatively and postoperatively, by measuring their circumference at intervals of 10 cm, starting from the palmar region up to the level of the proximal 1/3 of the arm. The data thus obtained were used to study the volumetry of the affected limb, in order to determine the amount of postoperative volume reduction.

In order to assess the results from the perspective of the impact they exert on the patients' degree of satisfaction with regard to the two surgical interventions performed, a questionnaire with 10 questions was developed, in which the patients could choose a value from 1 to 10, depending on personal experience regarding the applied therapeutic protocol (*Table 1*).

Surgical Procedure

Regarding the surgical technique used, free transfer of omentum harvested laparoscopically was opted for, with anastomosis at the level of the vessels in the axillary region. The

average size of the flaps was 11.3/7.6 cm, with an average of the lymph nodes included of 4.82 (3-7). Flap harvest in patients who had contraindications for laparoscopy was done by performing a minimal laparotomy.

The great omentum is the donor area for the lymph node flap based on the pedicle of the right gastroepiploic artery and the extended version of it (6). The artery has three anatomical variants (5), providing in 75% of the people at least three lymph nodes for the transfer, within the first 9 cm of its origin and 3 cm around it (15). The length of the pedicle is between 4-10 cm, with the diameters of the artery and vein approximated to 2-2.5 cm and 2.5-4 cm respectively (36).

Due to the fact that, in obese patients, the caliber of the vessels is larger, it facilitates the surgical approach of the anastomoses (5). On the other hand, in order to divide the greater omentum, it is suggested to perform four venous anastomoses, with the mention that their caliber decreases from the right side to the left of the flap (34).

The flap can be vascularized in two manners: arterial flow-through and end-to-end anastomoses and venous end-to-end anastomoses to either the superficial or deep veins of the limb (36). In selective cases, an arterio-venous fistula of the left gastroepiploic artery and vein can be performed, which will decrease the venous hypertension of the flap, with early mobilization of the patient (28).

All patients included in the study underwent preoperative and intraoperative lymphography using ICG, both for preoperative mapping (staging) of the lymphatic drainage system and for intraoperative monitoring of the quality of the anastomoses.

The data obtained through the preoperative mapping constituted the database for the postoperative monitoring carried out 12 months after the operation. In order to perform these imaging investigations, all patients included in the study expressed their written consent by completing the existing informed consent form at the level of the health unit where the study was carried out.

Table 1. Surgical impact on the quality of life based on the questionnaire

Domain	Question
General	To what extent did the surgical treatment influence your quality of life?
LVA	How satisfied are you with the LVA result? How likely you are to recommend LVA?
VOLNT	How satisfied are you with the VOLNT result? How likely you are to recommend LVA?

Table 2. Correlation between the number of LVAs/VOLNT and the degree of patient satisfaction

Domain	Question	Result
General	To what extent did the surgical treatment influence your quality of life?	9.3 (9 - 10)
LVA	How satisfied are you with the LVA result?	8.35 (7-9)
	How likely you are to recommend LVA?	8.17 (7-9)
VOLNT	How satisfied are you with the VOLNT result?	9.52 (8-10)
	How likely you are to recommend LVA?	9.76 (9-10)

Follow-up

After performing LVA, the patients were monitored at 3, 6, 12 months. After the VOLNT protocol was accomplished, the monitoring procedure continued through reevaluation at 3, 6, 12 months intervals.

During the reevaluation, the measurements were carried out according to the previously presented protocol, and the degree of satisfaction of the patients with regard to the postoperative result was also evaluated according to the questionnaire completed by the patients.

Demographic data, BMI, lymphedema stage before the surgery, the timeframe between the mastectomy and the lymphedema onset, edema location, number of LVAs performed previously, their location and the length of VOLNT surgery were recorded.

Furthermore, the authors followed up the patients for one year after the VOLNT surgery, assessing the upper limb circumferential reduction, the flap inset scar and the subjective perception of the quality of life.

Statistics

The statistics and graphics were performed in Microsoft Excel, linear correlation, slope, and intercept alongside with mean, average, and percentage were calculated.

Results

In this study, 17 women with upper limb secondary lymphedema met the inclusion criteria, with the left side being most prevalent (59%, exemplified). The average age was 57 years (range 45-69 years), with most of

the participants living in the urban area (65%). Moreover, the majority of patients were overweight preoperatively, with the average BMI of 26,47 kg/m² (range 22-29 kg/m²).

Following the processing of the statistical data obtained by completing the satisfaction questionnaire by all of the patients included in the study, the results revealed a significantly increased satisfaction level in all the analyzed indicators, after the surgical interventions.

