HAND/PERIPHERAL NERVE

Changes in the Lymph Structure of the Upper Limb after Axillary Dissection: Radiographic and Anatomical Study in a Human Cadaver

Hiroo Suami, M.D., Ph.D. Wei-Ren Pan, M.D. G. Ian Taylor, M.D. Melbourne, Victoria, Australia

Background: There have been very few anatomical reports on the changing lymph structure of the upper limb after axillary dissection despite its clinical significance for predicting skin cancer recurrence in the limb and secondary lymphedema. The authors used both upper limbs harvested from a fresh human cadaver that had undergone unilateral right radical mastectomy and radical axillary dissection for breast cancer.

Methods: Hydrogen peroxide was used to identify and inflate the lymphatic vessels. Individual channels were injected with a radiopaque lead oxide mixture and recorded on x-ray film.

Results: Results from the normal left upper limb were similar to results from the authors' previous studies. However, the right limb from the mastectomy side showed remarkable differences and revealed that the lymph node clearance in the axilla had been incomplete on that side. The major difference was the almost complete absence of the superficial lymphatic network in the right arm, proximal to the elbow, because of fibrosis and blockage of the lymphatic channels. A circuitous pathway was identified that bypassed the blocked lymphatics in the arm to reach the deep system. This was facilitated often by backflow through precollectors and avalvular lymph capillaries in the dermis of the forearm, to reach eventually the few remaining lymph nodes in the axilla.

Conclusions: Previously undetected lymph channels connecting the superficial and the deep lymphatic system had opened up because of the blockage of superficial lymphatic vessels caused by axillary dissection. It is presumed that these channels prevented lymphedema in this case. (*Plast. Reconstr. Surg.* 120: 982, 2007.)

Since Halsted¹ reported chronic edema of the upper limb after mastectomy for breast cancer, lymphedema has become a wellknown postoperative side effect. The treatment for acquired lymphedema of the upper limb after axillary dissection is a challenging problem for plastic surgeons. The cause of lymphedema is not fully understood and therefore at this time there is still no recognized cure. Although it is agreed that secondary lymphedema is caused by the inability of the lymphatic network to cope with the drainage of extracellular tissue fluid following ablation of the regional lymph nodes,

From the Jack Brockhoff Reconstructive Plastic Surgery Research Unit, Royal Melbourne Hospital, Department of Anatomy and Cell Biology, University of Melbourne.

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Copyright ©2007 by the American Society of Plastic Surgeons DOI: 10.1097/01.prs.0000277995.25009.3e it is difficult to predict before surgery which patients will be afflicted. Lymphangiographic studies²⁻¹⁵ of patients after axillary dissection describe changes in lymphatic pathways of the upper limb. However, lymphangiography requires the patient to remain in the same position for lengthy periods during the examination of just one vessel. It also uses an oil contrast medium, which can cause blockages and inflammation of the lymph channels, and the symptoms may become worse.¹⁶

Lymphoscintigraphy is now used more commonly for examination of the lymphatic system than lymphangiography. Lymphoscintigraphy is useful for quantitative diagnosis of lymphedema by checking the clearance time of injected radioactive substances.¹⁷ However, it is not suitable for accurately mapping the exact course of every lymph vessel. Early anatomical studies were undertaken using dye or mercury, and the results were usually only drawings.^{18–20} Gerota's method in 1896²¹ using blue oil painting color is still a common method of finding lymphatic vessels. However, it is not suitable for identifying and mapping the course of the collecting vessels.

There have been very few anatomical reports on the changing lymph structure of the upper limb after axillary dissection. There have been no reports comparing both upper limbs of a cadaver after unilateral mastectomy. Our new radiographic cadaver injection technique for investigating the lymphatic system^{22–24} has been applied to this study to examine the changes in the lymph structure after axillary dissection in one limb and to compare these results with those obtained from the opposite, normal limb (Figs. 1 through 8).

MATERIALS AND METHODS

The cadaver was an 81-year-old woman who had undergone a total right mastectomy with axillary node clearance 11 years previously. All nodes were clear of cancerous cells. She did not receive radiation treatment and she did not have any signs of lymphedema or cancer recurrence after the operation. Her death was caused by chronic heart failure. We used both upper limbs, including the armpits, as forequarter specimens.

