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Historical notes on the anatomy of the heart's lymphatic system

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Abstract

The heart's lymphatic system has been under research for many years both at a microscopic and a macroscopic level. The results so far significantly induce modern cardiologists to attribute pathologies of the heart to disorders of cardiac lymphatics. The current review is an effort to display the progress of the knowledge regarding the heart's lymphatic system through the work of the scientists devoted to the specific field. The reader will gain detailed and up to date information and will be able to comprehend thoroughly the anatomy of the cardiac lymphatics.

Key words

Anatomy, history, heart, lymphatic system.

A great matter but of minor concern until nowadays is the lymphatic system of the heart. What is known so far is that lymphatic vessels form subendocardial, myocardial and subepicardial plexuses, where the first two drain into the third one. Efferents from the subepicardial plexus form the left and the right cardiac collecting trunks. The lymphatic collectors contain valves and are arranged in pairs follow the subepicardial branches of the coronary arteries. They drain via the left coronary trunk into the right venous angle and via the right coronary trunk into the left venous angle (Wilting et al., 2007). The cardiac lymphatic system was not understood before the second half of the nineteenth century. The subendocardial lymph network in humans was discovered by Eberth and Belajeff in 1866, the epicardial ventricular lymph network by Sappey in 1874 and the epicardial atrial lymph network by Rainer in 1907 and Mouchet in 1909 (Olry, 1998). Patek in 1939 used India ink to demonstrate the lymphatic capillaries in the subendocardial and myocardial area and in the coming years investigators such as Miller, Drinker et al., and others provided precise information regarding the distribution and the physiology of the lymphatic cardiac system (Loukas et al., 2011).

Mascagni in 1784 had mentioned that presumably Olaus Rudbeck had been the first who described the lymphatics of the heart. In particular, Rudbeck in 1653 observed in dogs a few subepicardial lymphatics that likely drained into mediastinal lymph nodes (Patek, 1939). Mascagni mentioned that later on Rudbeck, Nuck

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and Cassebohm described the superficial lymphatic vessels, which corresponded to the subepicardial lymphatic channels (Mascagni, 1784; Kampmeier, 1928). Olaus Rudbeck, a professor of anatomy in Upsala, presented his work on the thoracic duct in 1652 and published his results in 1653. Rudbeck displayed his experiments to the court of Sweden, including direct presentations to Queen Christina, who took a great interest in his work, even allowing him to do numerous dissections in her presence (Woodhead, 1863; Loukas et al., 2011). Musschenbroek in 1715 injected air inside the lymphatic vessels and showed the presence of the subepicardial lymphatics with double valves (Musschenbroek, 1715).

William Cruikshank (1745-1800) discovered the subepicardial lymphatic system of the heart using a method further developed later by Ernest Alexandre Lauth (1803-1837). In specific, he injected arteries and veins with wax and let the specimen soak for some days. The development of gas in the lymphatic vessels made them more visible, and the previous injection of wax allowed an easy differentiation from arterial and venous vessels (Olry, 1997). Many of the specimens of human lymphatics injected with mercury in the Anatomy Museum at Glasgow are considered to be the fruit of Cruikshank's research (McDonald, 2015). Cruikshank published "The anatomy of the absorbing vessels of the human body" in 1786, which was a thorough account of all the illustrations of the lymphatic networks until that time (Thompson, 1942) and included a mercury injection tracing of the lymphatic drainage of the breast (Uren, 2003). William Cruikshank was educated at the Universities of Edinburgh and of Glasgow and joined William Hunter as his assistant in 1771. He was a gifted teacher as well an able researcher dealing with the research of lymphatics, early development of the embryo, regeneration of nerves and skin and perspiration (Thompson, 1942; Mc Dorland, 2015). Bourgery and Jacob, in their "Atlas d'anatomie humaine et de chirurgie" with the complete colored plates of 1831-1854, demonstrated distinct epicardial lymphatic trunks accompanying the right coronary, left coronary artery as well as its circumflex branch connecting with the pericardial lymphatic vessels and lymph nodes of the great vessels of the heart (Bourgery and Jacob, 1854). The subepicardial lymphatics of the heart were studied comprehensively by other authors such as Eberth et al. (1866), Sappey (1885) and Rainer (1909). Kampmeier (1928) considered that the subepicardial plexus becomes intricate and dense over the ventricular area and remains more simple and restricted over the auricular territories. Patek in 1939 noticed a subepicardial lymphatic plexus composed of large parallel capillaries overlying the slight depressions between neighboring muscle bundles accompanying small blood vessels receiving afferents lymphatics from the myocardium. The smaller vessels direct transversely between the muscle bundles. Shimada et al. (1990) ascertained that the subepicardial lymphatics were less extensive in the atria than in the ventricles.

