Anomalous atrium associated with persistent left superior vena cava

Fumihiro Shutoh,[1†] Tomoyuki Masuda,[2,3,#†] Tetsuya Sasaki,[1] Yosuke Takei[1,#]

[1]Department of Anatomy and Neuroscience, Faculty of Medicine, University of Tsukuba, Ibaraki 305-8577, Japan
[2]Department of Neurobiology, Faculty of Medicine, University of Tsukuba, Ibaraki 305-8577, Japan
[3]Department of Neurology, Faculty of Medicine, University of Tsukuba, Ibaraki 305-8575, Japan

[†]**Fumihiro Shutoh and Tomoyuki Masuda contributed equally to this work.**

[#]Correspondence:
Tomoyuki Masuda, tmasu@md.tsukuba.ac.jp
Yosuke Takei, ytakei@md.tsukuba.ac.jp

Running title: Anomalous atrium with PLSVC

Abstract

Persistent left superior vena cava (PLSVC) is the most common venous anomaly with an incidence of 0.3–0.5% in the general population. Here, we report a rare case of PLSVC with anomalous atrium in a cadaver during the student′s dissection session in the University of Tsukuba. In this case, the coronary sinus had merged with the right atrium to form an enlarged sac-like structure and received systemic venous flow including inflow from the PLSVC. The roof of the coronary sinus with the right atrium was thicker than that of the control cases. We further found that the distance between the sinoatrial node and the opening of the coronary sinus was slightly more than half of that in control cases. This variant appears interesting and is worth reporting for developmental and clinical consideration.

Keywords: Atria, Cardiovascular anomaly, Coronary sinus, Gross anatomy, Persistent left superior vena cava

Introduction

Persistent left superior vena cava (PLSVC) is a common cardiovascular malformation. This anomaly occurs in 0.3–0.5% of normal individuals and in 3–10% of patients with congenital heart diseases (Schummer et al., 2003; Schreve-Steensma et al., 2008). PLSVC is often detected during central venous catheterization, pacemaker implantation or open cardiac surgery. PLSVC is divided into several anatomical variations depending on the presence or absence of the right superior vena cava (RSVC) and where it drains into the heart (described later for the classification of PLSVC).

The atria are covered by atrial muscle layers and the ventricles are covered by ventricular muscle layers. Atrial muscle cells are smaller than ventricular ones and are diverse in nature (Inoue et al., 2010). The coronary sinus is surrounded by the venous wall consisting of a thin muscle layer, and its roof is composed of the epicardium and the muscle layer (Makino et al., 2006). Little is known about the tissue structure of the roof when the atrium and the coronary sinus are merged.

Here, we report a rare case of PLSVC with an anomalous atrium. In this case, the coronary sinus had merged with the right atrium to form an enlarged sac-like structure and received all the venous blood flow returning to the heart including inflow from the PLSVC. We examined this anomaly in detail by both gross anatomical and histological analyses.

Case Report

A cardiovascular anomaly with PLSVC was found in an embalmed cadaver of a

71-year-old Japanese female who had died from hepatic cancer with no history of cardiac disease. Her heart exhibited an abnormal appearance, especially in the dorsal view (Fig. 1a, b). A sac-like structure covered the upper half of the heart, to which the vena cava and pulmonary veins appeared to be connected. Dissected veins and arteries around the anomalous heart are shown in Fig. 1c and d. The azygos vein was normally connected to the RSVC with no visible anomalies (Fig. 1c, d). The vessel diameter of the LSVC and the RSVC was similar and about 4 times thicker than that of the left brachiocephalic vein (Fig. 1c, d). No other abnormal blood vessel branches were observed in the aortic arch. Furthermore, we cut the wall of the heart to view its inner structure (Fig. 1e, f). Inside the sac-like structure, the coronary sinus had merged with the right atrium without distinction and was connected to the PLSVC (Fig. 1e, f). The left atrium was separated from the coronary sinus by the septal wall (Fig. 1e, f). Pulmonary veins normally drained into the left atrium (Fig. 1e, f).

