MODIFIED CHARLES PROCEDURE AND LYMPH NODE FLAP TRANSFER FOR ADVANCED LOWER EXTREMITY LYMPHEDEMA

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Introduction: Treatment of advanced lymphedema remains a challenge in reconstructive surgery. Microsurgical techniques seem to be effective in early stage lymphedema, however in advanced stages their role is not well established. In this study, we present a novel approach for advanced lymphedema combining excisional procedure (Charles) with transferring lymph node flap. *Patients and method:* From 2010 to 2013, 24 patients (18 women, six men, mean age 53 years old) presented with late stage of lower extremity lymphedema. The modification of Charles procedure consisted of preserving the superficial venous system of the dorsum of the foot and the lesser saphenous vein, which were used for the venous anastomosis of the transferred lymph node flap. In 11 patients we transferred the inguinal lymph node flaps from the contralateral site, meanwhile in 13 patients supraclavicular lymph node flaps were used. *Results:* Maximum reduction of the lymphedema was achieved. No major complication was detected postoperatively. There were two patients with partial loss of the skin graft necessitated re-grafting. All the lymph node flaps survived well. The patients resumed normal daily activities within a period of 2 months. The mean follow-up was 14 months (3–26 months). During this period, no recurrence of the lymphedema was observed. *Conclusion:* The combination of the modified Charles procedure with vascularized transferring of lymph node flap is an effective method for treatment of advanced stage lymphedema. © 2014 Wiley Periodicals, Inc. Microsurgery 34:439–447, 2014.

Lower extremity lymphedema is a major source of morbidity. It can be either congenital or secondary following trauma or surgery for the treatment of cancer that includes removal of lymph nodes and/or radiotherapy. Congenital lymphedema may be caused by congenital aplasia or hypoplasia of peripheral lymphatics, congenital abnormalities of the abdominal or thoracic lymphatic trunk, and congenital valvular incompetence, usually associated with mega-lymphatics.[1] Primary or secondary lymphedema is characterized by the accumulation of the protein-rich lymph fluid in the subcutaneous tissue, which results in tissue hypertrophy, fibrosis, and lymphostatic elephantiasis.[2] In the medical literature have been described several staging systems of lymphedema. The International Society of Lymphology divides the severity of lymphedema in three stages.[3] Karri et al.[4] reported a modified staging system, dividing the severity of lymphedema in four stages. According to their system, the advanced lymphedema is characterized by irreversible skin fibrosis (stage IIIb) and nonpitting edema, with leather-like skin, skin crypts, and ulcers with or without involvement of the toes (stage IVa and IVb, respectively).

The surgical treatment of advanced lymphedema is a challenge reconstructive procedure. Microvascular techniques such as lymphaticovenous anastomosis and vascularized lymph node flap transfer seems to be effective at early stage lymphedema, with the last one to gain popularity among the plastic surgeons.[5–13] However, the role of these techniques in advanced lymphedema is not well established.

A variety of excisional procedures have been described for advanced lymphedema, notably by Charles, Sistrunk, Homans, Macey, and Auchincloss.[14–18] The Charles procedure consists of radical circumferential excision of the subcutaneous tissue and part of the fibrotic fascia of the affected limb and resurfacing with split-thickness skin grafts (STSG). Even though successful outcome after Charles procedure have been reported, potential complications of the procedure are the recurrence of the lymphedema especially at the foot necessitating resurfacing and re-grafting and toes amputation, skin graft loss, and poor cosmetic result.

On the basis of our previous experience in Charles procedure, we tried to improve the postoperative results eliminating the risk of recurrence and the need for secondary operations. In this report, we present a novel approach for advanced lymphedema combining a modified Charles procedure with vascularized lymph node flap transfer. To our knowledge, this is the first report of combination radical excisional procedure with vascularized lymph node flap transfer.

PATIENTS AND METHODS

From 2010 to 2013, 24 patients with severe lower extremity lymphedema underwent Charles procedure and

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Figure 1. Preoperative picture of patient with advanced lymphedema. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

vascularized lymph node flap transfer. The severity of lymphedema based on the staging system by the International Society of Lymphology and the proposed staging system by Karri and the senior author (H.C.C).[4] All the patients presented stage III and stage IIIb and IV according to the above staging systems, respectively.

