

Chapter 1

A General Outline of the Cardiac Lymphatic System

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Abstract The lymphoid system is a collection of freely permeable, thin-walled vessels dispersed throughout the entire body. Lymphatic vessels preserve circulatory homeostasis by clearing blood capillary ultrafiltrate along with excess protein from the interstitium and delivering them back to the venous circulation. Very little is known about the lymphatic system as it relates to the heart, and therefore, the subject is often neglected in textbooks. Many pathological conditions have been linked to obstruction of lymph flow and even, in rare cases, to cardiac lymphoma. The aim of this chapter is to review the anatomy of cardiac lymphatics based on current literature and emphasize the clinical significance of the system.

Keywords Thoracic duct • Lymphatic channels • Lymphatic vessels • Lymph nodes • Lymph drainage • Heart

Introduction

The lymphoid system is a collection of freely permeable, thin-walled vessels dispersed throughout the entire body [1, 2]. The capillary-like lymphatic vessels begin as blind sacs in the interstitial space and have three main functions [1–4]. First, the lymph vessels preserve circulatory homeostasis by clearing blood capillary

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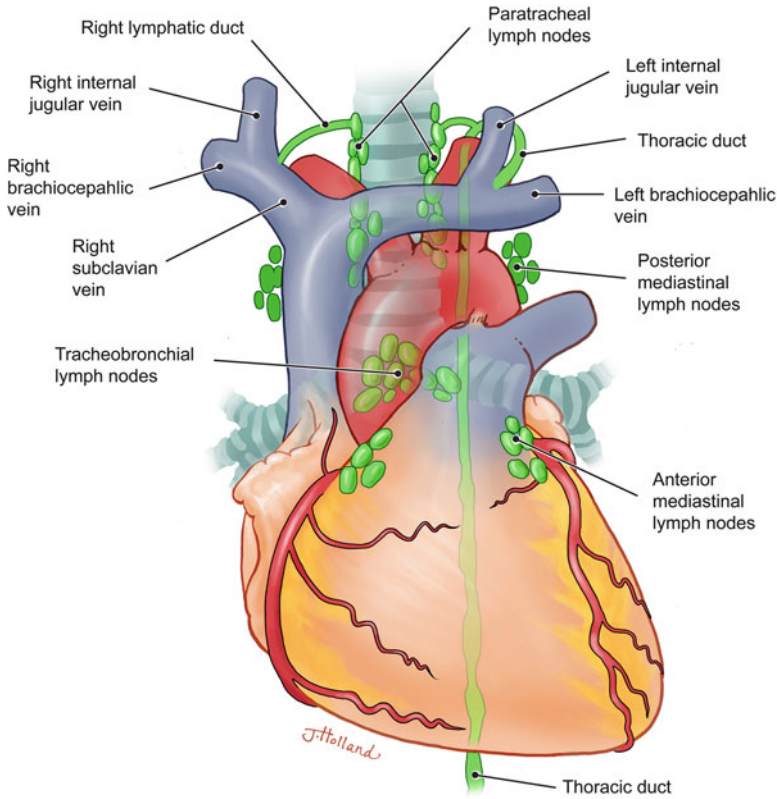


Fig. 1.1 A schematic representation of the lymphatic drainage of the heart

ultrafiltrate along with excess protein within the interstitium and delivering them back to the venous circulation [3, 4]. This clear, protein-rich fluid found in lymphatics is known as lymph [1, 4]. Second, lymphoid tissue in the intestinal tract aids in nutrition by absorbing digested fat [3]. Third, lymph vessels play a primary role in defense. Foreign antigens, bacteria, and lymphocytes found in the interstitium drain with the lymph to regional lymph nodes and trigger activation of the immune system [3]. The diagnosis, prognosis, and treatment of many diseases, not withholding malignancies, require thorough knowledge of lymph circulation and drainage. There are very few studies in the literature on the cardiac lymphatics in particular, and in fact, any mention of cardiac lymph drainage in textbooks is rare. This study focuses on lymphatics as they relate to the heart.

Lymphatics in the heart can be divided into three categories based on their size: minute valveless capillaries, medium lymphatic collecting vessels (usually valveless), and large valved lymphatic trunks [5]. In general, lymph flows from the sub-endocardium outward toward the subepicardial lymphatic plexus [1, 6, 7]. These plexuses feed into larger lymphatic vessels that follow the path of the main coronary

blood vessels in the anterior and posterior interventricular grooves and the coronary sulcus (Fig. 1.1) [1, 5, 7]. Kline [5] observed that these lymphatic vessels within the epicardium resembled white bands. Many pathological conditions have been linked to obstruction of lymph flow and even, in rare cases, to cardiac lymphoma [8–10]. The aim of this chapter is to review the current literature associated with the cardiac lymphatic system, with an emphasis on its clinical significance.