Next, we prepared paraffin-embedded sections (14 μm in thickness) for hematoxylin and eosin staining to examine the components and thickness of the roof of the heart at 3 points (points b–d in Fig. 2a). At point “b” (the roof of the coronary sinus with the right atrium proximal to the PLSVC), the roof was composed of the epicardium, atrial muscle layers, and presumptive coronary sinus muscle bundles (Fig. 2b). The thickness of the roof at point “b” appeared to be within the normal range. At point “c” (the roof of the coronary sinus with the right atrium distal to the PLSVC), the roof was composed of the epicardium, atrial muscle layers and presumptive coronary sinus muscle bundles (Fig. 2c). We further compared the thickness of the roof at point “c” with those of 5 control

hearts obtained from other cadavers (age 73–90, 83.8 ± 6.18, mean ± SD, 2 males and 3 females). The thickness in our case was 2.8 mm, whereas that of the control cases was 1.1 ± 0.24 mm (mean ± SD). At point "d" (the roof of the left atrium), the roof was composed of the epicardium and atrial muscle layers (Fig. 2d). The thickness of the wall at point "d" appeared to be within the normal range.

Furthermore, we examined the distance between the sinoatrial node (see Fig. 1b) and coronary sinus. Using a Stemi 2000 Stereo Microscope (Carl Zeiss, Germany), we first confirmed the position of the sinoatrial node by the observation of fine projection of autonomic nerve bundles. Next, we measured the distance between the sinoatrial node and the edge of the coronary sinus orifice. In our case, the distance was 24 mm, whereas that in the 5 controls was 41 ± 0.55 mm (mean ± SD).

Discussion

The present case is an example of congenital heart malformation with PLSVC. When we observed the surface of this heart, the coronary sinus and both the right and left atria seemed to have merged. After cutting open the heart to examine its lumen, we found that the left atrium was separated from the others. However, we also found that the right atrium had merged with the coronary sinus and that the PLSVC was connected to them. PLSVC itself is a common malformation, but it is a rare case when a large coronary sinus has merged with the right atrium.

The classification of PLSVC is roughly classified into 3 types depending on the presence or absence of other veins. First, PLSVC is classified into 2 types depending on

the presence or absence of the RSVC. PLSVC without RSVC is a less common anomaly and accounts for only 8–18% of all PLSVC cases (Webb et al., 1982; Schummer et al., 2003). Most PLSVCs (82–92%) have the RSVC, and the situation in which the left and right superior venae cavae (SVCs) are present is usually called double SVCs (Webb et al., 1982; Martínez-Villar et al., 2016). In the case of double SVCs, a further subdividion into 2 types is made depending on the presence or absence of the left brachiocephalic vein that connects both SVCs. Among double SVCs, the proportion of those with a communication (with the left brachiocephalic vein) is 60–65%, and that of double SVCs with no or small communication (without the left brachiocephalic vein or hypoplasia) is 35–40% (Webb et al., 1982). PLSVC in our present report possessed both the RSVC and the left brachiocephalic vein. We consider this case to be a major case in this PLSVC classification.

Furthermore, PLSVC is also classified into 2 types depending on where it drains. Most PLSVCs (about 90–92% of them) drain into the right atrium through the coronary sinus (Schummer et al., 2003; Ghadiali et al., 2006; Sheikh and Mazhar, 2014). The proportion of PLSVCs that drain directly into the left atrium is fairly low, even if the coronary sinus has not normally developed (8–10%; Schummer et al., 2003; Ghadiali et al., 2006; Sheikh and Mazhar, 2014). As the PLSVC in our report drained into the coronary sinus with the right atrium, this case is not rare even in this classification.

Our analyses revealed that the roof of the coronary sinus in this cardiac anomaly was thicker than that found in normal cases. Because the coronary sinus had merged with the right atrium in this case, it is highly likely that the atrial muscle layer of the right atrium

would have become a part of the roof of the coronary sinus. In fact, when we observed the roof of the coronary sinus in our sample, atrial muscles, which seem to have been derived from the right atrium, mainly constituted the thick inner layer of the roof. The epicardium and coronary sinus muscle bundles likely formed the outermost thin layers (see Fig. 2b and c).

