Lymph node transplant in Kenya: a case series of 20 patients

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Summary

Chronic limb lymphedema is a debilitating condition whose definitive management eludes medical practice to date. Lymph node transplant results in improvement of symptomatology amongst patients with lymphedema non-responsive to non-operative management. A retrospective audit of all patients who underwent lymph node transplant in Nairobi, Kenya for the period June 2014-June 2017 (three years) was done. We report improvement of symptomatology amongst patients with stage II lymphedema non-responsive to non-operative management. We also highlight surgical considerations taken during the management of these cases.

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Introduction

Lymphedema results from dysfunctional, non-functional or destroyed lymphatic channels. The chronically heavy extremity impairs utility of the limb. Abnormal accumulation of protein rich interstitial fluid predisposes the patient to recurrent episodes of ulceration, lymphangitis and or cellulitis. Physical therapy and compression therapy are the main non-operative management modalities to relieve the symptoms.[1] Lymph node transplant or free vascularized lymph node transfer (VLNT) is the transfer of functional lymph nodes with their blood vessels onto new sites to facilitate neo-lymphangiogenesis.[2] Where non-operative management fails, lymph node transplant is reported as a more effective modality compared to lymphaticovenular anastomosis or lymphatic-lymphatic bypass or lymphaticovenous bypass.[3, 4] Furthermore, these other physiologic surgical options are quite long and tedious and require supermicrosurgical skills. Surgical excision procedures are reserved for irreversible late stage procedures and often result in poor outcomes.[5] Lymph node transplant is a promising treatment modality and our retrospective case series adds to the growing evidence of its application. The objective was to evaluate the effectiveness of lymph node transplant on the preoperative symptomatology. This is the first experience reported from Kenya.

Patients and methods

In our setting, Nairobi, Kenya, microsurgery is a skill only found and practiced by plastic surgeons. For the period of the audit, there were only two operating microsurgeons. The procedure was undertaken in both the public hospital (Kenyatta National Hospital) and private hospitals (the Nairobi Hospital, Nairobi South Hospital, the Aga Khan University Hospital, and the M.P. Shah Hospital).

In this retrospective audit, we included all patients who underwent lymph node transplant for lymphedema during the period of June 2014 to June 2017. Lymphedema was defined as chronic swelling of an extremity confirmed by lymphoscintigraphy and graded according to the International Society of Lymphology (ISL). Lymph node transplant was defined as the transfer of functional lymph nodes utilizing microvascular anastomoses at the recipient site. A two team approach was incorporated: one team harvested the lymph nodes while the other evaluated and prepared the recipient site. Donor lymph nodes were harvested from the submandibular and inguinal lymph node basins for lower limb and upper limb lymphedema recipient sites, respectively. Microvascular anastomosis was done under microsurgical loupes 4.5x and 5x using nylon 9-0. Routine irrigation of vessels with heparinized saline solution (5000 units in 500 mls of normal saline) and 20% lignocaine was done. 5000 units of intravascular heparin units was given to patients where the anastomoses took

Table 1. Demographics and clinical profile of the patients (M=Male, F=Female)

Patient	Age (years)	Sex	Diagnosis	Site of lymphedema	Donor site	Donor vessels	Recipient site	Recipient vessels	Duration of lymphedema prior to surgery
1	6	M	Primary lymphedema	Right lower limb	Right submandibular	Facial vessels	Right groin	Superficial epigastric vessels	4 years
2	12	F	Primary lymphedema	Right lower limb	Right submandibular	Facial vessels	Right ankle	Dorsalis pedis vessels	6 years
3	13	M	Primary lymphedema	Right lower limb	Right submandibular	Facial vessels	Right groin	Superficial epigastric vessels	5 years
4	15	M	Primary lymphedema	Right lower limb	Right submandibular	Facial vessels	Right ankle	Anterior tibial vessels	5 years
5	16	M	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left groin	Superficial epigastric vessels	7 years
6	17	M	Primary lymphedema	Right lower limb	Right submandibular	Facial vessels	Right groin	Superficial epigastric vessels	7 years
7	25	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left groin	Superficial epigastric vessels	10 years
8	27	F	Secondary lymphedema (post mastectomy)	Left upper limb	Left inguinal	Superficial epigastric vessels	Left wrist	radial artery & cephalic vein	4 years
9	28	F	Secondary lymphedema (post trauma)	Right lower limb	Right submandibular	Facial vessels	Right groin	Femoral vessels	5 years
10	30	F	Secondary lymphedema (post mastectomy)	Left upper limb	Right cervical (lymph node flap)	Transverse cervical vessels	Left wrist	radial artery & cephalic vein	3 years
11	31	F	Secondary lymphedema (post mastectomy)	Left upper limb	Left inguinal	Superficial epigastric vessels	Left wrist	radial artery & cephalic vein	4 years
12	32	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left groin	Superficial circumflex iliac vessels	3 years
13	35	F	Secondary lymphedema (post mastectomy	Right upper limb	Left inguinal (lymph node flap)	Superficial circumflex iliac vessels	Right wrist	radial artery & cephalic vein	5 years
14	36	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	left ankle	Dorsalis pedis vessels	10 years
15	36	F	Secondary lymphedema (post mastectomy)	Left upper limb	Right cervical (lymph node flap)	Transverse cervical vessels	Left wrist	radial artery & cephalic vein	7 years
16	37	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left groin	Superficial epigastric vessels	6 years
17	40	M	Secondary lymphedema (post trauma)	Right lower limb	Right submandibular	Facial vessels	Right groin	Superficial circumflex iliac vessels	5 years
18	42	F	Primary lymphedema	left lower limb	Right submandibular	Facial vessels	Left groin	Superficial epigastric vessels	5 years
19	45	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left ankle	Dorsalis pedis vessels	16 years
20	50	F	Primary lymphedema	Left lower limb	Right submandibular	Facial vessels	Left ankle	Dorsalis pedis vessels	19 years
Mean ± SD (range)	28.7±12.1 (6-50)								6.8±4.1 (3-19)