History

Many authors credit Rudbeck as the first researcher to bring attention to the lymphatics in the heart [11, 12]. In 1653, Rudbeck [13] described the subepicardial lymph vessels of a dog, as reported by Patek [12]. The heart of a dog is often used as a surrogate model for the human heart when studying lymphatics because the two are nearly identical in anatomy [14]. Since Rudbeck, several anatomists have studied these lymphatics in more detail. According to Bradham et al. [15], Nuck discovered several decades later that mercury could be introduced directly into the cardiac lymph vessels. In 1924, Aagaard [16] discovered lymphatic plexuses in the subendocardial, myocardial, and subepicardial tissue layers after injecting dye into the heart muscle. In 1939, Patek [12] substantiated this finding using India ink. Patek [12] observed that lymph is drained outward in valveless channels from the subendocardial plexus through to the myocardial plexus and subepicardial plexuses and is finally collected into a large single trunk draining the entirety of the heart [12]. The following year, Drinker et al. [17] cannulated a major efferent lymphatic trunk to measure the flow, pressure, and composition of lymph leaving the heart.

Since 1940, several studies have confirmed these preceding basic anatomical findings. In 1966, Johnson and Blake [18] utilized hydrogen peroxide to distend the lumens of the cardiac lymphatic vessels and blood capillaries in an effort to investigate morphological differences, and in the process they demonstrated a vast network of subendocardial and subepicardial lymphatics [18]. In a study involving mongrel dogs, Bradham et al. [15] confirmed that a vast network of lymphatics is ubiquitous in the ventricular myocardium, even more so on the left side (Fig. 1.2). In 1982, Miller [19] outlined the path of cardiac lymph drainage from the major collecting trunks to the mediastinal lymph nodes, with the lymph finally emptying into the thoracic duct.

Embryological Studies

With his study of embryos and fetuses of humans, Kampmeier [20] utilized vital dye to show that lymph vessels of the heart originated from two plexuses. The first plexus began in the right ventricle, followed the right coronary artery proximally, ascended between the aorta and pulmonary trunk, and finally drained into the

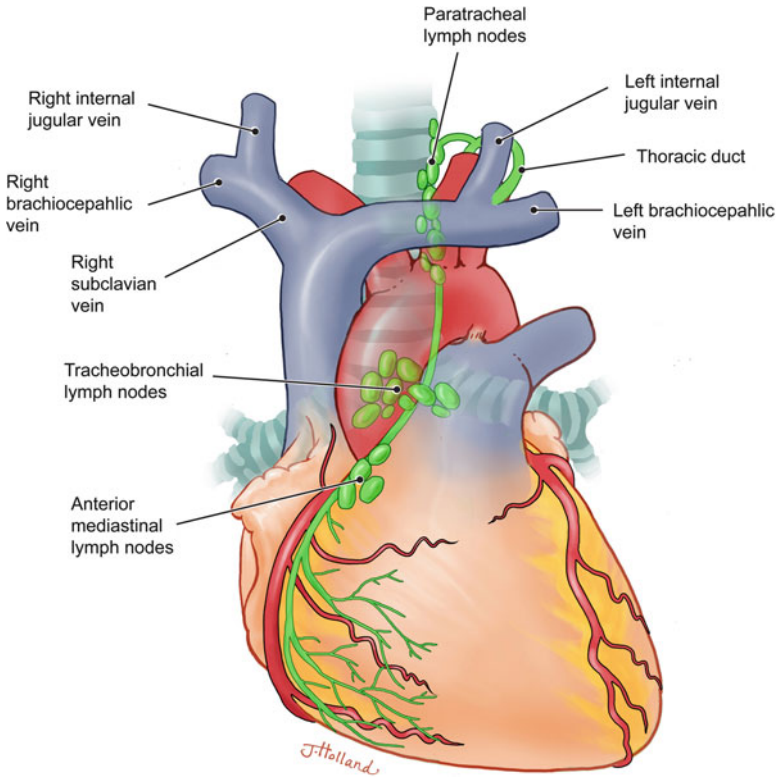


Fig. 1.2 A schematic representation of the right lymphatic drainage of the heart

upper thoracic duct adjacent to the left jugular lymph sac. The second plexus was observed to originate in the left ventricle, course proximally along with the left coronary artery, and drained into the right jugular sac (deriving from the pretracheal plexus) [20]. Kampmeier [20] inferred that these discrete efferent lymphatic paths persisted in adults. However, Feola et al. [21] disagreed with this conclusion. In their study, seven out of nine cadaveric specimens exhibited the left and right major lymphatic trunks unifying as one main lymphatic vessel superior to the heart [21]. In one of the earliest studies on lymphatic origin, Cash [22] demonstrated in embryo pigs that there is initially one large lymphatic plexus covering the entire surface of the heart, with vessels penetrating and networking deeper during late development.