Lauth in 1830 was the first investigator who described the presence of the subendocardial lymphatic vessels injecting mercury in the endocardium of the horse. Lauth (1830) noticed two independent plexuses, a superficial one composed of large vessels corresponded to lymphatics or veins and a deep plexus consisted of small like hair vessels directed parallel to the fibers of the myocardium. Presumably that deep plexus was the system of Purkinje fibers and not vessels (Lauth, 1830; Patek, 1939). Ernest Alexandre Lauth (1803-1837) belonged to a famous Strasbourg family of anatomists. He studied under Vincent Fohmann and carried out researches on the

lymph system in birds and in man. In his handbook in 1830 he provided detailed account of the injection and preparation of lymph vessels, a method which, as it has been mentioned, was used by William Cruikshank in order to study the lymph vessels of the heart (Olry, 1998). Later Eberth et al. (1866) described a net of subendocardial lymphatic vessels not displaying a remarkable difference from the morphology and density of subepicardial and myocardial lymphatics. Wedl (1871) could not show the existence of subendocardial lymphatics. Sappey in 1885 observed a widespread, loose net of subendocardial lymphatics utilizing direct mercury injection. Mouchet (1909) noted a deep subendocardial plexus consisting of sizeable vessels, whereas the superficial plexus was composed of thin vessels and was more compact. Aagaard and Hall in 1914 were the first researchers who noticed that the subendocardial lymphatics are located superficial and parallel to the Purkinje fibers. Cash in 1917 supposed that the lymphatics do not appear in the endocardium. It is impressive that Cash (1917) believed that the other investigators erroneously considered the bundle of His as subendocardial lymphatics (Cash, 1917). Kampmeier in 1928 "...did not deny the reality of lymph vessels in the inner lining of the heart". Patek in 1939 considered the subendocardial lymphatic plexus similar to the myocardial one, composed entirely of lymphatic capillaries. According to this author, the lymphatics were situated between the endocardium and the Purkinje fibers, were continuous with the papillary muscle plexuses, accompanied the chordae tendineae for a few millimeters and were uncommon in the valves (Patek, 1939).