The sinus venosus is incorporated into the right atrium and becomes the dorsal smooth wall of the right atrium, known as the sinus venarum (Faber et al., 2019). By this incorporation, a part of the sinus venosus differentiates into the sinoatrial node, the dominant cardiac pacemaker of the heart (Shiraishi, 2018). Interestingly, the sinoatrial node was positioned in a slightly different location (near the coronary sinus) in our case. A previous study reported that the location of the sinoatrial node is altered in the presence of PLSVC (Biffi et al., 2001). That finding is consistent with our case. An ectopic sinoatrial node may affect the coronary sinus rhythm and cause a change in the heart rate (Scherf and Harris, 1946; Scherf and Gurbuzer, 1958; Lancaster et al., 1965). Although it is well known that an increase in the heart rate induces ventricular muscle growth, resulting in cardiac hypertrophy, there is no evidence to indicate that an increase or decrease in the heart rate affects atrial muscle development. Therefore, it is unlikely that the roof of the coronary sinus, which had merged with the right atrium, had become thick due to the ectopic sinoatrial node.

It is unclear what genetic factors may affect the development of the sac-like coronary sinus shown in the present case. It is possible that the sac-like coronary sinus and PLSVC had formed as an independent congenital anomaly. The coronary sinus is

known to develop from the central side of the left superior vena cava during the fetal period (Furuki et al., 2015). It is also possible that the formation of the sinus may be enhanced by the presence of PLSVC.

We may also take into account the physical effects of double SVCs. The presence of PLSVC might have caused more venous blood flow into the coronary sinus than usual and exerted high pressure on the wall of the coronary sinus. In addition, because the coronary sinus had merged with the right atrium in our case, the venous blood flow from the inferior vena cava and the RSVC also drained into the coronary sinus, and the pressure applied to the wall might have been higher. It is possible that such physical stimulation might have promoted the wall hyperplasia, thus resulting in dysplasia of the coronary sinus.

Acknowledgments

We thank Dr. H. Nogami (Japan University of Health Sciences) for his advice and Mr. Y. Seya and Mr. K. Yabe (University of Tsukuba) for their technical support. We also thank the donor and her family for tissue donation and allowing us to publish this case report.

Compliance with ethical standards

Conflict of interest

The author declares that they have no conflicts of interest.

Ethical approval

Ethical approval was obtained from the Medical Ethics Committee of the University of Tsukuba (#1137). Informed consent was obtained from all donors and their families.

References

Biffi M, Boriani G, Frabetti L, Bronzetti G, Branzi A (2001) Left superior vena cava persistence in patients undergoing pacemaker or cardioverter-defibrillator implantation: a 10-year experience. Chest 120:139–144

Faber JW, Boukens BJ, Oostra R-J, Moorman AFM, Christoffels VM, Jensen B (2019) Sinus venosus incorporation: contentious issues and operational criteria for developmental and evolutionary studies. J Anat 234:583–591

Furuki H, Matsutani T, Hagiwara N, Nomura T, Uchida E (2015) A case of esophageal cancer in a patient with persistent left and absent right superior vena cava. Nihon Rinsho Geka Gakkai Zasshi 76:2422–2426 (**in Japanese with English summary**)

Ghadiali N, Teo LM, Sheah K (2006) Bedside confirmation of a persistent left superior vena cava based on aberrantly positioned central venous catheter on chest radiograph. Br J Anaesth 96:53–56

Inoue S, Makino M, Ota H, Sakai T, Saito T, Kobayashi Y, Ogawa G, Matsuyama T (2010) Anatomical construction of atrium and pulmonary veins and their arrhythmogenicity–from the histopathological viewpoint–. Jpn J Journal of Electrocardiol 30:268–274 (**in Japanese**)

Lancaster JF, Leonard JJ, Leon DF, Kroetz FW, Shaver JA (1965) The experimental

production of coronary sinus rhythm in man. Am Heart J 70:89–93

Makino M, Inoue S, Matsuyama T, Sakai T, Kobayashi Y, Katagiri T, Ota H (2006) Coronary sinus-anatomy and clinical implications. Shinzo 38:1181–1186 (**in Japanese with English summary**)

Martínez-Villar M, Gran F, Ferrer Q, Giralt G, Sabaté-Rotés A, Albert DC (2016) Persistent left superior vena cava with absent right superior vena cava. Rev Esp Cardiol (Engl Ed) 69:220–221