The lymph investigation was commenced in the abnormal right upper limb, and the normal left limb was preserved in a deep freezer. Applying our method,^{22–24} all of the lymph collecting vessels (approximately 0.3 mm in diameter) were de-



Fig. 1. Precollectors in the dermis (*PC*) and lymph collecting vessels (*LC*) in the subcutaneous tissue of the fingertip were identified using a mixture of blue ink and hydrogen peroxide. The lymph collecting vessels were injected with a radiopaque lead oxide mixture (*orange*). The *arrow* points to a valve that normally prevents backflow from the lymph collecting vessels.

tected. The study commenced at the fingertips. A mixture of blue drawing ink and hydrogen peroxide was injected into the dermis of the fingertips (Fig. 1). The epidermis and superficial part of the dermis were carefully removed. Precollectors situated in the dermal layer and lymph collecting vessels situated in the subcutaneous tissue were identified using blue ink and the oxygen bubbles absorbed into the lymph channels from the hydrogen peroxide. We used special finely stretched glass needles for cannulating the lymphatic vessels smaller than 0.3 mm and 30-gauge needles for the larger vessels.²³

The injection mixture consisted of 3 g of orange lead oxide, 0.5 g of powdered milk, and 20 ml of hot water (40°C). The lead oxide and milk powder were ground well using an agate mortar and pestle before adding hot water. A micromanipulator was used for the cannulation. The injection was begun gently by hand with a 1-ml syringe commencing in the index fingertip. Resistance in the syringe or leakage from the vessel at the injection point indicated the end of the injection. At this point, an unusual phenomenon occurred that is explained later. A blush of orange lead oxide was seen in the skin on the front of the forearm during injection into the finger (Fig. 6). The procedure was repeated for all the lymphatic vessels as they were identified in the hand and traced proximally up the forearm and arm. It is to be noted that the injectant sometimes stopped at an interval lymph node. When this occurred, hydrogen peroxide was injected directly into the lymph node so that the efferent lymph vessel could be identified and the injection continued. Injections were repeated until the injectant reached the subclavian vein. Subsequently, radiolucent venous injections using a mixture of blue color ink and gelatin were performed to compare the course of the veins with those of the lymphatic vessels.

The limb was radiographed and then an axial lateral incision line parallel with and close to the cephalic vein that avoided cutting the lymph vessels was made and the bones were removed. The specimen, including skin, deep fascia, and muscles, was spread on a board and radiographed (65 kV; 0.03 S; distance, 150 cm) (Figs. 2 and 3). A meticulous dissection was undertaken to obtain an accurate three-dimensional structure of the lymphatics and their relationship to the veins and the deep fascia. This involved a tedious, painstaking removal of epidermis, dermis, and fat globules from around and between the precollecting and



Fig. 2. Radiographs of the skin and soft tissues of the normal left upper limb (*right*) and abnormal right upper limb (*left*), including the deep fascia and muscles, for comparison. The integument has been split along the lateral border of the limb and unwrapped. Note that the number of lymph vessels was less in the abnormal right arm, especially above the elbow, and that there are still some lymph nodes in the axilla on this side following clearance (*arrows*).

collecting lymph channels. This method was repeated on the left arm (Fig. 4).

The radiographic images were scanned, the lymphatic vessels traced, and the channels color coded in relation to the deep fascia (Fig. 3). Finally, the lymphatic channels from the normal left upper limb were traced retrogradely from each regional lymph node and color coded to determine their territories (Fig. 5). Each upper limb required 5 weeks for injections and dissections to be completed.

RESULTS

Normal Left Upper Limb

The lymphatics of the digits were found to begin as a horizontal network of precollectors in the dermis and subdermal region. Valves were found at the junction between precollectors and the lymph collecting vessels that prevented backflow (Fig. 1). One to three lymph collecting vessels were found running beside the neurovascular bundle on each side of the finger.^{23,24} Once the vessels reached the web space, they changed their course toward the dorsal side of the hand. Thereafter, they repeatedly converged and diverged to interconnect, gradually changing their course toward the medial side of the upper arm above the level of the elbow joint. The diameter of the vessels remained uniform. We found the superficial lymphatic system to consist of a wavy network that often paralleled the cephalic and basilic veins, and the most superficial lymph vessels flowed into the regional lymph nodes in the armpit (Figs. 2 and 3, *right*). However, the lymph vessels that arose from the middle and ring fingers in the third web space coursed beside the cephalic vein on the lateral side of the forearm and arm. They did not head toward the medial side of the arm, as seen in previous studies,²⁴ but converged below the elbow to pass as a single vessel through three interval lymph nodes in the proximal arm (Figs. 3, right and 5). This vessel then bypassed the axillary lymph nodes and went straight to the subclavian vein.