The average age of the patients was 53 years (ranges, 37–78). There were 18 females and six males. All the patients presented with long lasting lymphedema (average, 7.2 years). Thirteen patients had secondary obstructive lymphedema, due to gynecological cancer resection followed by radiotherapy and/or chemotherapy. Four patients had post-traumatic lymphedema and seven patients had primary lymphedema (Fig. 1). All the patients had unilateral lymphedema.

The diagnosis was based on the clinical examination and the findings of the lymphoscintigraphy with technetium 99m, which showed delayed appearance of radioactivity with significant interruption of the lymphatic system. The contralateral leg was considered normal when the lymphoscintigraphy showed no dermal back-flow and the drainage was not blocked at 30 and 150 minutes.

All patients experienced at least one episode of infection. Preoperative antibiotics were given to the patients with persistent and long lasting cellulitis. All patients received preoperative conservative management, such as limb elevation and compression elastic bandage. We performed modified Charles procedure and vascularized lymph node flap transfer in all patients. In 13 patients the right supraclavicular lymph node flap based on the transverse cervical artery (TCA) were used, meanwhile the inguinal lymph node flap based on the superficial circumflex iliac artery (SCIA) and vein from the contralateral normal limb were transferred in 11 patients. Postoperative evaluation of the results such as regular measurement of the affected and the normal limb, recording of complications (recurrence of lymphedema, skin graft loss, cellulitis, and aggravation of lymphedema) was performed in all patients. Recurrence or worsening of lymphedema was defined as the increase of the limb circumference back to the preoperative status or even more, usually due to recurrent episodes of infection. Postoperative lymphoscintigraphy was performed at the 1 year follow-up in patients with groin lymph node flap transfer to evaluate the lymph drainage of the normal limb.

SURGICAL TECHNIQUE

With the patient under general anesthesia, two teams worked simultaneously, performing the Charles procedure and harvesting the lymph node flap. The Charles procedure was performed as it has been described analytically by Karonidis and Chen.[19] In brief, after pneumatic tourniquet was placed as proximal as possible, skin grafts were harvested from the diseased limb, and all the soft tissue above the deep fascia was excised. The proximal end of the resection was the middle of the thigh, and the distal end was the lateral and medial aspect of the foot, above the heel, and at the dorsum of the web spaces. In addition, two wedge excisions were made at the lateral and medial aspect of the thigh, in order additional reduction in the circumference of the proximal thigh, above the grafted area, to be achieved. The modification of the previously described Charles procedure was the preservation of the lesser saphenous vein and its superficial branches, which were used for the venous anastomosis with the transferred lymph node flap. The same team also prepared the recipient artery and the deep vein. Either the dorsalis pedis or the medial plantar artery with their concomitant veins could be used for anastomosis with the lymph node flap (Fig. 2).

At the same time, the second team harvested the lymph node flap. For the inguinal lymph node flap, the common femoral artery was palpated and then a skin paddle was designed about 2 cm below the inguinal

Figure 2. Intraoperative picture of Charles procedure. All the subcutaneous tissue was resected and a local flap on the dorsum of the foot was raised to cover part of the lymph node flap. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 3. Preoperative design of inguinal lymph node flap. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

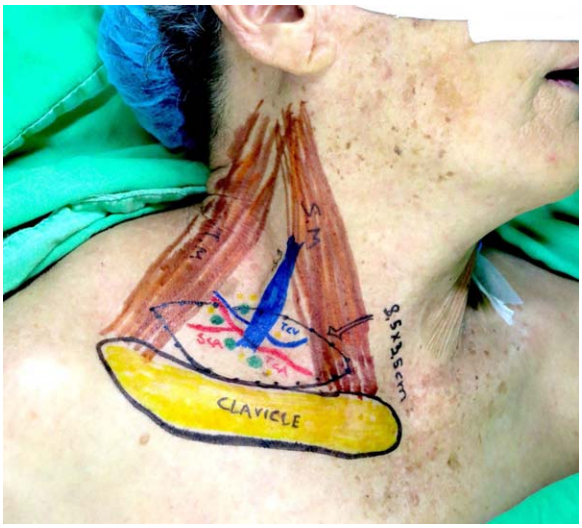

Figure 4. Preoperative design of supraclavicular lymph node flap with skin paddle. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