Patek (1939) was not able to demonstrate the presence of lymphatics within the mitral and tricuspid valves. Patek (1939) and Johnson et al. (1966) along with Shimada et al. (1990) observed a well-developed loose reticular fishnet-like arrangement of lymphatics located at the interventricular septum and papillary muscles of both ventricles. Marchetti et al. (1986) and Shimada et al. (1990) did not notice lymphatic capillaries in the subendocardium of the atria. Lymphatic capillaries are present in the atrioventricular valves and absent from arterial valves of the heart according to some authors (Miller et al., 1961; Johnson et al., 1966; Shimada et al., 1990). Very early Eberth et al. in 1866 observed a plexus of endocardial lymphatics which enter into the flaps of the mitral and tricuspid valves (Eberth et al., 1866). Miller et al. (1961) observed lymphatic vessels in atrioventricular valves of living dogs, whilst Bradham et al. (1973) did not succeed to visualize such vessels in dogs. Noguchi et al. (1988) noticed lymphatic capillaries in dogs being restricted to the subendocardial area of the atrial side and mentioned that the lymphatic capillaries are well developed in the anterior cusp of the mitral valve. Ratajska et al. (2014) reported that lymphatics are absent from the tricuspid valve of human hearts. As regards the lymphatic drainage of the conduction system of the heart, it has been shown that the lymphatic vessels of the sinus-atrial node drain through the subepicardial lymphatics of the right atrium into the right main lymphatic trunk of the heart, directly or indirectly (Golab, 1977). The lymphatics of the atrioventricular node and the upper portion of the atrioventricular bundle reach the subendocardial lymphatics at the area of the septal cusp of the tricuspid valve. From that point the lymph directs backwards to the posterior branch of the left lymphatic trunk and ventrally into the inferior tracheobronchial nodes (Eliska and Eliskova, 1980). It has been shown that the lymphatic drainage of the elements of the conduction system is made by the myocardial lymphatics and afterwards the lymph is directed to subendocardial or subepicardial lymphatic plexus

(Golab, 1977). Prior to discovery of the precise nature of the Purkinje system, the latter one was considered mistakenly as lymphatic vessels. In particular, Patek (1939) thought that the deep layer of the subendocardial lymphatic plexus is composed presumably of the Purkinje system. The first investigators who mentioned such an error in the identification of lymphatics were Eberth and Belajeff in 1866. Aagaard and Hall (1914) differentiated more precisely the fibers of the Purkinje system from the subendocardial lymphatics.

As regards the lymphatic vessels of great vessels, such as aorta, very early in 1883 Hogan et al. observed a subendothelial lymphatic plexus only in vessels in which the muscular layer is absent (Hogan and Hogan, 1883). Schiefferdecker in 1897 demonstrated the existence of lymphatic net just under the endothelium of pig's aorta. Lee in 1922 observed an extensive net of lymphatic capillaries at the junction of the media and the adventitia in the thoracic aorta of the cat. Moreover, he noted superficially in the adventitia a plexus of large lymphatic vessels (Lee, 1922). Lymphatics have been also noticed within the wall of coronary arteries (Johnson, 1969; Smolich et al, 1990). It has been stated that the lymphatics of the coronary arteries penetrate the adventitia and reach the outer zone of the media coat of the arterial wall (Johnson, 1969; Pappadia and Setti, 1972). However, Eliska et al. (2006) found myocardial lymphatics to appear only in the periadventitial region, but not in the adventitia of the coronary arteries. These authors noted, also, that the intramural coronary arteries are surrounded by an extensive plexus of myocardial lymphatics as compared to the epicardial coronary arteries (Eliska et al., 2006).

In the second half of the nineteenth century, a debate existed as regards the likely presence of lymph spaces inside the myocardial tissue or myocardial lymphatic vessels. The first investigator who mentioned that the myocardium contains lymphatic vessels was Leyh (1859). Later in 1863 Wilhelm His was the first who demonstrated lymphatic vessels within the interstitial connective tissue of the myocardium, a discovery based on microscopic observation (His, 1863). The same year as Wilhelm His, Luschka (1863) noted myocardial lymphatic vessels draining the lymph into a vessels's plexus at the vortex of the heart, i.e. where superficial myocardial fibres form vortices at the apices of both ventricles. Henle, in 1868, claimed that within the myocardium there are intermuscular spaces and fissures filled with lymph. These spaces have been termed "Henle spaces". Later Salvioli (1878) noted a rich interfascicular plexus of lymphatic vessels within the myocardium. Albrecht (1887) concluded that large lymphatic trunks lay in the spaces between the muscle cells. These vessels were differentiated from blood vessels since they showed multiple and acute branching and ran at about right angles to the long diameter of the cardiac muscle (Albrecht, 1887). Bock (1905) established the presence of myocardial lymphatic vessels noticing that for every muscle fiber one or even two lymphatic vessels existed parallel to the muscle fiber. Cash (1917) mentioned that lymphatics never form a capillary bed, but a well-woven plexus of vessels, of which the smallest are larger than capillaries. Cash stated that lymphatics become fewer and smaller deep in the myocardium, with their number being exceedingly small near the endocardium. On the contrary other researchers supported that inside the myocardial tissue one could not observe the appearance of distinct lymphatic vessels (Eberth and Belajeff, 1866; Sappey, 1855). Hewson (1774) was the first who made no mention about myocardial lymphatics in a haddock that had been dissected by himself.