Regarding the lymphedema stages measured on lymphoscintigraphy, most participants were diagnosed with second stage of the disease (76% of women), with the forearm being the most affected part (75% of cases). In addition, in the majority of cases, the symptoms were noticed, on average, one year after the mastectomy (47% of cases, range 6 months – 3 years).

Regarding the correlation between the stage of lymphedema and the postoperative reduction of the volume of the affected limb, its value was -0.26, for the slope to reach the value of -0.33, under the conditions of an intercept value of 2.64 (*Diagram 1*).

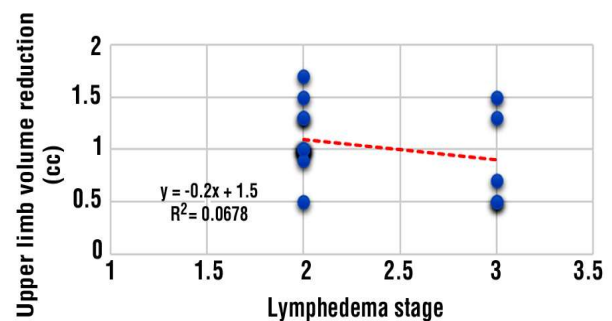


Diagram 1. Correlation between stage of lymphedema and post-operative volume reduction

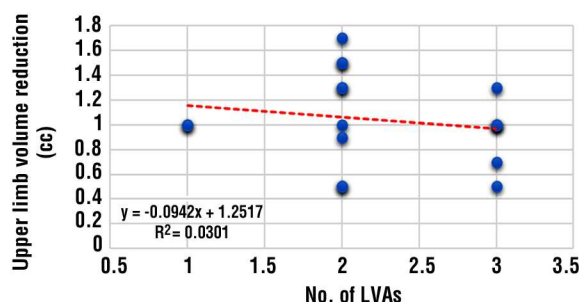


Diagram 2. Correlation between the number of LVAs and postoperative volume reduction

Preoperatively, at least one LVA was performed in every patient, with an average of two (58% of cases, range 1-3 LVAs). The most common site was the forearm (82% of cases). Nevertheless, in 18% of the women, LVAs were performed in both the forearm and the hand. Regarding the correlation between the number of LVAs performed and the postoperative reduction in the volume of the affected limb, its value was -0.17, for the slope to reach the value of -0.31, under the conditions of an intercept value of 2.56 (*Diagram 2*).

The patients met the criteria for receiving VOLNT after at least two years' timeframe from the LVA surgery, but not later than three years. Most of the participants were scheduled for the second surgery two years and six months after the LVAs (29%). The VOLNT transfer was performed in a multidisciplinary manner. The first team, composed of general surgeons, raised the great omentum flap based on the right gastroepiploic artery, by laparoscopic approach, and the second one, comprising plastic surgeons, did the vascular end-to-end anastomoses in the axilla, with the inset of the flap (*Fig. 1*).

The average time of the surgery was three hours and 50 minutes (range 3 hours – 4 hours and 30 minutes). In most cases, the surgical time was reserved to four hours (29% of cases). *Figure 2* shows the evolution of the upper right limb of a one of the patients, before and after the procedure. After performing VOLNT, the volume difference between the upper limbs decreased from 15% to 5%, for a global decrease of 66%.



Figure 1. The vascularized omentum lymph node flap in the axilla

The statistical analysis carried out using Excel also focused on establishing the correlation between the degree of satisfaction obtained after LVAs, respectively VOLNT. The T(test) result provided a p(value) of 5.20, in the conditions of a group of 17 patients. It should be mentioned that the standard deviation in the case of patients who benefited from LVAs reached a value of 0.78 and for its value in the case of patients with VOLNT of 0.43. In this context, there is a greater predictability of a high degree of satisfaction in the context of VOLNT, therefore deepening the research in the direction of using the VOLNT technique as the only therapeutic solution represents an objective for the research team.



Figure 2. Zoomed aspect of the hand before the VOLNT surgery (A) and one year postoperatively (B).

The results of the analysis of the satisfaction questionnaires after performing LVA revealed the fact that the average degree of satisfaction of the patients with regard to the postoperative result was 8.35 (7-9). The rate of recommending surgical intervention (after LVA) to other patients was 8.17 (*Diagram 3*).

Regarding the analysis of the patients' degree of satisfaction after performing the VOLNT, an average of 9.52 (8-10) was obtained, the probability of recommending the procedure to another patient reaching a value of 9.76 (*Diagram 4*).