ligament, and lateral to the femoral artery. In cases, that we harvested the flap without skin paddle a lazy "S"-shape incision, 6–8 cm in length was made 2 cm below the inguinal ligament as well. The flap can be harvested either from medial to lateral, identifying first the SCIA and vein, or from lateral to medial. Of note, a "patch" of the femoral artery can be harvested to increase the diameter of the arterial distal end. The femoral artery is then repaired with 5-0 prolene (Fig. 3).

Harvesting of the right side supraclavicular lymph node flap has been described in our previously published article.[20] In brief, an incision was made 1.5 cm above the clavicle, and a free style lymph node flap was harvested based on the TCA. The anatomical landmarks of the flap were the sternocleidomastoid muscle anteriorly, the trapezius muscle posteriorly, the clavicle inferiorly, and the external jugular vein, which was also included with the flap and used for the second venous anastomosis (Fig. 4). The main lymph nodes are deep to the omohyoid muscle, and careful dissection should be performed not to separate the lymph node from the underlying TCA. The concomitant vein was also identified and included with the flap. In three cases, we harvested the flap with skin paddle. The size of the skin paddle was about 4 × 8 cm. Of note, direct perforator from the TCA to the skin, was difficult to be identified due to its small size, however the skin paddle could be harvested with safety, unless careless dissection separate the skin from the underlying soft tissue.

After the Charles procedure was completed and the lymph node was harvested, one arterial and two venous anastomoses were performed at the recipient site. In our initial cases, the dorsum of the foot was used as recipient site and the flap was totally being covered by STSG. In the last 11 cases, where the medial plantar artery was used, a local flap was raised at the medial aspect of the ankle and the lymph node flap was almost completely covered by the skin flap, leaving a small part to be covered by STSG (Fig. 5). For venous anastomoses, one deep and one superficial vein, branch of the lesser saphenous vein, were used. Postoperative the patients remained

Figure 5. Intraoperative picture after implantation of the lymph node flap at the ankle. A skin flap was raised to cover the lymph node flap. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

inpatient for 5–7 days with the leg elevated and then discharged. Compression garment for the foot, leg, and thigh, was used after 1 month, when the skin graft was stabilized.

RESULTS

Two patients experienced partial skin graft loss, and required re-grafting. In these cases, skin graft was harvested from the proximal thigh. All the lymph node flaps survived well. However, in one case, where the supraclavicular lymph node flap was harvested with skin paddle, partial loss of the skin flap occurred. In addition, in six cases where the lymph node flap was grafted on the dorsum of the foot, we had partial loss of the skin graft, however re-grafting was not necessary, and the wound healed secondary with conservative treatment. From the 11 cases that the lymph nodes were covered by a skin flap at the ankle and partially by STSG only in one case presented partial skin graft loss, which also healed conservatively. All the patients had 100% reduction of the affected limb (Fig. 6). All the patients followed physiotherapy, and were able to return to their normal daily activity within the first 2 months following the operation. All patients were encouraged to begin wearing compression elastic bandage 1 month after the operation, when the skin graft was complete healed, for a period of 3–4 months. No complication of the lymph node flap donor site was also noted. Similarly, we didn't have any complication when a "patch" of femoral artery was used to increase the diameter of the SCIA. During the follow-up period, no difference in the circumference of the donor site limb was noted. The operation time was about 6 hours (ranges, 5–8 hours).