In animal studies, the atrioventricular (AV) valves of both adult dogs and puppies have been observed to have lymphatic capillaries [23]. The capillaries visualized in the adults were more developed, which supported the theory that lymphatic vessels of the heart continue to develop into adulthood [23]. In contrast, human cardiac lymphatics have been demonstrated to conclude development in early stages of fetal growth [24].

The Subendocardial Plexus

As stated above, the network of lymphatic vessels in the subendocardium are extensive [18]. Uhley et al. [25] observed the branches of these vessels crossing at myriad angles. It has been reported that small lymphatic capillary systems, such as the subendocardial plexus, originate from the blood endothelium and basement membrane and are observed as sizeable dilatations [26]. Lupinski [26] approximated that 1,300 blood capillaries drain into each lymphatic capillary. As discussed, lymph flow in the heart progresses outward from the subendocardial plexus to the myocardial plexus [12]. Lupinski [26] opined that there is no clinical significance to this pattern of outward flow.

Myocardial Plexus

Studies detailing the myocardial plexus are scarce. Anatomy and pathology textbooks forego the topic all together [27], or else only note that they exist [1]. Nevertheless, Bullon and Huth [28] described the intricate anatomy of lymphatic vessels in the myocardium. They found that myocardial lymphatic capillaries were sparse compared to blood capillaries, and it was noted that a continuous basal membrane was absent [28]. Bullon and Huth [28] suggested these lymphatics possessed the ability to adjust immediately to an increased functional load as a result of the multitude of cellular junctions encompassing the vessels. In addition to blood capillaries, Bullon and Huth [28] reported that the basement membranes of nerves, fibrocytes, and myocytes were in direct contact with the adjacent myocardial lymphatic vessels.

Recent research by Lupinski [26] has expanded on prior knowledge of the myocardial lymphatic plexus. He described the numerous lymphatic capillaries as “basket-like” and confirmed they are positioned adjacent to blood capillaries in the interstitium [26]. Lymph from the myocardial plexus collects into channels, which drains to the subepicardial plexus via channels in the connective tissue septum [26].

Subepicardial Plexus

Patek [12] discovered the subepicardial plexus network of lymphatic capillaries, with accompanying collecting channels between the myocardial and epicardial muscle layers, by injecting India ink into the subepicardium. According to Patek [12], lymphatics can be classified into five types that are determined by the region being drained. The first type includes all of the lymphatics initially flowing into the capillary plexuses, and the second type involves the lymphatic vessels that make up the capillary plexus. As the diameter of the lymphatic collecting vessels increase,

the type numbers increase correspondingly with type five being the largest lymphatic trunk [12]. Patek's [12] results were substantiated by Johnson and Blake [18], in humans, as well as in other species. In addition, Johnson and Blake [18] observed the efferent lymphatic vessels flowing into larger lymphatic trunks in the AV grooves and finally emptying within the main lymphatic collecting trunk of the heart. More recent studies also support their findings [26].

Pericardial Lymphatics

Prior to 1977, the consensus was that the right lymphatic duct drained the majority of cardiac lymph. However, Leeds et al. [29] observed multiple pathways of lymphatic drainage from the parietal pericardium into both the right and thoracic lymphatic ducts of canines using radiolabeled lymph. Following the canine pericardial lymph drain more proximally, Miller et al. [30] showed the lymphatic ducts emptying into the left and right upper mediastinal nodes and further to the parasternal internal thoracic chain of lymphatics bilaterally.

