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Morphometric characteristics of myocardial sleeves of the pulmonary veins

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Abstract

Background: The pulmonary veins are covered by a myocardial layer, which is often an electrical substrate for atrial fibrillation. The aim of this study was to study the morphologic characteristics of the myocardial sleeves of pulmonary veins by examining a large group of freshly autopsied human material.

Methods and Results: The study macroscopically examined a total of 498 pulmonary veins draining the left atrium (120 unpreserved human hearts). In 75.0% of specimens, a classical pulmonary venous pattern was observed. The remainder of specimens either had an additional middle right pulmonary vein (20.0% of cases) or a common left pulmonary vein (5.0% of cases). Among all the veins seen in the classical pulmonary venous drainage type, the left superior pulmonary vein had the longest myocardial sleeves (9.4 ± 4.6 mm; coverage = 60.1 ± 19.4%), followed by the left inferior pulmonary vein (6.6 ± 3.5 mm; coverage = 47.6 ± 18.3%), the right superior pulmonary vein (6.0 ± 2.7 mm; coverage = 50.5 ± 13.9%) and then the right inferior pulmonary vein (5.0 ± 2.8 mm; coverage = 45.6 ± 16.2%; analysis of variance $p < .001$). In hearts with an additional right pulmonary vein, this vessel had the shortest myocardial sleeves (2.7 ± 1.1 mm; coverage = 36.0 ± 11.6%). In hearts with a common left pulmonary vein, the myocardial sleeves had the longest course for the common vein (13.7 ± 4.4 mm; coverage = 79.7 ± 4.9%).

Conclusions: Myocardial sleeves of the pulmonary veins were seen in each examined specimen, however, their length varied significantly. In hearts with a classical venous drainage pattern, the left superior pulmonary vein had the longest sleeves. When present, an additional middle right pulmonary vein had the shortest myocardial sleeves, while the left common pulmonary vein had the longest sleeves.

KEYWORDS

ablation, atrial fibrillation, cardiac anatomy, left atrium, myocardial sleeves, pulmonary veins

1 | INTRODUCTION

Pulmonary veins play a significant role in the pathogenesis of supraventricular tachycardias.[1] More specifically, the myocardial sleeves of the pulmonary veins are a known arrhythmogenic substrate capable of initiating and sustaining atrial fibrillation.[2] These structures are the short and slim extensions of the left atrial myocardium which covers the venoatrial junction and a distal portion of the pulmonary veins, which gradually thin out along the course of the pulmonary veins.[3–5] The cellular and electrophysiological characteristics of these myocytes differ from the surrounding atrial tissue.[6,7] Morphological and electrophysiological studies have identified pacemaker-like cells in the pulmonary myocardial sleeves that have abnormal automaticity and spontaneously triggered electrical activity.[8] Due to this trait, it has been suggested that left atrial tachyarrhythmias are caused by a reentry phenomenon generated by the myocardial sleeves or at the venoatrial junction.[9]

Several isolation techniques can be used to eliminate abnormal electrical activity from the pulmonary veins. The more popular procedures, such as radiofrequency circular ablation and cryoballoon ablation, achieve this goal by functionally disconnecting the myocardial sleeves from the atrial myocardium.[10–12] Thus, due to its electrophysiologic significance, clinicians should be familiar with the morphometric features of myocardial sleeves and their accompanying pattern of pulmonary venous drainage. Although several studies exist about the characteristics of these anatomical entities, the collected data has been gathered from small sample groups (ranging from 10 to 43 hearts) and from highly processed cardiac tissue (preserved, dehydrated, and stained).[13–16] Furthermore, the results from these studies are inconsistent and are most likely not reflective of the properties of myocardial sleeves in their in vivo state. The aim of this study was to address those shortcomings and to study the characteristics of the myocardial sleeves of the pulmonary veins on a large sample of fresh human autopsied material.

2 | MATERIALS AND METHODS

A total of 120 random adults (of which 37.5% were female) were selected for this investigation. They had a mean age of 51.8 ± 14.5 years and an average measured body mass index of 26.7 ± 4.0 kg/m^2. All subjects died of a noncardiac-related cause and had no history of persistent atrial fibrillation. The specimens were obtained from routine forensic medical autopsies performed at the Department of Forensic Medicine of the Jagiellonian University Medical College in Cracow, Poland. The study was conducted according to the principles expressed in the 1975 Declaration of Helsinki and was approved by the Bioethical Committee of the Jagiellonian University in Cracow, Poland.

The hearts and lungs were dissected from the chest cavity in a routine manner. They were briefly inspected and washed to remove excess blood. The left atrium and the ostia of the pulmonary veins were identified and labeled. The distal portions of the pulmonary veins along with their direct tributaries were bluntly dissected from the surrounding tissue. The dissected veins were cut-off from the rest of the pulmonary vasculature. We measured the length of the pulmonary vein's main trunk (defined as the vessel located between the last tributary [most proximal to the heart] and the venoatrial junction). We then assessed the length of the myocardial sleeves and the amount of coverage that they had on the pulmonary veins. This was easily accomplished due to their distinct color and characteristic fiber trajectory. The extent of myocardial sleeve coverage on the pulmonary veins was calculated by dividing the sleeves' length by the length of the pulmonary vein trunk and this value was reported as a percentage. All measurements were done with a 0.03-mm precision electronic caliper (YT-7201; YATO, Poland). To reduce human bias, two independent researchers performed the same measurements on the same sample. If their results varied by >10%, the specimen was reassessed and the mean of the two new values was calculated and reported as the final value.