The mean follow-up was 14 months (ranges, 3–26 months). During this period, no recurrence of lymphedema was observed. One patient experienced infection 13 months after the operation, which was treated with antibiotics. Special observation was made on the toes, which were preserved during the Charles procedure and were vulnerable to infection and aggravation of lymphedema. However, none of the patient experienced severe

Figure 6. Postoperative result 1 year after Charles procedure and lymph node flap transfer at the dorsum of the foot. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

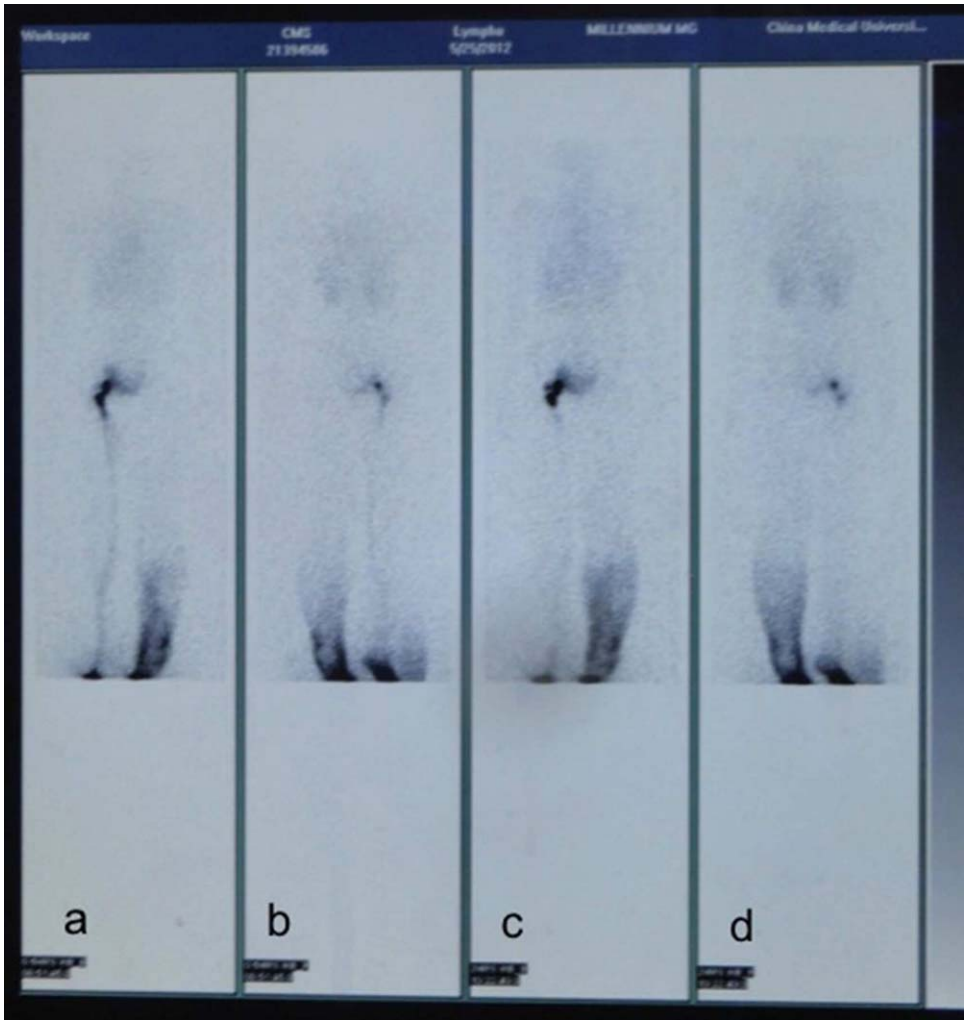

*Figure 7. The proeoperative lymphoscintigraphy of a patient with left lower limb lymphedema showed significant dermal back-flow of the radiotracer and impaired lymphatic function on the left side with no visualization of the left groin lymph nodes. On the right leg, normal lymphatic function was noted (**a**: front view, **b**: back view). Thirty minutes later the drainage was still blocked on the left leg, meanwhile the right leg had normal clearance of the radiotracer (**c**: front view, **d**: back view). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]*

infection of the toes or worsening of lymphedema, and no need for toes amputation was noted. Five patients with groin lymph node flap transfer completed 1 year follow-up and received lymphoscintigraphy, which didn't show impairment of the lymphatic function of the donor site limb.