In humans, lymph in the pericardial space has been shown to drain by several different pathways [31]. Anteriorly, lymph from the upper aspect drained toward the phrenic neurovascular bundle, turned superiorly to the brachiocephalic veins, and ultimately emptied into both anterior mediastinal lymph nodes (Fig. 1.1). Lymph from lower regions either drained toward the phrenic neurovascular bundle and then moved inferiorly to enter the diaphragm or coursed ventrally, entering the prepericardial lymph nodes at the juncture between the diaphragm and pericardium. Laterally, lymph from the upper aspect of the pericardium mostly flowed superiorly into the peribronchial and tracheobronchial lymph nodes. The lower part mirrored that of the anterior pericardial space. A posterior part of the lateral pericardium drained to a chain of lymph nodes ventral to the esophagus and dorsal to the inferior vena cava. Lymphatics from the posterior pericardium, including the cupula, ultimately drained superiorly to the tracheobronchial lymph nodes. Finally, lymph from the diaphragmatic pericardium followed several different pathways. The right side drained into the right pericardial lymph node, the ventral aspect into the prepericardial nodes, and the central aspect into the posterior mediastinal or tracheobronchial lymph nodes (Figs. 1.2 and 1.3) [31]. In addition, Eliskova et al. [31] observed a second layer of lymphatics within the adipose and areolar tissues.

Lymphatics of the Cardiac Valves

The presence of lymphatics within AV valves is a point of contention [32]. However, Miller et al. [33] demonstrated lymphatic vessels in the valves of live canines. In 1988, Noguchi et al. [23] utilized various methods, including light and electron microscopy, to substantiate this finding. Within the atrial region of the leaflets of all

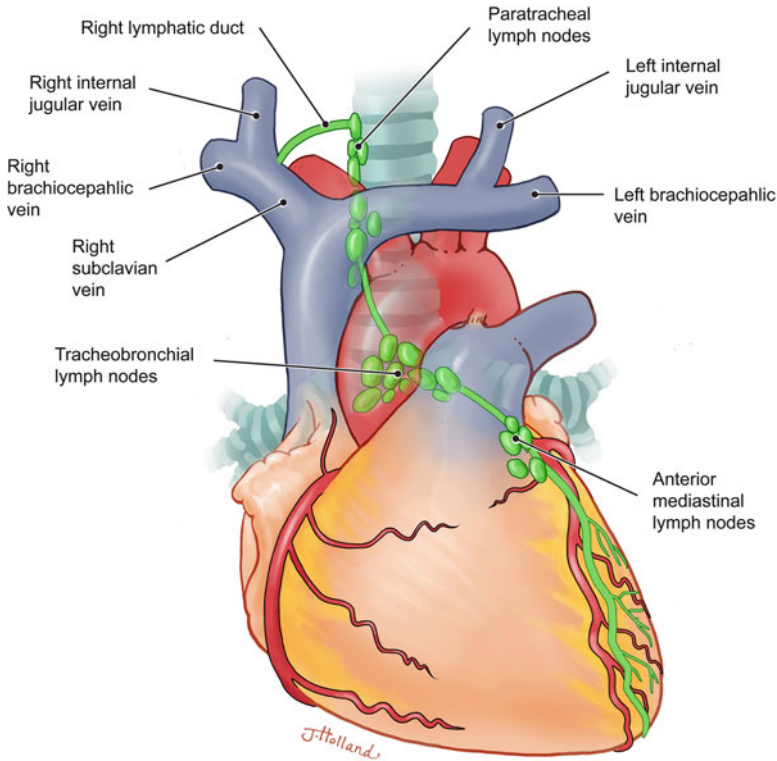


Fig. 1.3 A schematic representation of the left lymphatic drainage of the heart

the valves, especially the mitral valve, they discovered subendocardial lymph-filled capillaries. Noguchi et al. [23] found the majority of the lymphatic vessels of the leaflets were more proximal, diminishing as they approached the free border. The following year, Ichikawa et al. [34] observed the lymphatic vessels originating as a single endothelial cell projecting into the chordae tendineae from the papillary muscles. Miller et al. [33] suggested that it is highly probable that the pathways of lymphatics of the AV valves are connected with the corresponding aortic and pulmonary valves.

Right-Sided Cardiac Lymphatic Pathways

Riquet and Hidden [35] investigated lymphatics of the right atrium and ventricle in cadaveric specimens. After dye was injected at the right cardiac border, they observed lymph flow to the main right efferent lymphatic collecting vessel and continue superiorly toward the left anterior mediastinal lymphatic chain.

Riquet and Hidden [35] introduced dye within the interventricular groove and observed it drain into the thoracic duct, passing through the right paratracheal lymph nodes on the way. Prior to this study, it was demonstrated that the right subendocardial aspect of the ventricular septum contained the more substantial lymphatic network [36].

