

Anatomy and Physiology of Lymphatics

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It is important to understand lymphatic system to treatment of lymphedema, and to provide basic and precise knowledge of the anatomy and physiology of the lymphatic system. Review articles and textbooks about lymphatic system, lymphedema, and vascular problems. The lymphatic system consists of lymphatic vessel and lymphatic organ. Lymphatic vessel is consisted of lymph capillary, precollector, collector, and lymphatic trunk. Lymphatic organ is made up of primary organ such as thymus and secondary as lymph node, spleen, tonsil, and lymph follicles. The lymphatic system has many functions including body fluid homeostasis, immune surveillance, and lipid absorption. Knowledge of the normal anatomy and physiology of lymphatics is important to treat and investigate lymphedema.

Key Words: Anatomy • Physiology • Lymphatics • Lymphedema

INTRODUCTION

Lymphatic or lymph vessels constitute a lot of vessels of the whole body and they are potentially larger in size than capillary. Lymphatics vessels are two types: smaller, non-contractile initial lymphatics and larger contractile lymphatics such as collectors and trunks.

Lymphatic system is related to drain materials from the interstitial tissue spaces. Large molecules like protein included this category. Bacterial and other micro-organisms are channelled through lymphatics, presumably as a protective mechanism to prevent waste materials to the blood stream. Cellulitis is frequently recurred in lymphedema patients because the failure of filtering role. Lymphatics serve as a conduit to drain excess interstitial fluid, which role of the lymphatic acts as a buffer against fluid overload.

LYMPHATIC VESSEL STRUCTURAL ANATOMY

Healthy lymphatics provide a unidirectional, blind-

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ended conduit of fluid from the interstitial tissue to the central venous circulation. The initial lymphatics are in direct contact with the intercellular tissue, and there fluid acquires entry into the lymphatics vessel. The fluid from interstitial tissue is lymph, which enter into lymphatic endothelial-lined cavity of the initial lymphatics-lymphatic capillaries. Alitalo [1] reported that the caliber of lymphatic capillary is 10-30 μm . Lymphatic capillaries are consisted of inconsecutive basement membrane and smooth muscle cells. And the initiation of lymph drainage to next lymphatic system is dependent on the elastic fibers of the extracellular matrix to initiate lymph drainage. Baluk et al. [2] reported that the specialized lymphatic endothelial cells have a distinct oak-leaf shape adorned by unique button-like junctions that characterize these the interfaces among cells and comprise the flap-like portals of entry into the lymphatic capillary. Tal et al. [3] reported that large potential openings facilitate the entry of immune cells and larger structures into the lymph. Pericytes are absent from these circulatory conduits. The endothelial cells of the initial lymphatics are attached to the collagen fibers of the extracellular matrix through specialized anchoring filaments. The elastic fibers of the extracellular matrix are very important role for fluid transit to lymphatics, because of absent basement membranes and smooth muscle cells.

Baluk et al. [2,4] reported that stream of lymph from the lymphatic capillary flow to precollectors. Precollec-

tor has a little of smooth muscle cells, and its caliber is 100 μm . Some portion has valve, which through lymph pass to prefascial collector, and prevent backflow to lymphatic capillary. The precollectors coalesce into collecting ducts with vasomotor activity. The collecting ducts have thick walls, 100-600 μm , but continue to demonstrate the monolayer of endothelial cells that surrounds the lumen. Dejana et al. [5,6] described that the transition to the collecting vessels, located deeper within the dermis, is demarcated by the presence of a distinct periendothelial smooth muscle cell layer with the intima and media in axial and oblique configuration, a basement membrane, continuous interendothelial junctions and regularly, recurrent, intraluminal bi-leaflet valvular structures. The latter separate the lymphatic collecting vessel into distinct functional units called lymphangions, which small functional unit of lymphatics. Eisenhoffer et al. [7] described that the length of lymphangion is 6-20 mm, and superficial collector of upper limb is consisted of sixty to eighty lymphangions, and that of lower limb is of eighty to a hundred. In a healthy lymphatic system, these valvular structures prevent the backflow of lymph.

Lymph trunk has thicker muscle layer than lymph collector, and is consisted of several efferent lymphatics from a group of lymph nodes. Thoracic duct, most large lymph trunk, is consisted of bilateral lumbar and gastrointestinal trunk and drain lymph amount of about 2-4 liters per day to left venous angle.

Skin area is the territory drained to one precollector, and is overlapped near other skin areas. Skin zone is skin areas of several precollectors drained to one superficial collector. Skin territory is skin zones of several collectors, which constitute of lymph bundle. Skin zones are connected with each other through cutaneous lymph network or near collectors. Lymphatic watershed is area of lack of collectors between skin territories.