Even though the patients' quality of life was not investigated with accurate scale, all the patients reported satisfied with the final result, as they were able to perform their daily activities independently.

CASE REPORT

A 53-year-old woman presented with left lower limb lymphedema after ablative surgery for stage IB cervical cancer, lymph node dissection, and adjuvant chemoradiotherapy performed 7 years ago. The duration of lymphedema was 6 years. The preoperative measurement of the limbs showed that the patient suffered from stage III lymphedema as the left limb was 42 and 36% larger than the right at the middle of the thigh and the middle of the knee, respectively. The preoperative lymphoscintigraphy showed significant dermal back-flow of the radiotracer and impaired lymphatic function on the left leg, with no visualization of the left groin lymph nodes. On the right leg, the examination showed normal lymphatic function (Fig. 7). We performed modified Charles procedure and supraclavicular lymph node flap transfer on the dorsum of the foot. The dorsalis pedis artery and the concomitant vein were used as recipient vessels. During the Charles procedure, a superficial vein connected with the lesser saphenous vein was preserved and used for second

*Figure 8. (**a**) Preoperative picture of a patient with advanced left lower limb lymphedema (**b**) postoperative result. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]*

venous anastomosis. The postoperative period was uneventful. Maximum reduction of the lymphedematous limb was achieved, with no recurrence at the 1 year follow-up (Fig. 8).

DISCUSSION

Lymphedema is a chronic, progressive, and debilitating condition, which negatively affects the quality of life. It can be either primary or secondary after cancer ablation with or without radiotherapy and chemotherapy. Even though the pathogenesis and the pathophysiology of this condition is well established, the treatment remains a challenge for the reconstructive surgeon. Several methods have been described for the treatment of lymphedema. Surgical procedures are indicated when previous conservative method failed to improve the lymphedema. They can be categorized as excisional, in which the diseased soft tissue is removed, or physiologic, in which an attempt is made to improve the lymphatic flow. Among the physiologic procedures that have been used for the treatment of lymphedema, the lymphaticovenous by-pass transferring vascularized lymph node flap is gaining popularity.

Felmerer et al.[21] proposed the microsurgical lymphatic vessel transplantation as a method for bypassing the obstructed lymph pathway with satisfactory results in 14 patients with secondary lymphedema of the limb, face, and genital. On the other hand, the mechanism of the lymph node flap transfer is based on the spontaneous generation of lymphatic channels between the transferred lymph nodes and the surrounding tissues. The lymph is absorbed by the vascularized lymph nodes and drained to the venous system through the lympaticovenous connections inside the flap.

In 1990, Chen et al.[22] investigated the efficacy of transferring lymph node flap into lympoedematous limbs. Experimental studies in Mongrel dogs showed that 3–6 months after lymph node flap transfer, the transferred lymph nodes inside the flap had normal architecture. Furthermore, the circumference of the limb was reduced after transplantation and postoperative lymphangiography demonstrated regeneration of the lymphatic system. In addition, the authors noticed that lympholymphatic anastomosis between the lymph node flap and the surrounding lymphatics was neither necessary nor beneficial.

The medical literature is limited regarding the efficacy of the vascularized lymph node flap transfer in

lower extremity lymphedema. Cheng et al.[23] reported reduction of the limb circumference after transferring submental lymph node flap at the ankle. Similarly, Althubaiti et al.,[24] using also vascularized supraclavicular lymph node flap transfer for lower extremity lymphedema, presented satisfactory postoperative results. Our previous experience using either inguinal or supraclavicular lymph node flap transfer for lower extremity lymphedema agree with the above studies that the lymph node flap transfer is able to reduce the circumference of the lymphedematous limb and relieve the subjective symptoms at the early stages of disease. Furthermore, several studies prove the efficacy of the lymph node flap transfer in postmastectomy upper extremity lymphedema.[6–9,25] Important factor for the positive outcome after lymph node flap transfer is the appropriate selection of the patients, as the lymph node flap transfer is able to improve significant the lymphedema at the early stage. When the disease is long lasting, and permanent changes of the limb has been established such as extensive fibrosis and skin changes with hyperkeratosis, the role of lymph node flap transfer is not well established and can offer only limited improvement.