Aagaard (1924) noticed that the myocardial interfascicular net of lymphatic vessels consisted of small deep vessels coursing parallel to the muscle fibers and drained into the large superficial lymphatic vessels accompanying the blood vessels. According to Patek (1939) the myocardial lymphatics form a loose plexus distributed throughout the whole myocardium. The lymphatics lie within the interfascicular connective tissue surrounding the muscular fascicles. One group of lymphatics lie parallel to the muscle fibers, whereas the other group directs transversely or obliquely across the muscle fibers. Patek (1939) commented that large myocardial blood vessels are accompanied by one or two communicating lymphatics. The same author mentioned that the myocardial lymphatic plexus contain few valves and presumably the entire plexus is composed of lymphatic capillaries. The myocardial lymphatic plexus, in general, is thought to be more sparse than that (Bullon and Huth, 1972). Kampmeier (1928) considered that during diastole the blood's pressure in ventricles drives lymph from subendocardial to myocardial lymphatics, whereas during systole the contraction of heart's muscle drives the lymph from the myocardial to the subepicardial lymphatics. At the end, the pressure of the heart against the pericardium forces the lymph from subepicardial lymphatics to principal lymphatic of the heart. On the contrary, Cui (2010) thought that the force driving the lymph out of the subepicardial lymphatics is the powerful subepicardial muscular contraction. Cui believed that the effectiveness of subepicardial myocardium to pump lymph from the heart may require an asymmetric contraction and relaxation between the subepicardial myocardial and the rest of the myocardium. Michael et al. (1979) considered that the active movement of the heart produces a rhythmic compression on the myocardial lympatics. On the contrary, Szabo et al. (1974) stated that lymph flow was independent of heart rate.

With respect to the likely presence of epicardial lymph nodes of the heart there is no reference in the literature. Mouchet (1909) noticed small lymph nodes located in the epicardium overlying the intrerventricular sulci in the dog and horse; however, he was not able to find such lymph nodes in human hearts. Millard (1922) stated that the absence of lymph nodes in the heart is explained by the active drainage through the efferents. The same author considered that the nodes are practically unnecessary and if they were present in various heart disorders they could induce undue pressure to the pressure sensitive heart. As regards the lymphatics that drain the heart Heuer (1909) designed a vessel from the thoracic duct that reaches the aortic plexus having the appearance of going to the heart. Cunningham (1909) described two main lymphatic trunks, the anterior and the inferior trunk that accompany the left and the right coronary artery, respectively. Ultimately, these lymphatic trunks at the upper portion of the heart pass backwards, at the sides of the pulmonary artery, terminating in the lymph nodes located around the birfucation of the trachea. Sabin (1913, as cited by Cash, 1917) suggested that the lymphatic vessels of the heart are evidently those coming from the right lymphatic duct. Later Cash (1917) in embryo pigs noticed that there are two lymphatic trunks one from the right lymphatic duct coursing behind the aortic arch and the pulmonary artery and one from the tracheal plexus at the base of the heart. These two lymphatic trunks become plexiform in nature and pass under the pulmonary artery, lying between it and the left auricle and forming a primary plexus on the anterior surface of the heart. That plexus gives rise to two main branches which follow the course of the right and left coronary artery (Cash, 1917).