Table 2. Patient outcomes
S=small, M=medium, L=large, XL=extra-large, XXL=extra-extra-large; N/A – not applicable (symptomatology not present).

Patient	Change in compression stocking size	Change in episodes of lymphangitis +/ cellulitis (per year)	Change in episodes of ulcerations (per year)	Utility of limb	Fibrosclerotic changes	Change in skin pliability	Follow up period
1	M to S	N/A	N/A	Improved	N/A	Yielding to supple	12 months
2	L to M	N/A	N/A	Improved	N/A	Yielding to supple	26 months
3	L to M	1 to 0	2 to 0	Improved	Improved	No change	16 months
4	L to M	N/A	N/A	Improved	N/A	Yielding to supple	27 months
5	XL to M	N/A	N/A	Improved	N/A	Yielding to supple	14 months
6	No change	N/A	N/A	No change	N/A	No change	6 months
7	XL to L	3 to 1	N/A	Improved	Improved	Firm to yielding	10 months
8	XL to L	2 to 0	N/A	Improved	N/A	Yielding to supple	17 months
9	XL to L	N/A	N/A	Improved	N/A	Yielding to supple	18 months
10	XL to L	N/A	N/A	Improved	N/A	Yielding to supple	23 months
11	XL to L	-	-	-	-	-	Lost to follow up
12	XXL to L	4 to 1	N/A	Improved	Improved	firm to supple	25 months
13	XL to L	N/A	N/A	Improved	N/A	No change	20 months
14	XL to L	3 to 1	3 to 0	Improved	Improved	Firm to yielding	14 moths
15	XL to L	1 to 0	N/A	Improved	N/A	No change	22 months
16	XXL to XL	5 to 1	4 to 0	Improved	improved	Firm to yielding	29 months
17	XL to L	N/A	N/A	Improved	N/A	Yielding to supple	18 months
18	XL to L	3 to 0	2 to 0	Improved	Improved	Firm to yielding	20 months
19	XXL to XL	3 to 1	2 to 0	Improved	Improved	Firm to supple	24 months
20	XXL to XL	2 to 0	1 to 0	Improved	Improved	Firm to yielding	24 months
Mean ± SD (range)	-	-	-	-	-	-	19.2±6.2 (6-29)

Table 3. Compression stocking size chart
S=small, M=medium, L=large, XL=extra-large, XXL=extra-extra-large

Lower limb stocking size chart			
Size	**Ankle circumference (cm)**	**Calf circumference (cm)**	**Thigh circumference (cm)**
S	19-22	28-34	42-57
M	22-24	32-38	48-64
L	25-27	36-42	54-71
XL	28-30	40-46	60-78
XXL	30-32	42-50	65-85
Upper limb stocking size chart			
Size	**Wrist circumference (cm)**	**Mid-forearm circumference (cm)**	**Mid-arm circumference (cm)**
S	14-20	18-23	22-40
M	16-22	23-29	27-45
L	18-24	29-34	33-51

Figure 1. Post-operative healed sites of donor right submandibular region and recipient left ankle region