Scherf D, Harris R (1946) Coronary sinus rhythm. Am Heart J 32:443–456

Scherf D, Gurbuzer B (1958) Further studies on coronary sinus rhythm. Am J Cardiol 1:579–583

Schreve-Steensma AM, van der Valk PHM, ten Kate JBL, Kofflard MJM (2008) Discovery of a persistent left superior vena cava during pacemaker implantation. Neth Heart J 16:272–274

Schummer W, Schummer C, Fröber R (2003) Persistent left superior vena cava and central venous catheter position: clinical impact illustrated by four cases. Surg Radiol Anat 25:315–321

Sheikh AS, Mazhar S (2014) Persistent left superior vena cava with absent right superior vena cava: review of the literature and clinical implications. Echocardiography 31:674–679

Shiraishi I (2018) Basic and comprehensive outlines of cardiovascular embryology and morphogenesis. Pediatr Cardiol Cardiac Surg 34:88–98 (**in Japanese with English summary**)

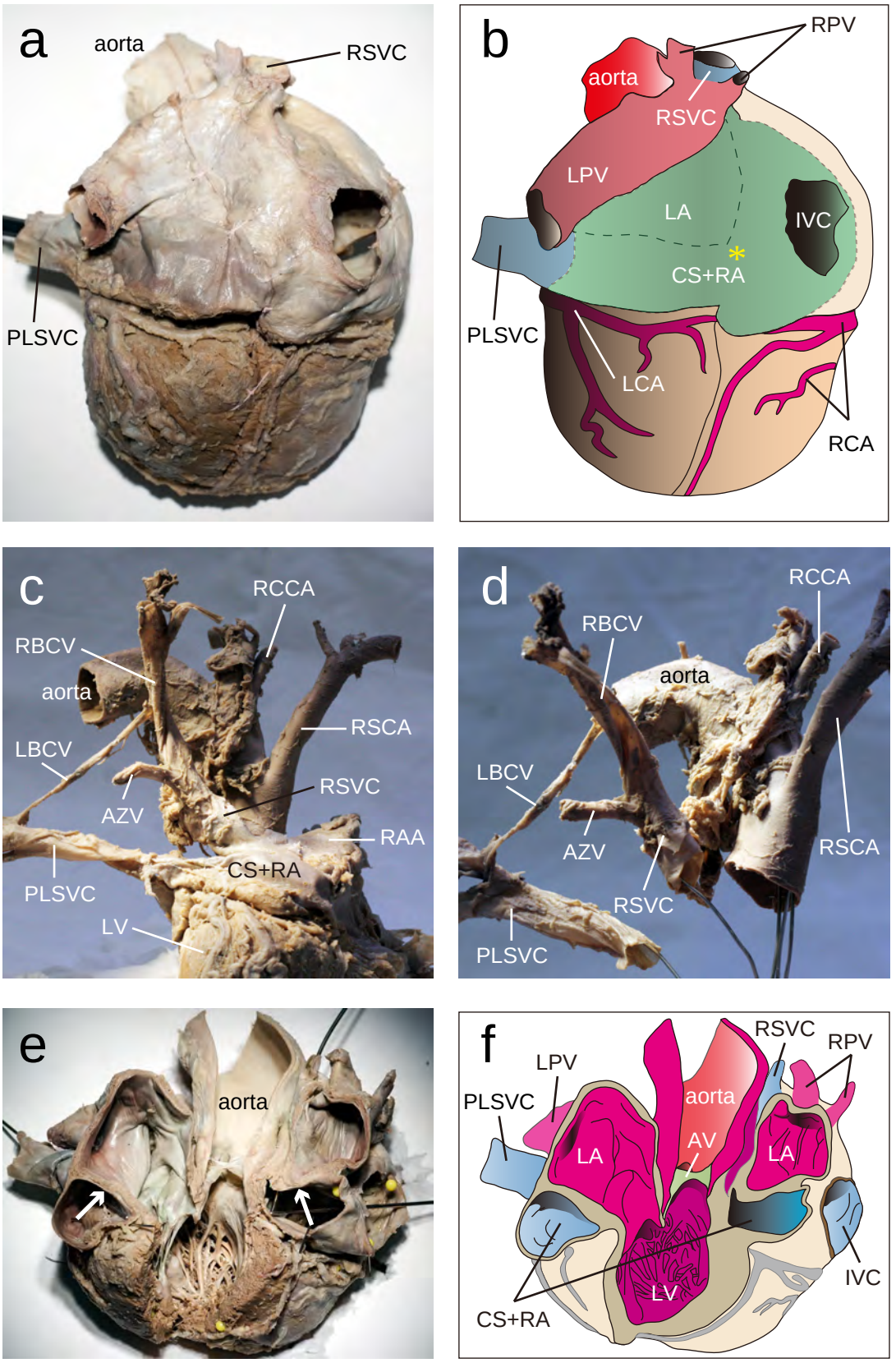
Webb WR, Gamsu G, Speckman JM, Kaiser JA, Federle MP, Lipton MJ (1982) Computed tomographic demonstration of mediastinal venous anomalies. AJR Am J Roentgenol 139:157–161