Left-Sided Cardiac Lymphatic Pathways

Studying the left side of the heart as well, Riquet and Hidden [37] again utilized dye, this time within the left principal efferent ducts. They demonstrated lymph traversing the pulmonary trunk posteriorly and draining into the right pretracheal lymphatic chain, eluding the left side of the heart. Dye was also reported to enter the right principal collecting trunk on several occasions, but generally, variations of the left side are less frequent than the right [37]. Eliskova et al. [38] found similar results in Macaque monkeys.

Atrial Lymphatics

Previously, many were unable to detect lymph capillaries in the atria. More recent studies utilizing light and electron microscopy have shown scant lymphatics in the subepicardium of atria [39, 40]. Marchetti et al. [40] opined that lymphatic vessels have only been noted in the subepicardium of the atrium as a consequence of its very thin walls.

Ventricular Lymphatics

As one would expect, lymphatic vessels in the ventricles are consistent with the organization of subendocardial, myocardial, and subepicardial plexuses, as noted above [36, 41]. In a study in canines, Uhley and Leeds [42] showed that papillary muscles contained an extensive lymphatic system. Burch et al. [43] suggested that disruption of the lymphatics in papillary muscles would cause derangement of the mitral valvular complex and therefore malfunction of the mitral valve. Uhley and Leeds [42] observed an intricate reticulation of lymph capillaries articulating the surface of both papillary muscles of the mitral valve. In addition, they demonstrated thin spikes of lymphatic vessels projecting down the chordae tendineae [42].

Lymphatics Related to the Cardiac Conduction System

Studies have shown a significant anatomical association of the lymphatic capillaries in the subendocardium with the right bundle branch [25]. Uhley et al. [25] suggested that pathology related to cardiac lymph flow may delay or even block conduction along the fascicle, with an endpoint of fibrosis. Uhley et al. [25] speculated that the AV node region drained lymph from the inferior part of the chambers on the right side of the heart. They proposed that damaged tissue released large amounts of potassium that could reach the AV node in this fashion and disrupt its extracellular environment, which could explain the transient manifestations of AV conduction delays associated with an inferior infarction [25]. Uhley et al. [25] also described an anterior septum infarction leading to potassium-rich lymph draining to the right bundle, delaying conduction and creating the possibility of a complete bundle branch block.

Golab [44] demonstrated that lymph originating in the conduction system drains via the myocardial plexus. He found that most of the lymphatics from the AV node emptied directly into the main left lymphatic trunk and the majority of lymph collected from the sinoatrial node flowed directly into the main right lymphatic trunk [44].

Etiology and Sequelae of Disruption to Cardiac Lymph Flow

As stated above, lymphatics play a key role in clearing protein-rich fluid from the interstitium [3, 4]. Inhibition of lymph flow elsewhere in the body can lead to serious complications, and it is no different in the heart. Disruption of cardiac lymphatics was shown to cause subsequent build up of excess interstitial fluid and proteins [45]. This lymphedema has been found to initiate many pathological processes, such as interstitial fibrosis and pericardial effusion, thus impairing cardiac function [46, 47]. It is important to consider the etiology and sequelae of the obstruction of lymph flow in the heart because they are clinically significant.

The literature supports many different sources of impairment to lymph flow, which could be roughly separated into pathological and iatrogenic origins. We propose the pathological causes could be further divided into three groups: those causing lymph stasis due to decreased myocardial contractility, those causing lymphatic obstruction by compression of the vessels, and those damaging lymphatics through inflammation and fibrosis.

The flow of cardiac lymph is completely dependent on the contractions of the heart [3, 7, 48]. Myocardial ischemia, increased superior vena caval pressure, ventricular fibrillation, and pulmonary artery hypertension have all been shown to decrease cardiac contractility and are associated with compromised cardiac lymph flow [5, 19, 49]. In contrast, Feola et al. [50, 51] noted an increase in lymph flow following acute myocardial ischemia in canines. They suggested cardiac lymphatics

were essential in the reduction of ischemic damage by decreasing interstitial edema and anaerobic tissue metabolites [50, 51]. Cui [52, 53] also supported the benefits of improved cardiac lymph flow ensuing myocardial infarction.

Tumors of the heart have also been shown to disrupt lymph flow by mechanical compression of the vessels. It was reported that metastatic cardiac tumors were a more common cause of mass effect on lymphatics [49]. Primary cardiac tumors, as discussed later, are rare.