Regarding complications, in this study, none has been noticed at the donor area, while at the flap inset the following ones are worth mentioning: seroma (five patients), hematoma (two patients), partial skin graft congestion (three patients), partial skin graft marginal necrosis (two patients) and hypertrophic scars (three patients).

All patients came for the follow-up at one, three, six and 12 months. Most of the patients whose upper limbs were measured at one year follow-up, registered a 1 cc circumference reduction (47% of the women). Fifteen mentioned an improved quality of life, while in two cases no modifications were subjectively reported.

Discussions

The study confirms the effectiveness of VOLNT in the case of patients for whom LVAs did not provide the expected effects. The vast experience of the authors regarding the treatment of patients diagnosed with lymphedema by using LVAs, places this type of approach as the first intention in the treatment of lymphedema for the patients with favorable response to conservative treatment.

However, under the conditions of obtaining satisfactory results through the use of LVAs,

Diagram 3. Correlation between the number of LVAs and the degree of patient satisfaction

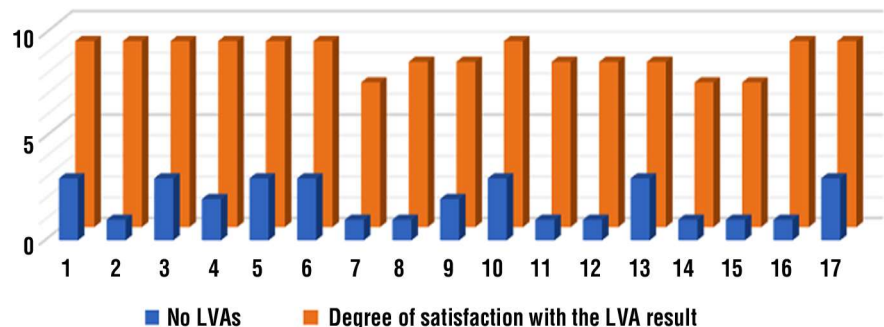
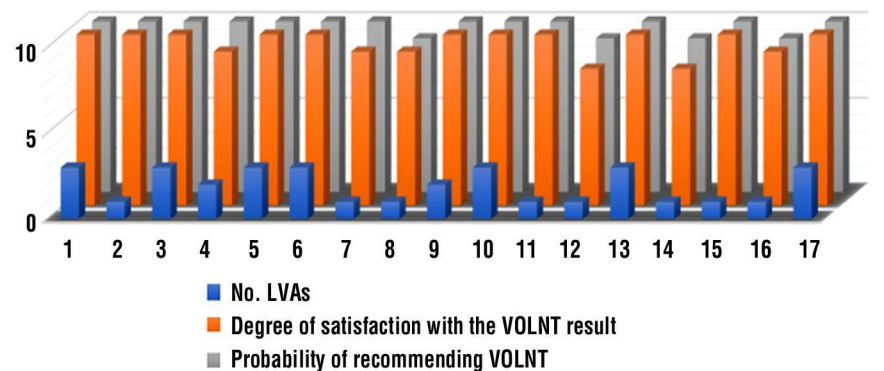


Diagram 4. Correlation between the number of LVAs and the degree of patient satisfaction after performing the VOLNT



the VOLNT procedure proved to be an effective solution, which contributes both to the improvement of the physical parameters, quantified by direct measurement, and to the increase of the degree of satisfaction of the patients regarding the result of the surgical treatment. In a systematic review, the authors concluded that after performing VOLNT a significant circumferential reduction of the affected limb was observed at the regular measurements. Also, they noticed a decreased incidence of complications such as cellulitis (4). Furthermore, in patients treated with the double VOLNT a functional improvement in half of the cases has been noticed, evaluated on lymphoscintigraphy and 20% on ICG lymphangiography (38).

The suggested treatment plan for stages II-III of lymphedema consists of sustained conservative treatment for at least six months preoperatory, one week of complex decongestive physiotherapy before surgery, followed by wearing compression garments for at least one year postoperatively and manual lymphatic drainage for at least 6 months. The patient's follow-up should be performed at one, three, six and 12 months after the surgery (6).

The vascularized omentum lymph node transfer (VOLNT), first reported in 1960 by Goldsmith et al. (12), has been described in literature as a suitable donor area for secondary lymphedema treatment, rich in lymphatic tissue (13), spread on a relatively large area (14).

Surgical indications for the treatment of secondary lymphedema are represented by: unsatisfactory results of conservative treatment, stages 2-4 objectivized by ICG, failure of lymph node transplantation and the presence of cellulitis (27).