Figure Legends

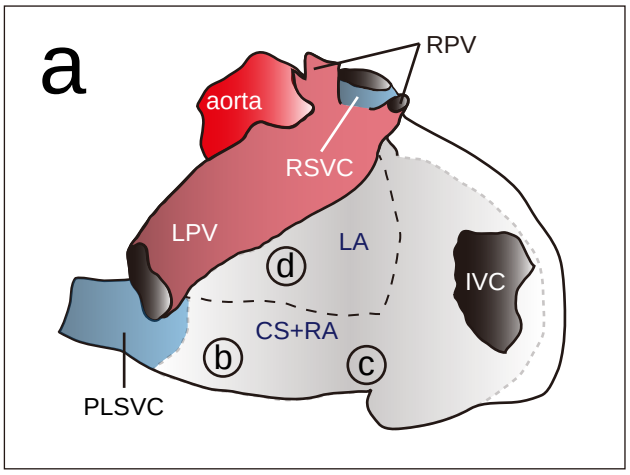
Fig. 1 Gross anatomy of the anomalous heart. **a** Dorsal view of the heart. **b** Schematic drawing of "**a**." The dashed line indicates the position of the septal wall between the cavity of the left atrium (LA) and the cavity of the coronary sinus that had merged with the right atrium (CS + RA). The green area indicates the sac-like structure. The sinoatrial node existed in a deep position marked with the yellow asterisk. **c** Dissected veins and arteries with the anomalous heart. **d** Dissected veins and arteries without the heart. **e** The dorsal inside view of the heart after cutting from the left ventricle to the ascending aorta. White arrows show the septal wall between the left atrium and the coronary sinus with the right atrium. **f** Schematic drawing of "**e**." *AV* aortic valve, *AZV* azygos vein, *IVC* inferior vena cava, *LBCV* left brachiocephalic vein, *LCA* left coronary artery, *LPV* left pulmonary vein, *LV* left ventricle, *PLSVC* persistent left superior vena cava, *RAA* right atrial appendage, *RBCV* right brachiocephalic vein, *RCA* right coronary artery, *RCCA* right common carotid artery, *RPV* right pulmonary vein, *RSCA* right subclavian artery, *RSVC* right superior vena cava

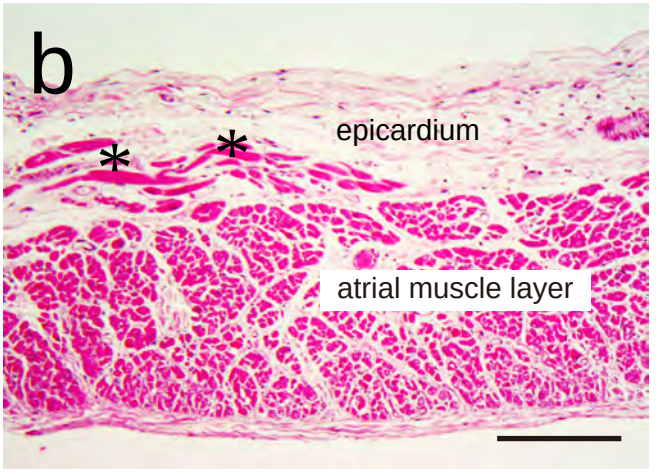
Fig. 2 Histological images of the anomalous heart following hematoxylin and eosin staining. **a** Schematic drawing of the heart. The dashed line indicates the position of the septal wall between the cavity of the left atrium (LA) and the cavity of the coronary sinus merged with the right atrium (CS + RA). The gray area indicates the sac-like structure. Positions of sampling (**b**–**d**) are shown. **b** Section of the roof in the coronary sinus with the right atrium proximal to the persistent left superior vena cava (*PLSVC*). **c**