Another source of injury to lymphatics is inflammation. Lupinski [54] reported on mediastinal lymph nodes that were damaged after infection, causing blockage of distal lymph flow, and injury to the cardiac lymphatic vessels. The author suggested rheumatic arteritis, endocarditis, syphilis, and tuberculosis as sources of inflammation. On the other hand, the reverse has also been shown to be true. Maurice et al. [55] argued that impaired lymph drainage renders the heart more susceptible to inflammation and infection. Miller [14] provided support to this study and added that cardiac lymphedema predisposed the tissue to fibrosis and fibroelastosis. Several studies, human and animal, have substantiated the idea of lymphatic obstruction initiating a cascade of significant fibroblastic proliferation leading to endocardial and interstitial fibrosis [5, 56–59].

Many have commonly accepted that the mediastinal lymphatics are nonessential with no harmful consequences to their abolition, but the proposed evidence has opposed that theory. Several cardiac surgical procedures, such as valve replacement and cardiac transplant, result in removing or scarring of mediastinal and intrathoracic lymphatic vessels [46]. Lupinski [26] described the destruction of cardiac lymphatic vessels during open-heart surgery as a result of cross-clamping. The ramifications of cardiac lymphatic obstruction have been thoroughly outlined above. Kong et al. [59] suggested lymphatic obstruction is rarely avoidable in cardiac transplantation and that the root of allograft failure was a result of injury to the myocardium from the obstruction. Mehlhorn [48] reported that dysfunction of the left ventricle and myocardial edema after surgery contributed to the compromised lymphatic flow.

Lymphoma of the Heart

Malignant cardiac lymphoma is an infrequent, but significant cause of cardiac lymphatic obstruction. The heart is not often initially involved at the time of diagnosis, but metastases of lymphomas to the heart have been observed in 20 % of cases, based on autopsy reports [8, 9, 60]. The prevalence of primary cardiac lymphoma is extremely low, constituting only 1.3 % of all heart tumors and 0.5 % of all extranodal lymphomas [61]. Primary cardiac lymphoma is commonly defined as a non-Hodgkin lymphoma presenting exclusively in the heart, or having the majority of the tumor mass in the heart or pericardium [8, 60]. Jeudy et al. [61] suggested that an increasing prevalence of cardiac lymphomas in transplant recipients and acquired immunodeficiency syndrome patients is a result of the Epstein-Barr virus.

Cardiac lymphomas are most commonly found in, but are not limited to, the right-sided chambers of the heart [8, 60], and the most common sign observed with the lymphomas are pericardial effusions [9]. Because patients with severe disease can be asymptomatic, and clinical suspicion is usually low with imaging findings being nonspecific, cardiac lymphomas tend to be more advanced at the time of diagnosis and therefore are generally associated with a poor prognosis [9, 60, 62]. Widespread dissemination and underlying immunodeficiency also add to the grave outcome [9, 60]. Polychemotherapy including anthracycline was shown to increase survival, with combination radiation and chemotherapy being the most effective [60].

Conclusion

In spite of the fact that most textbooks neglect the subject, the cardiac lymphatic system may play a significant role in the pathophysiology of many diseases. Furthermore, a clear understanding of the anatomy and physiology of cardiac lymphatics may be an important part of successful thoracic operations including improved postoperative outcomes. Although further studies are required, the authors hope this distillation of current knowledge serves as an overview of the cardiac lymphatic system for both the morphologist and the clinician.

References

1. Moore KL, Dalley AF, Agur AMR (2010) Clinically oriented anatomy, 6th edn. Lippincott Williams and Wilkins, Baltimore, MD, p 43
2. Berne RM, Levy MN (1992) Cardiovascular physiology: the microcirculation and lymphatics. Mosby Year, St. Louis, MO, p 168
3. Levick JR (1990) An introduction to cardiovascular physiology: lymph and the lymphatic system. Butterworth Heinemann Ltd., Oxford, pp 159–163
4. Smith JJ, Kampine JP (1990) Circulatory physiology: microcirculation and the lymphatic system, 3rd edn. Williams and Wilkins, Baltimore, MD, pp 136–137
5. Kline IK (1969) Lymphatic pathways in the heart. Arch Pathol 88:638
6. Hollinshead WH (1956) Anatomy for surgeons, vol 2. Paul B. Hoeber, Inc., New York
7. Alexander RW, Schlant RC, Fuster V (eds) (1998) Hurst's the heart, arteries and veins: anatomy of the heart, vol 1, 9th edn. McGraw Hill, New York, pp 52–53
8. Ceresoli GL, Ferreri AJ, Bucci E, Ripa C, Ponzoni M, Villa E (1997) Primary cardiac lymphoma in immunocompetent patients: diagnostic and therapeutic management. Cancer 80:1497–1506
9. Gill PS, Chandraratna PA, Meyer PR, Levine AM (1987) Malignant lymphoma: cardiac involvement at initial presentation. J Clin Oncol 5:216–224
10. Zaharia L, Gill PS (1991) Primary cardiac lymphoma. Am J Clin Oncol 14:142–145
11. Miller AJ (1963) The lymphatics of the heart. Arch Intern Med 112:501–511
12. Patek PR (1939) The morphology of the lymphatics of the mammalian heart. Am J Anat 64:204–239
13. Rudbeck O (1953) [Nova exervitatio anatomia exhibens ductus hepatico aquosus et vasa glandularum serosa, nune primum inventa, aeneisque figuris delineate]. Lauringerus, Euchar. Latin.