No connections were found between the superficial and deep lymphatics in the hand and forearm when the former vessels were injected. The connections between the superficial and the deep lymphatic system were found only above the elbow along the basilic vein. Lymph vessels that arose from the remaining sides of the middle, ring, and little fingers ran posteriorly along the side of the forearm. When they passed above the elbow joint, they took a short turn toward the basilic vein and pierced the deep fascia to form a single channel. This deep lymph vessel followed the basilic vein beneath the deep fascia. It passed through two interval lymph nodes before reaching the regional lymph nodes in the axilla.

We found a second deep lymph vessel running under the deep fascia in the forearm. The vessel was found near the wrist joint, but its origin was unknown. It coursed beside the radial artery and passed through several interval lymph nodes before reaching a lymph node in the axilla (Fig. 3). In this specimen, we could not find lymph vessels around the ulnar artery. The significant difference between the superficial and deep lymph vessels was that the former vessels went straight to the regional lymph nodes in the axilla, whereas the latter first passed through several interval lymph nodes before reaching the armpit. Thereafter, lymph vessels passed through several lymph nodes before merging into one vessel to reach the subclavian vein (Fig. 5).

Abnormal Right Upper Limb

Initially, the pattern of the lymph collecting vessels in the distal third of the finger was similar to the pattern in the left hand. Thereafter, their pathways were interrupted and diverted at frequent intervals because of segments of blocked lymph channels, subsequently found to be caused by fibrosis, narrowing, and blockage of these channels (Figs. 2 through 4, 6, and 7).

In the index and middle fingers, because of obstruction, the lymph collecting vessels that ran



Fig. 3. Tracing of lymphatics of the abnormal right limb (*left*) and the normal left limb (*right*) with regard to the depth of each vessel. The lead oxide backflow from the collecting lymphatic channels to the precollectors (*orange*) can only be seen in the abnormal right upper limb. Note in the abnormal limb that the lymphatic flow has been diverted into the deep system above the elbow, that interval nodes are prominent in this region, and that some nodes still exist in the axilla.



Fig. 4. Comparison of the dorsal side of both hands after the lead oxide injection. The left hand (*right*) revealed a normal appearance of lymph vessels (*orange*). On the right hand (*left*), however, not many lymph vessels could be found. Note the unusual vessel (*arrows*) traversing the hand.



Fig. 5. Tracing of lymphatics distally from each regional lymph node, color coded to define their territories in the normal left upper limb (compare with Fig. 3, *right*). The color chart shows the hierarchy of lymph vessels draining the third web space. Note that the orange vessel bypasses the axillary lymph nodes and that one sentry node (*gray*) drains the largest area.

along their contiguous sides did not drain through the second web space to the dorsum of the hand. Instead, their pathways were diverted across the back of each finger to their opposite sides by backflow through precollectors in the dermis (Figs. 2 and 3, *left*). From the ulnar side of the index finger, the lymphatic pathway was again diverted through a channel that passed through the second web space to emerge in the palm and course with the palmar metacarpal artery. When the vessel reached the thenar eminence, it was again diverted by reverse flow through a network of precollectors in the dermis and subdermis before reaching collecting vessels at the wrist.

On the dorsum of the hand, few vessels could be found, unlike the left limb. However, a peculiar vessel was seen to connect the lymph vessels transversely (Fig. 4, *left*). An orange stain in the skin in the forearm region, noted previously (see above), was found to be caused by lead oxide backflow into precollectors in the dermis. The radiograph showed clearly the precollector network that connected adjacent lymph collecting vessels (Fig. 6).