Transport of lymph is influenced by contraction of lymphangion, active and passive exercise of body, arterial pulsation, muscle contraction, massage, and breathing. Lymph is actively transported by contraction of lymphangion, and active and passive exercise of body is helpful to transport of lymph by compression of lymphatic vessels.

The drainage interruption may occur by the injury of a part of collectors or removal of local lymph nodes. After injury of lymphatic vessels, the function of drainage can be recovered by transport from edema area to contiguity area through lymphatic capillary plexus, transition to adjacent collectors through fascial plexus,

transportation to deep lymphatic collectors through perforating vessel, derma backflow from precollectors to lymphatic capillary plexus, and new lymphatic vessel formation.

1. Lymph nodes

Lymph nodes are small, bean-shaped organs that filter lymph. Lymph nodes vary in size but are usually less than 2.5 cm (1 inch) across. There are many lymph nodes throughout the body. The number of lymph nodes varies from one part of the body to another. Lymph nodes filter biologically the hazardous material of interstitial tissue into blood stream, create lymphocytes related to immune response, and control the density of proteins in lymph. Lymph enters into lymph node through afferent vessel and drain out through efferent vessel. If a large number of materials are filtered through a lymph node or group of nodes, they may swell and become tender to the touch.

2. Regional lymph node and lymphatic drainage

1) Head

Lymphatic drainage of head is divided to superficial and deep lymph node. Superficial lymph nodes are scattered whole head, and deep lymph nodes are in lingual and retropharyngeal area.

Superficial occipital lymph node is near greater occipital nerve and artery. Deep occipital lymph node is on obliquus capitis superior which connected with superficial occipital lymph node. Mastoid lymph node related to retroauricular and parietal skin area. Superficial parotid lymph node is on superficial surface of parotid gland and divided to infraauricular and preauricular lymph nodes. Deep parotid lymph node is within parotid gland, around which facial nerve passed. Submandibular lymph node is on submandibular triangle, and submental lymph node is on submental triangle. Lingual lymph node is around genioglossal area, retropharyngeal lymph node is between pharynxes and atlas.

2) Neck

Anterior cervical lymph node is divided to superficial and deep anterior cervical lymph nodes. These are connected with lymphatic stream of head

3) Chest

Lymph node on chest divided to parietal lymph node and visceral lymph node in mediastinum.

Parietal lymph node

Intercostal lymph node and juxtavertebral lymph node are alternative if cisterna chyli or thoracic duct are not developed. Supraphrenic lymph node is between pericardium and xiphoid process, lateral pericardiac lymph node is conduit of bronchial cancer to diaphragm. Parasternal lymph node is between sternum and ribs.

Visceral lymph node

Brachiocephalic angle lymph node is drained from thyroid and larynx. Cardiac lymph node is inside of phrenic nerve. Botallo's lymph node is around Botallo's ligament. Retropulmonary lymph node is named pulmonary hilar and interlobar lymph nodes according to location. Extrapulmonary lymph node absorb lymph from retropulmonary lymph node, drain to chest lymph nodes. Posterior mediastinal lymph nodes are around bronchial division area, esophagus area, between esophagus and aorta, and retro-aortic area.

4) Upper limb

Axillary lymph nodes are related to drainage of upper limb, shoulder, and supra-umbilical area. Usually there are 10-12, and 0.1-8 cm sized.

Lateral axillary lymph node is located according to axillary vein. They absorb lymph from superficial and deep collectotrs of upper limb and drained to central, subscapular, subclavicular, and supraclavicular lymph nodes. Subscapular lymph node is around subscapular and thoracodorsal nerves. Central lymph node is large and located around intercostobrachial nerve. Pectoral lymph node is 1st thing that happened metastasis of breast cancer. Infraclavicular lymph node gets lymph from all axillary lymph node and chest muscles, breast glands, and deltoid muscle. Drainage of lymph of this node connected to supraclavicular lymph node and lymphatic duct of right side, and vein of left side. Interpectoral lymph node absorbs lymph from breast glands and drain to sub-pectoral and infraclavicular lymph nodes. Lymphatic drainage of upper limb is divided superficial and deep area. Deep area is drained according to vessels, and superficial area is divided several areas. Radial, ulnar, and middle areas are in forearm, and central,

dorsomedial, and dorsolateral areas in upper arm.

5) Lower limb

Superficial inguinal lymph nodes are located on femoral triangle according to great saphenous nerve, and drainage of infra-umbilical area, external genitalia, buttock, and peritoneum.

Superficial inguinal lymph node is related to back, lateral abdomen, upper buttock, and external genitalia. Superomedial inguinal lymph node and inferomedial inguinal lymph nodes get lymph from external genitalia. Inferolateral lymph node is related to drainage of lower limb, and presaphenous or central lymph node exist in just 15% of people.

Deep inguinal lymph node is related to muscle, joint, internal genitalia, and superficial inguinal lymph nodes and drain to external iliac lymph nodes.