14. Miller AJ (2011) The grossly invisible and generally ignored lymphatics of the mammalian heart. *Med Hypotheses* 76:604–606
15. Bradham RR, Parker EF, Barrington BA Jr, Webb CM, Stallworth JM (1970) The cardiac lymphatics. *Ann Surg* 171:899–902
16. Aagaard OC (1924) *Les Vaisseaux Lymphatique du Coeur Chez l'Homme et Chez Quelques Mammiferes*. Levin, and Munkegaard, Copenhagen
17. Drinkier CK, Warren MF, Maurer FW, McCarrel JD (1940) The flow, pressure, and composition of cardiac lymph. *Am J Physiol* 130:43
18. Johnson RA, Blake TM (1966) Lymphatics of the heart. *Circulation* 33:137–142
19. Miller AJ (1982) *Lymphatics of the heart*. Raven, New York
20. Kampmeier OF (1928) On the lymph flow of the human heart, with reference to the development of the channels and the first appearance, distribution, and physiology of their valves. *Am Heart J* 4:210
21. Feola M, Merklin R, Cho S, Brockman S (1977) The terminal pathway of the lymphatic system of the human heart. *Ann Thorac Surg* 24:531–536
22. Cash JR (1917) On the development of the lymphatics in the heart of the embryo pig. *Anat. Rec.*, 13: 451–464. doi:[110.1002/ar.1090130706](https://doi.org/10.1002/ar.1090130706)
23. Noguchi T, Shimada T, Nakamura M, Uchida Y, Shirabe J (1988) The distribution and structure of the lymphatic system in dog atrioventricular valves. *Arch Histol Cytol* 51:361–370
24. Riquet M, Briere J, Dupont P, Pennhouat G, Hidden G (1993) The embryonic and early fetal development of the lymphatics of the heart and lungs in humans. *Surg Radiol Anat* 15:369–370
25. Uhley HN, Leeds SE, Sung MA, Patel S, Lobos E (1972) The subendocardial lymphatics of the canine heart. *Am J Cardiol* 29:367–371
26. Lupinski RW (2009) Aortic fat pad and atrial fibrillation: cardiac lymphatics revisited. *ANZ J Surg* 79:70–74
27. Gould SE (1960) *Pathology of the heart*, 2nd edn. Charles C. Thomas, Springfield, IL
28. Bullon A, Huth F (1972) Fine structures of lymphatics in the myocardium. *Lymphology* 5:42–48
29. Leeds SE, Uhley HN, Meister RB, McCormack KR (1977) Lymphatic pathways and rate of absorption of ¹³¹I-albumin from pericardium of dogs. *Lymphology* 10:166–172
30. Miller AJ, DeBoer A, Pick R, Van Pelt L, Palmer AS, Huber MO (1988) The lymphatic drainage of the pericardial space in the dog. *Lymphology* 21:227–233
31. Eliskova M, Eliska O, Miller AJ (1995) The lymphatic drainage of the parietal pericardium in man. *Lymphology* 28:208–217
32. Johnson RA (1969) The lymphatic system of the heart. *Lymphology* 2:95–108
33. Miller AJ, Pick R, Katz LN (1961) Lymphatics of the mitral valve of the dog. *Circ Res* 9:1005–1009
34. Ichikawa S, Uchino S, Hirata Y (1989) Lymphatics of the cardiac chordae tendineae with particular consideration of their origin. *Lymphology* 22:123–131
35. Riquet M, Hidden D (1991) Lymphatic drainage of the right atrium and ventricle of the heart. *Surg Radiol Anat* 13:235–237
36. Marchetti C, Poggi P, Calligaro A, Casasco A (1985) Lymph vessels of the rabbit heart: distribution and fine structure in ventricles. *Lymphology* 18:90–95
37. Riquet M, Hidden D (1991) Lymphatic drainage of the left atrium and ventricle of the heart. *Surg Radiol Anat* 13:238–240
38. Eliskova M, Eliska O, Miller AJ, Palmer A, DeBoer A, Usman Z (1992) The efferent cardiac lymphatic pathways in the Macaque monkey. *Lymphology* 25:69–74
39. Shimada T, Morita T, Oya M, Kitamura H (1990) Morphological studies of the cardiac lymphatic system. *Arch Histol Cytol* 53:115–126
40. Marchetti C, Poggi P, Calligaro A, Casasco A (1986) Lymph vessels of the rabbit heart: distribution and fine structure in atria. *Lymphology* 19:33–37