On the dorsal side of the forearm, a connection between the superficial and the deep lymphatics was observed. At first, the vessel ran axially but changed its path and coursed deep. It penetrated the deep fascia and ran along the posterior interosseous artery and then reached a small in-

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Fig. 6. (*Above*) An orange stain caused by lead oxide backflow into the dermis was observed in the right forearm region. (*Center*) Higher magnification shows precollectors filled with lead oxide in the dermis. (*Below*) A radiograph of the same area showing that the precollectors (*PC*) connected lymph collecting vessels (*LC*).

terval lymph node near the humeroulnar joint (Figs. 2, *left* and 3, *left*).

In the upper arm, superficial lymph vessels could not be found. Histologic examination



Fig. 7. The results of histologic studies for comparing normal lymph vessels harvested from the normal left arm (*above*) and atrophic lymph vessels harvested from the abnormal right arm (*below*). The image *below* shows that the vessel wall is much thicker than that in the image *above*.

showed the differences between a normal vessel from the left arm and a vessel harvested from the right arm. The vessels from the mastectomy side were encased with a thick fibrous layer (Fig. 7). This observation suggested a chronic inflammatory reaction around the vessel.

Deep lymphatic vessels were found beside the radial and ulnar arteries at the wrist. The vessel that ran along the ulnar artery coursed superficially and became a superficial lymph vessel. The course of the deep vessel beside the radial artery was similar to the lymphatic pathway demonstrated in the left arm. Above the elbow joint, the vessel ran beneath the deep fascia with the basilic vein and passed through several interval lymph nodes before it reached the axilla (Figs. 2, *left* and 3, *left*). Clearly, the interval lymph nodes in the right arm from the mastectomy side were far larger than those from the normal left arm (Fig. 8).



Fig. 8. Images depicting the epitrochlear lymph nodes in the left arm (*above*) and in the right arm (*below*). It is clear that the lymph nodes from the abnormal right arm (*below*) are much larger. The *arrow* indicates the direction of lymphatic flow.

Histologic examination revealed no evidence of cancerous cell metastasis to account for the large size of the interval nodes in the right arm.

DISCUSSION

Although one case study is presented, we were able to compare the lymphatic pathway in the limb on the side of the axillary clearance, which did not develop lymphedema, with the opposite, normal extremity. This study has revealed much information that may lead to a better understanding of the pathogenesis of lymphedema and the spread of secondary cancer deposits.

Lymphatics in the Normal Left Arm

We have investigated 23 upper limb lymphatic studies and published the results from 14 of these studies.²⁴ The results of this left arm from the normal side showed no significant differences from our previous results.



Fig. 9. The lymphatic territories of each sentinel lymph node in the normal left limb, colored to match Figure 5. One lymph node (*gray*) almost covers the entire anterior region. However, the posterior side is divided into several lymph territories.

The color-coded tracing of the lymphatic vessels of the arm is summarized in Figures 5 and 9. All the lymph vessels that ran along the anterior surface of the limb passed into one main (sentry) lymph node (gray). However, lymph vessels that ran along the posterior surface revealed more variety. Some lymph vessels that ran in the midposterior surface drained into a small regional lymph node in the axilla, and lymph vessels that ran beside the cephalic vein bypassed the regional lymph nodes in the axilla.

Lymphatics in the Abnormal Right Arm

Several types of unusual lymph pathways that we had never seen before were identified in this study. We have summarized our findings as schematic diagrams in Figures 10 and 11. These show the sites where these lymphatic pathway changes were observed.

Type A represents backflow to precollectors and the avalvular lymphatic capillaries in the dermis. It is caused by incompetent valves situated between precollectors and lymph collecting vessels similar to that seen in the pathogenesis of varicose veins in the skin. There have been many reports describing this observation under some



Fig. 10. Schematic diagrams showing lymphatic pathway changes after a blockage of the lymph collecting vessel. *Type A*, backflow to precollectors in the dermis; *Type B*, connection between the superficial lymph collecting vessel; *Type C*, connection between the superficial and deep lymph collecting vessel; *Type D*, becoming atrophic; *Type E*, formation of lymphovenous shunt.

pathologic conditions.^{2,7-12,25} In particular, it is apparent in studies of lymphedematous limbs. This seems also to be relevant to in-transit recurrence of skin malignancies, which often deposit in the dermis.