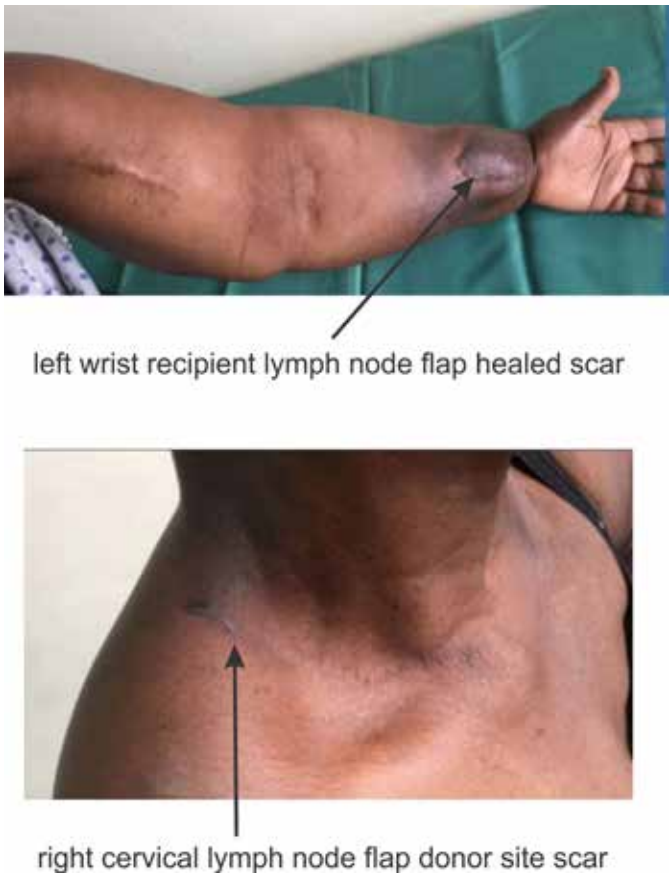

Figure 2. Post-operative healed sites of donor right cervical region and recipient left wrist region in lymph node flap

longer than anticipated. No other adjunct procedures were performed. Postoperative protocol included antimicrobials (amoxicillin/clavulanate 45 mg/kg/day or ceftriaxone 1–2 g/day for 1 week plus clindamycin 15 mg/kg/day for 2 weeks), analgesics (paracetamol 45 mg/kg/day, diclofenac 2 mg/kg/day plus an opioid), enoxaparin (0.5 mg/kg/day) for 5 days, low dose aspirin (4 mg/kg/day) for 2 weeks, limb elevation for 3 months and postoperative compression therapy (started 2 weeks post-surgery and continued for one year). The compression stockings were changed every 3 months. In patients with ulcerations, lymphangitis and or cellulitis, surgery was performed after treatment and resolution of the infection and healing of the wound.

Data was collected from patient medical records – perioperative and review consultation notes, operating theatre notes, treatment prescriptions and radiology results. Data recorded included patient demographics, length of symptoms and postoperative outcomes (change in limb size, change in skin pliability, fibrosclerotic skin changes and change in episodes per year of ulcerations and lymphangitis/cellulitis, improvement in limb utility) and the perioperative surgical protocol. Change in limb size was determined by change in stocking size. Skin pliability tactile assessment was a modification of the parameter from the Vancouver Scar scale: normal, supple, yielding, firm (in order of reducing pliability). Limb utility was subjective report given by the patient during reviews (either improved or not improved). Fibrosclerotic skin changes was determined and assessed by the clinician. Perioperative reviews was done by the operating surgeon. Data was analyzed using descriptive statistics; the mean was calculated. Follow up period was for three years (still ongoing). Approval was sought and granted by the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee (KNH/UON ERC).

Results

Twenty patients (n=6 male, n=14 female; median age: 30.5 years; and range 6 to 50 years) with lymphedema underwent lymph node transplant from the period of June 2014 to June 2017. Six patients underwent the procedure in the public hospital.

Of all the patients (n=20), the majority had primary lymphedema (13 patients) and the lower limb was mainly affected (15 patients) (See Table 1). Mean duration of lymphedema prior to surgery was 6.8 years. One patient was lost to follow-up. The mean duration of follow up was 19.2 months.

Most of the patients had improved utility of the affected limb and improved skin pliability (See Table 2). All the patients experienced reduction in limb size as determined by

reduction in compression stocking size (See Table 3). Patients with prior episodes of ulcerations and lymphangitis/cellulitis experienced reduction in occurrence.

All patients had an uneventful recovery and wounds healed well (See Figure 1 and 2). There were no complications.

Discussion

This is the first experience on lymph node transplant from Kenya spanning three years. Patient selection is key to success and the criteria reported was based on the senior surgeon's preference and experience in other free flap procedures.