Popliteal lymph nodes are divided to superficial and deep area, and related to deep tissue below knee.

Drainage area is divided to ventromedial, dorsolateral territory, and dorsolateral territory of thigh, dorsomedial territory of thigh. When ventromedial territory is injured, edema of lower limb may occur.

PHYSIOLOGY OF LYMPHATIC FUNCTION

Lymph differs very little from interstitial fluid, and the process of lymph drainage starts at the point of net plasma filtration from the blood stream. From there three independent steps occur. Transport of fluid and other materials (prelymph) across the interstitial space and into initial lymphatics, movement of lymph through the network of non-contractile initial lymphatics, and active pumping of lymph through the series of contractile collecting trunks. Interstitial fluid becomes lymph upon entry into the initial lymphatics. Rockson [8] reported that the protein content of lymph is various according to lymphatic organs. The interstitial fluid protein concentration of most of body is approximately 2 g/dL, but 3-4 g/dL in mesenteric lymph, and 3-5 g/dL in central lymph of the thoracic duct.

Aukland and Reed [9] explained that interstitial fluid pressure is important to enter in and drain out of interstitial fluid into the lymphatic capillary, and it is subatmospheric in the steady state. Zawieja [10-13] reported that when interstitial pressure is slightly higher than atmospheric pressure, lymph drain to lymphatic capillary maximally. Therefore Lymph flow is partly dependent on dynamic interstitial pressure gradient. Olszewski

[14] reported that systemic driving forces dependent on intrinsic, rhythmic contraction of the lymphangions is another factor influenced on lymph flow. Zawieja et al. [10,15-18] reported that the lymphatic muscle cells influence intrinsically on lymph flow by rapid, coordinated contractions. These contractions produce a decrease in lymphatic compliance, an increase in the local lymph pressure, and the ejection of lymph into the next lymphangion. And by electrical pacemaker located within the muscle layer of the lymphatic wall, next contractions are started.

Sjoberg and Steen S [19-25] reported that the physical and humoral factors affect the rate and amplitude of the intrinsic contractions, and the rate of lymph transport substantially altered. Lymphatic contractility and flow will enhance in response to tissue edema, positional increases in hydrostatic pressure, exercise, massage and pneumatic compression, and temperature changes.

LYMPHATIC ORGANS

There is lymphatic vasculature distributed in the whole body and within each tissue and organ except of the central nervous system. Lymphatic system is comprised of both conduits and lymphoid cells within organized lymphoid tissues. Olszewski [26] reported that lymphoid tissue includes the lymph nodes, the spleen and thymus, the intestinal Peyer's patches, and the lymphoid tissue that is present in lungs, liver, and bone marrow. Lymphatic organ is divided primary and secondary lymphatic organ. Primary lymphatic organ is related to creation, maturation, and selection of immune cells. Especially, T- , and B- lymphocytes mature in Thymus and red bone marrow, respectively. The lymphocytes acquired immune function reside in secondary lymphatic organ, where antigen transport, cell proliferation, antibody formation are occurred. Spleen, lymph nodes, mucosa associated lymphatic tissue (MALT), bronchus associated lymphatic tissue (BALT), gut associated lymphatic tissue (GALT), Peyer's patch, and vermiform appendix.

Lymphatic organs of direct contact with the external environment, such as the skin, gastrointestinal tract, and lungs, are the protective function of the lymphatics against hazardous. Dietary fat is absorbed through lymphatic uptake of chylomicrons from the intestine, with transport of the chylous lymph to the liver. Szuba et al. [27] reported that the lymphatic system also transports macromolecules and obligate fluid, metabolic waste, and cellular debris from the interstitium to the systemic

circulation.

The lymphatic system is a very important organ and also complex organ system responsible for fluid homeostasis, immune surveillance, and lipid absorption. Knowledge of the anatomy about lymphatic channels and lymph nodes and the physiology of their interaction with the extracellular environment and the venous vascular system provides precious basis of lymphedema treatment and investigation.

Conflicts of Interest

All authors declare no conflicts of interest.