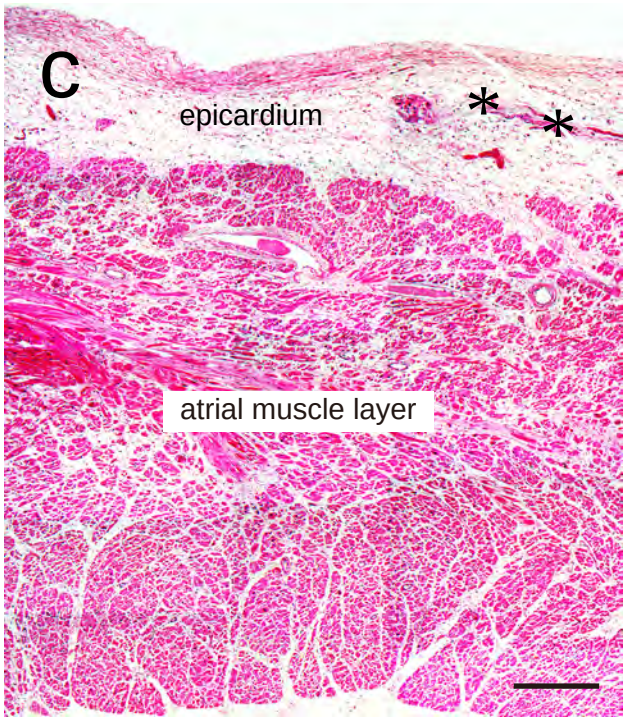
Section of the roof in the coronary sinus with the right atrium distal to the PLSVC. **d** Section of the roof of the left atrium. Asterisks indicate presumptive coronary sinus muscle bundles. Scale bars: 300 μm. *IVC* inferior vena cava, *LPV* left pulmonary vein, *RPV* right pulmonary vein, *RSVC* right superior vena cava

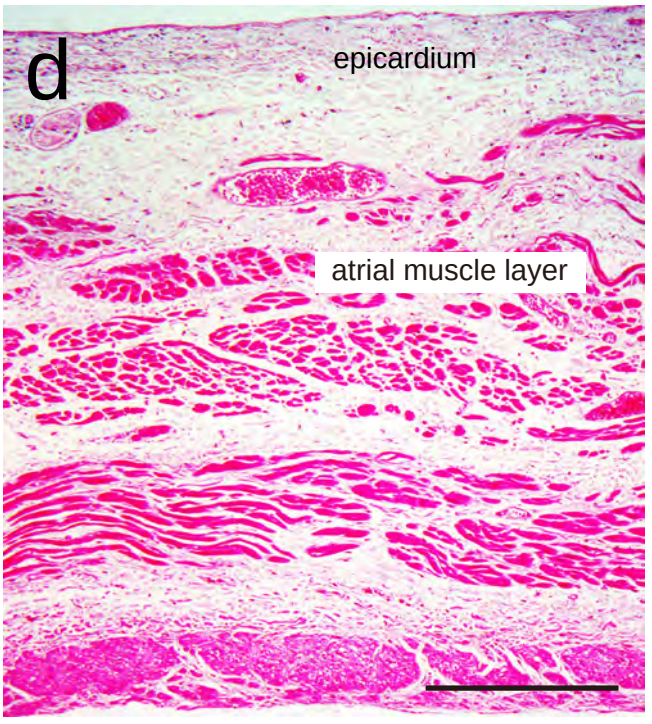


Shutoh et al. Fig. 1









Shutoh et al. Fig. 2