41. Takada K, Otsuki Y, Magari S (1991) Lymphatics and pre-lymphatics of the rabbit pericardium and epicardium with special emphasis on particulate absorption and milky spot-like structures. *Lymphology* 24:116–124
42. Uhley HN, Leeds SE (1976) Lymphatics of the canine papillary muscles. *Lymphology* 9:72–74
43. Burch GE, Depasquale NP, Phillips JH (1963) Clinical manifestations of papillary muscle dysfunction. *Arch Intern Med* 112:112–117
44. Golab B (1977) Lymphatic vessels of the conducting system of the human heart. *Folia Morphol* 4:317–322
45. Caro DM, Berjon A, Teijerira J, Duran CG (1972) [Anatomical study of the cardiac lymphatics. Their pathogenic role in pericardial effusions]. *Ann Chir Thorac Cardiovasc* 11:373–376, French
46. Cui Y, Urschel JD, Petrelli NJ (2001) The effect of cardiopulmonary lymphatic obstruction on heart and lung function. *Thorac Cardiovasc Surg* 49:35–40
47. Ishikawa Y, Akishima-Fukasawa Y, Ito K, Akasaka Y, Tanaka M, Shimokawa R et al (2007) Lymphangiogenesis in myocardial remodeling after infarction. *Histopathology* 51:345–353
48. Mehlhorn U, Davis KL, Burke EJ, Adams D, Laine GA, Allen SJ (1995) Impact of cardiopulmonary bypass and cardioplegic arrest on myocardial lymphatic function. *Am J Physiol* 268:H178–H183
49. Huth F (1983) Disease of cardiac lymph vessels. In: Silver MD (ed) *Cardiovascular pathology*, vol 1. Churchill Livingstone, New York, Edinburgh, pp 171–190
50. Feola M, Glick G, Pick R (1973) Interrelations between cardiac lymph and experimental infarction in dogs. *Clin Res* 21:418
51. Feola M, Glick G (1975) Cardiac lymph flow and composition in acute myocardial ischemia in dogs. *Am J Physiol* 229:44–48
52. Cui Y (2010) The role of lymphatic vessels in the heart. *Pathophysiology* 17:307–314 [Epub ahead of print]
53. Cui Y (2010) Impact of lymphatic vessels on the heart. *Thorac Cardiovasc Surg* 58:1–7
54. Lupinski RW (2004) Lymphatic aneurysm of the heart. *Lymphology* 37:141–150
55. Maurice SM, Palmer AS, Miller AJ, Greene R (2001) Lymphatic drainage of the heart in the laboratory rat. *Lymphology* 34:145–148
56. Miller AJ, Pick R, Katz LN (1963) Ventricular endomyocardial pathology following chronic impairment of cardiac lymph flow in the dog. *Br Heart J* 25:182–190
57. Kline IK, Miller AJ, Pick R, Katz LN (1964) The relationship between human endocardial fibroelastosis and obstruction of the cardiac lymphatics. *Circulation* 30:728–735
58. Gibbs NM, Haworth JC, Rendle-Short J (1957) Endocardial fibroelastosis with generalized lymphadenopathy, oedema, and rash. *Br Heart J* 19:193
59. Kong XQ, Wang LX, Kong DG (2007) Cardiac lymphatic interruption is a major cause for allograft failure after cardiac transplantation. *Lymphat Res Biol* 5:45–47
60. Gowda RM, Khan IA (2003) Clinical perspectives of primary cardiac lymphoma. *Angiology* 54:599–604
61. Jeudy J, Kirsch J, Tavora F, Burke AP, Franks TJ, Mohammed TL et al (2012) From the radiologic pathology: archives cardiac lymphoma: radiologic-pathologic correlation. *Radiographics* 32:1369–1380
62. Tanaka T, Sato T, Akifuji Y, Sakamoto M, Shio H, Ueki J et al (1996) Aggressive non-Hodgkin's lymphoma with massive involvement of the right ventricle. *Intern Med* 35:826–830