REFERENCES

1. Alitalo K. The lymphatic vasculature in disease. *Nat Med* 2011;17:1371-1380.
2. Baluk P, Fuxe J, Hashizume H, Romano T, Lashnits E, Butz S, et al. Functionally specialized junctions between endothelial cells of lymphatic vessels. *J Exp Med* 2007;204: 2349-2362.
3. Tal O, Lim HY, Gurevich I, Milo I, Shipony Z, Ng LG, et al. DC mobilization from the skin requires docking to immobilized CCL21 on lymphatic endothelium and intralymphatic crawling. *J Exp Med* 2011;208:2141-2153.
4. Schulte-Merker S, Sabine A, Petrova TV. Lymphatic vascular morphogenesis in development, physiology, and disease. *J Cell Biol* 2011;193:607-618.
5. Dejana E, Tournier-Lasserre E, Weinstein BM. The control of vascular integrity by endothelial cell junctions: molecular basis and pathological implications. *Dev Cell* 2009;16:209-221.
6. Norrmén C, Tammela T, Petrova TV, Alitalo K. Biological basis of therapeutic lymphangiogenesis. *Circulation* 2011; 123:1335-1351.
7. Eisenhoffer J, Kagal A, Klein T, Johnston MG. Importance of valves and lymphangion contractions in determining pressure gradients in isolated lymphatics exposed to elevations in outflow pressure. *Microvasc Res* 1995;49:97-110.
8. Rockson SG. Physiology, Pathophysiology, and Lymphodynamics: General Overview. In: Lee B, Bergan J, Rockson S, editors. *Lymphedema: A Concise Compendium of Theory and Practice*. London: Springer; 2011. p. 59-61.
9. Aukland K, Reed RK. Interstitial-lymphatic mechanisms in the control of extracellular fluid volume. *Physiol Rev* 1993;73:1-78.
10. Zawieja DC. Contractile physiology of lymphatics. *Lymphat Res Biol* 2009;7:87-96.
11. Negrini D, Moriondo A, Mukenge S. Transmural pressure during cardiogenic oscillations in rodent diaphragmatic

- lymphatic vessels. *Lymphat Res Biol* 2004;2:69-81.
12. Moriondo A, Mukenge S, Negrini D. Transmural pressure in rat initial subpleural lymphatics during spontaneous or mechanical ventilation. *Am J Physiol Heart Circ Physiol* 2005;289:H263-269.
13. Grimaldi A, Moriondo A, Sciacca L, Guidali ML, Tettamanti G, Negrini D. Functional arrangement of rat diaphragmatic initial lymphatic network. *Am J Physiol Heart Circ Physiol* 2006;291:H876-885.
14. Olszewski W. Contractility patterns of normal and pathologically changed human lymphatics. *Ann N Y Acad Sc* 2002; 979:52-63; discussion 76-79.
15. Zawieja DC, Davis KL, Schuster R, Hinds WM, Granger HJ. Distribution, propagation, and coordination of contractile activity in lymphatics. *Am J Physiol* 1993;264:H1283-1291.
16. Van Helden DF. Pacemaker potentials in lymphatic smooth muscle of the guinea-pig mesentery. *J Physiol* 1993;471: 465-479.
17. von der Weid PY, Crowe MJ, Van Helden DF. Endothelium-dependent modulation of pacemaking in lymphatic vessels of the guinea-pig mesentery. *J Physiol* 1996;493:563-575.
18. Toland HM, McCloskey KD, Thornbury KD, McHale NG, Hollywood MA. Ca (2+)-activated Cl (-) current in sheep lymphatic smooth muscle. *Am J Physiol Cell Physiol* 2000; 279:C1327-1335.
19. Sjoberg T, Steen S. Contractile properties of lymphatics from the human lower leg. *Lymphology* 1991;24:16-21.
20. Brautigam P, Vanscheidt W, Foldi E, Krause T, Moser E. Involvement of the lymphatic system in primary non-lymphogenic edema of the leg. Studies with 2-compartment lymphoscintigraphy. *Hautarzt* 1997;48:556-567.
21. Suga K, Uchisako H, Nakanishi T, Utsumi H, Yamada N, Oohara M, et al. Lymphoscintigraphic assessment of leg oedema following arterial reconstruction using a load produced by standing. *Nucl Med Commun* 1991;12:907-917.
22. Olszewski WL, Engeset A. Intrinsic contractility of prenodal lymph vessels and lymph flow in human leg. *Am J Physiol* 1980;239:H775-783.
23. McGeown JG, McHale NG, Thornbury KD. The role of external compression and movement in lymph propulsion in the sheep hind limb. *J Physiol* 1987;387:83-93.
24. Ikomi E, Zweifach BW, Schmid-Schonbein GW. Fluid pressures in the rabbit popliteal afferent lymphatics during passive tissue motion. *Lymphology* 1997;30:13-23.
25. Meeusen R, van der Veen P, Joos E, Roeykens J, Bossuyt A, De Meirleir K. The influence of cold and compression on lymph flow at the ankle. *Clin J Sport Med* 1998;8:266-271.
26. Olszewski W. Lymphology and the lymphatic system. In: Olszewski W, editor. *Lymph Stasis: Pathophysiology, Diagnosis and Treatment*. Boca Raton (FL): CRC Press; 1991. p. 4-12.
27. Szuba A, Shin WS, Strauss HW, Rockson S. The third circulation: radionuclide lymphoscintigraphy in the evaluation of lymphedema. *J Nucl Med* 2003;44:43-57.