Aagaard (1924) described the subepicardial plexus and traced its drainage to the mediastinal lymph nodes, without however mentioning on the terminal pathway into the venous system. Kampmeier (1928) in human embryos and fetuses observed two main lymphatic trunks of the heart, one arising from the pretracheal plexus and following the left coronary artery and the other from the upper portion of the thoracic duct following the right coronary artery. These trunks reach the fetal heart at 4 months. The same author found valves inside the subepicardial lymphatics being most numerous on the anterior surface of the heart, not so numerous on the phrenic surface and only a few on the atria (Kampmeier, 1928). Patek (1939) in dogs detected a vessel of the so-called by him fifth order, that was one principal coronary lymphatic trunk formed by the union of the right and left coronary lymphatics, or vessels of the fourth order. The right coronary lymphatic trunk accompanies the homonymous artery passing superiorly on the anterior surface of the pulmonary artery, after receiving tributaries from the right ventricle. The left coronary lymphatic trunk begins as posterior interventricular trunk accompanying the homonymous artery, is overlapped by the left auricle and after receiving branches from the left ventricle joins the right trunk on the anterior aspect of the pulmonary artery. The diameters of the two lymphatic trunks are usually equal. Only in a few instances the two trunks don't unite to from a single vessel (Patek, 1939).

Drinker et al. (1940) believed that the complete flow from the heart is collected by a single lymphatic trunk that enters in a constantly placed lymph node situated between the superior vena cava and the brachiocephalic trunk. The single lymphatic trunk of the heart passes behind the pulmonary artery and the arch of the aorta and bends to the right mediastinum to terminate into the above mentioned cardiac lymph node (Drinker and Yoffey, 1941). Miller (1982) considered that most heart's lymphatics cross the anterior surface of the pulmonary artery to reach the pretracheal and the cardiac lymph nodes. Afterwards, lymphatics course proximally to enter the right lymphatic duct. Feola et al. (1977) noticed a subepicardial plexus which tended to cover the area of the left ventricle in the region delineated by the atrioventricular sulcus and the anterior and posterior interventricular sulci. The lymphatic channels accompanied the coronary artery and their branches. The right and left coronary lymphatic channels converged toward the root of aorta forming one main supracardial channel in 77,78% cases. This channel coursed behind the pulmonary artery, in front of the trachea, to the cardiac lymph node. The efferent lymphatics from that node emptied into either the right lymphatic duct or directly into the right angulus venosus. In 11.11% of cases the right coronary lymphatic channel remained separate from the left one and drained into the thoracic duct. Moreover, the posterior interventricular trunk emptied into the left coronary lymphatic channel (Feola et al., 1977). Michael et al. (1979) found the cardiac lymph node being clearly visible in 98% cases of their material, composed of dogs. Only in 7.14% of the cases the lymph flow bypassed the cardiac lymph node and the lymphatics proceeded to the thoracic duct on the left side. Shimada et al. (1990) described one left and one right cardiac lymphatic trunk mainly terminating into the tracheobronchial lymph nodes. Riquet et al. (2002) observed that the right lymphatic trunk of the heart drained mostly lymph from the right ventricle, reached mainly the left anterior mediastinal lymph node chain and terminated in the majority of cases into the arch of thoracic duct. The left lymphatic trunk drains the left ventricle, then joins the right paratracheal lymph

nodes and the efferent pathway presumably terminates into the right lymphatic duct (Riquet et al., 2002). Miller (2011) supported that the left ventricle has the most lymphatic concentration and mostly drains to the right lymphatic duct.

The cardiac lymphatic system is a topic of great interest and still under research. Heart diseases, myocardial ischemia included, are related and possibly attributed to disorders of the heart lymphatic system. The clarification and full mapping of the lymph drainage will be a decisive step to comprehend diseases which are lurking. The cardiologists of the future will probably have to insert in differential diagnosis obstructions and disorders of the cardiac lymphatics.

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