In the cases, with advanced lymphedema, significant improvement can be achieved with excisional procedures, in which the lymphedematous tissues are partially or totally removed. Sistrunk[15] first described the staged excision of the subcutaneous tissues in 1918. Modification of this technique was later presented by Miller et al.[26] and Homans.[16] Salgado et al.[27] tried to eliminate potential complications after partial excision of the lymphedematous tissue such as skin necrosis. According to their technique, medial and lateral skin flaps are raised through incisions on the anterior and posterior leg, preserving a 4-cm skin bridge in the central portion of the incisions. The skin flaps are reduced to 5 mm in thickness, except in the vicinity of the lateral and medial septae, which contain perforators from the posterior tibial and peroneal arteries. Postoperative complications were cellulitis in three of 15 patients and seroma and hematoma in one patient. Even though the authors didn't report aggravation or recurrence of lymphedema, a retrospective study from Kim et al.,[28] about the efficacy of excisional surgery in advanced lymphedema, showed that improvement was achieved in 75% of the cases, and in the rest 25% the lymphedema progresses to the postoperative status.

More radical reduction of the lymphedematous limb can be achieved with Charles procedure, which involves radical excision of the skin, subcutaneous tissue, and fascia, and then resurfacing of the limb with STSG. Potential complications of the procedure are wound breakdown, hyperkeratosis, ulceration, and aggravation of foot lymphedema. Van der Walt et al.[29] presented a modified Charles procedure, applying negative-dressing after the initial debulking surgery and then they delayed the skin grafting by 5–7 days. Three from eight patients required re-grafting, however the results showed dramatic functional improvement in quality of life and a high overall satisfaction rate.

Karri et al.[4] performed Charles procedure in 27 patients with late-stage lower extremity lymphedema. According to their results, the 59.3% of the patients required secondary minor operations. The most frequent complication was a single, short period of cellulitis, affecting five of 27 patients (18.5%). Furthermore, self-reported mobility was either the same or improved at 6 months and appearance of their limbs satisfactory.

In our clinical study, we included 24 patients who presented with unilateral late-stage lower extremity lymphedema. The diagnosis was based on the difference of the circumference between the normal and the affected limb and the findings of the lymphoscintigraphy with technetium 99m, which confirmed the impaired lymphatic function of the lymphedematous limb compared to normal clearance of the radiotracer on the contralateral side. Due to previous failure of the conservative treatment and the long-lasting advanced disease modified Charles procedure combined with lymph node flap transfer was planed. In 11 patients, we transferred the inguinal lymph node flaps from the contralateral site, meanwhile in 13 patients supraclavicular lymph node flaps were used. The supraclavicular lymph node flap was harvested from the right side to avoid potential injury of the main lymphatic duct on the contralateral side.

Viitanen et al.[30] evaluated the long-term donor site morbidity after inguinal lymph node flap transfer. Even though none of the patients developed lymphedema, in six of 10 patients postoperative lymphoscintigraphy showed minor changes in lymphatic flow on the donor site and two of 10 patients the semiquantitative evaluation of lymphatic drainage was considered slightly abnormal.

Vignes et al.[31] reported that two of 26 patients developed lower limb lymphedema after harvesting groin lymph node flap. Similarly, Pons et al.[32] reported only one of 42 patient with secondary iatrogenic lymphedema lymphedema after vascularized lymph node flap transfer.

In our five cases, with groin lymph node flap transfer who received postoperative lymphoscintigraphy at the 1 year follow-up no difference in the pre and postoperative findings were noted and the circumference of the donor site limb remained the same. Similarly, none of patients during the follow-up period experienced increase in the circumference of the donor site limb.