On-table confirmation of functional arterial and venous anastomoses is essential to avoid "lymph node grafting". Due to the edema and or fibrosclerosis, most of the recipient vessels have weak walls; and it may take quite some time to identify a suitable vein. A clear understanding of the varied vascular anatomy of the limb aids in prompt vessel dissection and identification. Patience is an attribute often tested in such circumstances. At the recipient site, the most suitable vessels (good length, caliber and blood flow) were chosen for anastomosis. We recommend a two-team approach: one for harvesting and another for recipient anastomosis to avoid fatigue and mistakes. We opted for and recommend donor lymph nodes of the neck for relative ease of dissection, large caliber donor vessels and limited donor site complications.[6] The risk of donor site lymphedema of the neck is also quite low as the neck has a robust lymphatic network.[7] We report neither donor site nor recipient site complications. Contrary to Lee et al., we had no incidence of donor site lymphedema.[8] While Nguyen at al. encountered other donor site complications, reports from Saaristo et al. and Viitanen et al. indicated recipient site complications.[9-11] Comparison to these three studies is not appropriate as their patients underwent simultaneous breast reconstruction with VLNT; a more technically demanding procedure.

Use of enoxaparin was limited to the five days when the patient was on strict bed rest post surgery, following which ambulation was initiated. Anti-platelet use was based also on surgeon experience and preference. Postoperative compression therapy was routinely initiated at two weeks when the anastomosis was expected to have healed/matured. Compression therapy was done both pre and post-surgery; based on surgeons experience it hastens improvement in skin pliability. Patient adherence to rehabilitation protocol and compression therapy is also a significant contributor to success of the procedure. Whereas reports by Granzow et al. and Becker et al. highlight ability to reduce and discontinue postoperative compression therapy, there is no analysis of this ability to lymphedema stage.[12,13] We opt for long term compression therapy for our stage II lymphedema patients, whose spontaneously irreversible lymphedema often relapsed and retarded any improvement in limb size reduction.[14]

In the earlier years (year 2014–2015), the third author opted for ankle region as the recipient site in lower limb lymphedema. During that period, the groin was utilized only when the limb had severe verrucous changes with notable dilated and weak vessels. A paradigm shift in the latter years has seen the groin recipient as the standard. The lymph node flap was utilized to ensure tension-free closure in a region with significant edema. All the patients were unwilling to undergo a postoperative lymphoscintigraphy due to the high cost.

Lymph node transplant resulted in reduction in limb size and improved utility of the affected limb. Utility of the limb was reported by the patient as improved ability to utilize limb in daily activities. Despite the majority of our patients reporting improved limb utility, we cannot equate this to patient satisfaction. Patient satisfaction, which has been reported to be high post VLNT by Patel et al. and Gharb et al., is a reflection of multiple quality of life factors.[15,16] Although subjectively assessed, our report of reduction in limb size is concordant to studies by Patel et al. and Chen et al.[17,18] The only patient reporting no change in limb utility and size has only been reviewed six months post-surgery. All patients with prior episodes of ulceration (n=6), lymphangitis and or cellulitis (n=10) have noted reduction in their occurrence. Studies by Cheng at al. also indicated reduction in frequency of infections post VLNT.[19,20] We further noted improvement in fibrosclerotic changes. This is the first study to report on positive changes in episodes of ulcerations and fibrosclerotic changes.

Success in management of lymphedema using lymph node transplant has been variously reported and our study affirms the same[21-23] In our experience, the most dramatic changes that we noted and were appreciated by the patients were the reduction in frequency of ulcerations, lymphangitis and or cellulitis and improvement in fibrosclerotic changes.

Limitations of the Study

Our study is limited by: small sample size, surgeon bias as there was no independent assessor and inadequate measure of limb utility. However, there are no objective measures of limb utilization that have been validated in assessing lymphedema treatment modalities. We further acknowledge our study's drawback in assessing changes in limb size. Despite having regular changes in stockings, they stretch and are unreliable compared to the standard limb circumference measurement. We also did not record when the patients stopped physiotherapy.

Recommendations

We recommend identification and validation of functional (limb utility) and quality of life assessment tools to objectively assess lymphedema treatment modalities. For example: the six minute walk test for lower limb, isometric muscle strength for both upper and lower limbs, the 36-Item Short Form Health Survey questionnaire and the WHOQOL-BREF questionnaire.[24-26] We also recommend utilization of photographs to objectively assess changes in skin fibrosclerosis.

Conclusion

Based on our small series of patients, lymph node transplant results in improvement of symptomatology amongst patients with stage II lymphedema non-responsive to non-operative management.

Conflict of interest

None

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None

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