Vascularized lymph node transfer (VLNT) is a microsurgical procedure consisting of functional lymph nodes (LNs) transferred on a region with impaired lymphatic drainage. This way, the lymphatic flow is restored (13). One of the advantages of this method is the fact that it presents no risk of donor site iatrogenic lymphedema (28). Another one might be the surgical approach itself: the

omentum flap harvest could be performed either as laparotomy (29) or as a minimally invasive manner, such as laparoscopy (30) or even robotically assisted procedure (14,31), with its single port variant (32). The surgical procedure could be performed in a multidisciplinary team (general surgeons and plastic surgeons) (33).

Various lymph node donor areas have been described, such as the axilla, elbow and wrist for the upper extremity and the groin, ankle and knee for the lower one (34). Despite the fact that the groin (submental nodes) and the neck are the most frequently chosen regions (2), the greater omentum is considered a good option for the patients associating cellulites because of its rich immune cells density. Ciudad et al. suggested a combined surgical approach for advanced lymphedema, a centered placement of the second VLNT (the cubital fossa), together with a distal lymph node transfer (at the wrist).

This arrangement improves the fluid absorption through the pump mechanism (4), assuring the clearance of excess fluid into the venous system due to the pressure gradient between the arterial inflow and venous outflow. This also occurs because of the longitudinal placement of the flap along the limb which increases its absorption surface (34). It has been shown that the use of computed tomography and magnetic resonance imaging for the surgery planning and the ultrasound intraoperatively have been helpful in all of the healthcare systems worldwide (39, 40). Moreover, computed tomography angiography has a 90% sensitivity and specificity, which enhances the finding of a perforator with a wider caliber than 0.3 mm (5). Postoperatively, an important reduction of the risk of cellulitis recurrence (6), improvement in the fibrosis in the dermis, and an decreased fat hypertrophy (28) have been reported.

Several advantages have been described. Firstly, the greater omental lymph node flap consists of an abundant resource of lymphoreticular bodies ("milky spots" or "lymphatic lakes" – the omentum being associated with lymphoid tissue composed of

clusters of macrophages, lymphocytes and mast cells (34)) which drain into the main lymphatic collecting system and from there to consistent efferent lymphatic vessels (28). These allow the flap to be split for more than one recipient site (28). Secondly, the flap is well vascularized, with a pedicle of a suitable diameter, able to cope with a longer period of ischemia (28). Thirdly, it has an easy access through a laparoscopic approach (5) and a decreased risk of iatrogenic donor site lymphedema (2). The limitations of the study consist of a reduced number of participants, followed-up for a relatively short period of time (one year).

Literature has described single and double vascularized omental lymph node transfers performed either by laparotomy, or laparoscopy (4, 37). The advantages of the double flap consist of another VLNT donor area for patients who have already had a lymph node dissection at the recipient site (4), scar removal through a transverse axillary incision (starting from the lateral chest wall, where the thoracodorsal vessels and the axillary vein could be visualized, until fat with a healthy aspect is encountered in the proximal 1/3 of the arm) and the possibility of the decompression of the axillary vein by connecting the gastroepiploic vein with the circumflex scapular one (38).

In clinical practice, the results of the study confirm the effectiveness of VOLNT for the treatment of forms of lymphedema that did not have the expected response to LVA, representing from this point of view a lifesaving solution for these patients.

However, considering the complexity of VOLNT, LVAs represent the first line treatment for forms of lymphedema whose favorable response to the initial conservative treatment creates the conditions for a good local evolution after LVAs.

Conclusion

Despite the fact that BCRL has impacted a significant number of women, the various treatment options bring them hope. We

consider this step to be highly important in the economy of the surgical procedure, as, in our experience, this tends to be the most sensitive stage. If there are no contraindications, we highly recommend laparoscopic procedure, due to shorter recovery time, and less aggressive approach.

Data in literature, together with authors' good results, recommend the great omental lymph node as a versatile flap and a safe option for the patients with stage II-III of lymphedema, with stable results in time.

Author's Contribution

A.B. conception and design of the manuscript. A.B., A.B., F.B. data extraction, drafted the paper. I.P. performed the analysis. A.B. supervised, reviewed and edited the manuscript, verified the methodology. All authors reviewed the results and approved the final version of the manuscript.

Conflicts of Interests

The authors have no conflicts of interest.

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Ethical Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Bagdasar-Arseni Clinical Emergency Hospital Bucharest, Romania (Protocol No. 4943/02.02.2023). An informed consent for using personal unidentifiable data for publication was signed on admission by all patients' parents.

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