Furthermore, based on the previous experience of the senior author in the groin lymph node flap for the upper extremity lymphedema, no donor site complications were noted.[8] Careful dissection of the flap preserving the deep inguinal lymph nodes is essential to prevent of

development lymphedema on the donor site. However, due to this potential risk our first choice for lymph node flap transfer is becoming the supraclavicular lymph node flap. Further advantages of the supraclavicular lymph node flap are the following: (1) constant vascular anatomy (2) adequate size of vessels compared to groin flap (3) most of the time during the flap harvesting lymph nodes can be visualized due to the size, making the dissection more precise. Even though patent blue dye can be injected half an hour before dissection in order the lymph nodes to be visible easily, it is not absolutely necessary as the color and the shape of the lymph nodes are different from the surrounding fat under magnification during the flap harvesting.

Several studies have shown that the indocyanine green lymphography can be useful tool in lymphedema surgery. Yamamoto et al.[33] reported that the lymphography findings were classifiable into two patterns according the severity of lymphedema. Mild cases of lymphedema were characterized by a linear lymphatic channel pattern. In more severe cases, lymphatic channels demonstrated retrograde lymphatic flow (dermal backflow pattern) and diminution or absence of linear channel patterning. Ogata et al.[34] showed that the lymphography using indocyanine green dye for near-infrared fluorescence labeling is helpful in identification of the lymphatic channels eliminating the time of the operation. Similarly, Yamamoto et al.[35] showed that the microscopic ICG lymphography helps the supermicrosurgeon to find and dissect lymphatic vessels easier.

A new method for easy detection of functional lymphatic vessels in the superficial layer is reported.[36] In a clinical trial, lymphography using indocyanine green dye for near-infrared fluorescence labeling in lymphaticovenular anastomoses was performed in five patients with lymphedema. The technique is simple and enables a minimally invasive operation to be performed. The results indicate that this technique is useful for acceptance as one of the examinations to evaluation of lymphedema.

The modification of the Charles procedure consists of preserving the lesser saphenous vein along with its superficial branch on the dorsum of the foot. The superficial venous system is preserved to be used for the second venous anastomosis with the lymph node flap. The main mechanism of the lymph node flap transfer is the lymphaticovenous bypass. After the implantation of the lymph nodes spontaneous regeneration of lymphatic channel between the lymph nodes and the surrounding lymphedematous tissue is occurred and then the lymph is drained to the venous system through the normal lymphaticovenous connections inside the lymph node flap. On the basis of this mechanism, we supercharged the lymph node flap with two venous anastomoses maximizing the lymph drainage into the venous system. However, more studies are necessary to confirm if two venous anastomoses are more beneficial than one.

The disadvantages of the Charles procedure are the poor cosmetic outcome, recurrence, and the progresses of the disease on the remaining tissues. To eliminate these complications, we combined the excisional procedure with lymph node flap transfer. In our cases, none of the patients experienced aggravation of the lymphedema on the foot as the transferred lymph node flap had protective role. In addition, in our cases we had low incidence of postoperative infection as only one patient developed cellulitis 8 months after the operation. The transferred lymph node flap contain macrophages and lymphocytes, which have the ability to capture, phagocytose, and destroy pathogens draining from sites of infection. This immunological mechanism of the lymph nodes can explain the reduction of the infection rate of the diseased limb after lymph node flap transfer.

Even though the lymph node flap is buried, the postoperative monitoring is not tedious, as the overlying skin graft is meshed and the observation of the flap is relative easy. In addition, in three cases, we harvested supraclavicular lymph node flap with skin paddle. The skin paddle was used for the postoperative monitoring of the flap, without any influence on the clinical outcome. One patient had partial loss of the skin flap due to venous congestion, necessitating debridement. However, the underlying lymph nodes were viable.

As a conclusion, the treatment of the lower limb late-stage lymphedema remains challenging. A novel approach combining excisional procedure such as Charles with microvascular lymph node flap transfer seems to be reliable method for treating advanced stage of lower limb lymphedema, preventing from potential complications such as recurrence, infection, and aggravation of the disease. However, more clinical studies and longer follow-up is necessary for safer conclusions.

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