Types B and C describe the opening of a channel between lymph collecting vessels. Type B is a connection between the superficial vessels and type C is a connection between the superficial and deep vessel. Crockett²⁵ reported a collateral route of drainage from an obstructed superficial trunk into an unobstructed deep system using amputated limbs in the case of a Marjolin carcinoma of the lower limb. Malek et al.²⁶ observed these communications using lymphangiography in the lower leg of a patient with lymphedema.

Type D illustrates what happens when lymph vessels become atrophic and disappear in the proximal upper arm. It is these atrophic vessels that we used for histologic examination (Fig. 7). The histologic results show chronic inflammation around lymph vessels, and this is considered to be one of the reasons for lymph vessel blockage. The literature reports^{3,5,7} absence or obstruction of distinct lymphatic channels at different levels after axillary dissection. Espe-



Fig. 11. Radiograph showing the sites in the abnormal right arm where types A, B, C, and D were observed as illustrated in Figure 10.

cially in the case of a patient suffering from lymphedema, very few lymph vessels were found at the wrist. Altorfer et al. reported in their experimental study of dogs that the vessel walls of precollectors and lymph collecting vessels were thickened and sclerosed.²⁷

Type E describes the formation of a lymphovenous shunt in the peripheral region. In our study, this type of communication was not found. However, Aboul-Enein et al. proved the existence of a lymphovenous shunt in a case of a nonedematous postmastectomy arm.¹⁵ They used lymphangiography. Several articles suggest the possibility that lymphovenous shunts form in some pathologic conditions, such as postoperatively, in congenital lymphedema, and in cancer.^{6,13}

There have been no reports about the differences in the size of interval lymph nodes. Lymphadenopathy is caused mostly by cancer metastasis or immunologic reaction against inflammation. In this case, the patient had been free from cancer for 11 years; therefore, breast cancer metastasis to the lymph nodes is unlikely. Histologic examination also showed no sign of cancerous cells in those nodes. We propose two reasons for the interval lymph node swelling: (1) inflammatory reaction to the superficial lymph vessels, which were blocked by the axillary dissection; and (2) work hypertrophy in compensation for ablated lymph nodes in the axillary region.

That the right arm was not lymphedematous appears to be attributable to (1) patency of the deep lymphatic system together with some residual axillary lymph nodes that had not been removed at the original gland dissection; (2) unusual communication between the superficial and deep lymphatic system; and (3) cross-connections between superficial collecting lymph channels facilitated by reverse flow through precollectors, whose valves have become incompetent, and lymphatic capillaries in the dermis, which have no valves.²⁸ Goffrini et al.,⁴ using lymphangiography, studied the cases of 63 radical mastectomy patients that lacked swelling of the arm. They demonstrated the regeneration of an axillary lymphatic network anastomosing the severed arm lymph channels as a fourth pathway. We described also an intact deep lymphatic pathway from the upper limb to the subclavian vein in the abnormal arm. However, our results do not confirm that the pathway regenerated but rather that it was preserved.

In recent years, the sentinel lymph node biopsy technique offers less morbidity to breast cancer and melanoma patients. However, we have little knowledge of lymphatic structure changes after surgical treatment. We need more studies to confirm our findings of lymph network changes in the postoperative cadaver following axillary dissection and especially to obtain further comparative studies of the upper limb with and without lymphedema.

CONCLUSIONS

We had a rare opportunity to investigate the lymphatic system of both upper limbs harvested from a cadaver after unilateral mastectomy and axillary gland clearance. In the normal left arm, there was no communication seen between the superficial and deep lymphatics except in the epitrochlear region. However, the lymphatic pathways of the right arm on the mastectomy side showed significant differences: obliteration of superficial lymph vessels, dermal backflow, unusual communication between the superficial and deep lymphatics, and interval lymph node enlargement. These changes seem to facilitate lymph drainage after sporadic blockage of the lymph tract, especially proximal in the limb. We hope this study provides further information about the

cause of lymphedema and recurrence of malignant skin tumors after primary surgery.

> *Hiroo Suami, M.D., Ph.D.* The Jack Brockhoff Reconstructive Plastic Surgery Research Unit, E533 Medical Building Department of Anatomy and Cell Biology University of Melbourne Grattan Street Parkville 3050, Victoria, Australia hsuami@unimelb.edu.au

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DISCLOSURE

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this article.

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