The data was presented as mean values with its corresponding standard deviations. Shapiro–Wilk tests were used to determine if the quantitative data was normally distributed. Levene's test was performed to verify the relative homogeneity of variance. Student's *t* tests and the Mann–Whitney *U* tests were used for statistical comparisons. The analysis of variance or nonparametric Kruskal–Wallis test was used to compare the values between different groups. Detailed comparisons were performed using Tukey's post hoc analyses. Qualitative variables were compared using χ^2 tests of proportions with Bonferroni corrections to account for the multiple comparisons. A $p < .05$ was considered statistically significant. Statistical analyses were performed using StatSoft STATISTICA 13.1 software for Windows (StatSoft Inc., Tulsa, OK, USA).

3 | RESULTS

We identified and analyzed 498 pulmonary veins draining the left atrium. In 90 of the examined hearts (75.0%), we observed a classical venous pattern consisting of two right-sided and two left-sided pulmonary veins. An additional middle right pulmonary vein was observed in the remaining 24 hearts (20.0%) and 6 hearts (5.0%) had one single left-sided common pulmonary vein.

Myocardial sleeves were present in each examined vein, although their characteristics varied significantly from specimen to specimen. Table 1 presents the length of the pulmonary vein trunk, the length of the myocardial sleeves and their associated percentage coverage in hearts with a classical pulmonary venous drainage. Analysis of individual veins in these hearts showed that the left superior pulmonary vein had the longest trunk, the longest myocardial sleeves, and the largest myocardial sleeve coverage. Meanwhile, the right inferior pulmonary vein had the lowest values for the above-mentioned parameters (Table 1). It was observed that left-sided veins were significantly longer than right-sided veins, although no such difference was found when comparing superior and inferior veins on the same side (Table 1). When compared to the myocardial sleeves of the left inferior pulmonary vein, the myocardial sleeves of the left superior vein were significantly longer and covered a larger percentage of the trunk (Table 1). This trend was not observed between right-sided veins (Table 1). Generally, the superior veins had longer myocardial sleeves and enveloped a larger area of the trunk than the inferior veins, but in paired comparisons, this trend was found to only be statistically significant for left-sided veins.

Table 2 presents results from hearts with a nonclassic pulmonary venous drainage pattern. A comparison of individual corresponding veins revealed no significant differences between hearts

TABLE 1 Morphometric features of the pulmonary vein trunk and myocardial sleeves for classical pulmonary vein drainage type (mean ± *SD*)

						Pairwise comparisons *p* values					
Pulmonary vein	**Left superior ($n = 90$)**	**Left inferior ($n = 90$)**	**Right superior ($n = 90$)**	**Right inferior ($n = 90$)**	***p* Value ANOVA**	**Left superior vs. left inferior**	**Right superior vs. right inferior**	**Left superior vs. right superior**	**Left inferior vs. right inferior**	**Left superior vs. right inferior**	**Right superior vs. left inferior**
Trunk length (mm)	15.1 ± 4.6 (range: 8.0–27.0)	13.5 ± 4.0 (range: 6.1–22.3)	11.8 ± 4.0 (range: 3.8–22.0)	11.0 ± 3.7 (range: 4.0–22.2)	**<.001**	NS	NS	**<.001**	**<.001**	**<.001**	**.028**
Myocardial sleeve length (mm)	9.4 ± 4.6 (range: 1.0–21.0)	6.6 ± 3.5 (range: 1.0–18.3)	6.0 ± 2.7 (range:1.0–13.2)	5.0 ± 2.8 (range: 1.0–19.0)	**<.001**	**<.001**	NS	**<.001**	**<.001**	**<.001**	NS
Myocardial sleeve coverage (%)	60.1 ± 19.4 (range: 9.6–91.0)	47.6 ± 18.3 (range: 11.6–90.7)	50.5 ± 13.9 (range: 11.3–83.8)	45.6 ± 16.2 (range: 17.3–92.1)	**<.001**	**.0049**	NS	**<.001**	NS	**<.001**	NS

Note: Statistically significant values are given in bold.

Abbreviations: ANOVA, analysis of variance; NS, not significant.

with classical venous drainage and those with nonclassical venous drainage. In the hearts that had an additional right pulmonary vein, the extra vessel was shorter than all the other veins and it had the shortest myocardial sleeves and the lowest trunk coverage (Table 2; all $p < .05$). Moreover, the additional middle right pulmonary vein trunk was found to be significantly shorter than the right superior vein (7.8 ± 3.2 vs. 11.8 ± 4.0 mm, $p < .001$) and the right inferior vein (7.8 ± 3.2 vs. 11.0 ± 3.7 mm, $p < .001$) of hearts with classical venous drainage. The same tendency was observed when analyzing the length of the myocardial sleeves (2.7 ± 1.1 vs. 6.0 ± 2.7 mm, $p < .001$ and 2.7 ± 1.1 vs. 5.0 ± 2.8 mm, $p < .001$, respectively) and the myocardial sleeve coverage (36.0 ± 11.6% vs. 50.5 ± 13.9%, $p < .001$ and 36.0 ± 11.6% vs. 45.6 ± 16.2%, $p = .007$, respectively). In hearts that had a single common left pulmonary vein, this vessel was found to be significantly longer than the left inferior pulmonary vein of classical hearts (17.4 ± 6.1 vs. 13.5 ± 4.0 mm, $p = .028$). However, this trend was not statistically significant when comparing the common left pulmonary vein with the left superior vein (17.4 ± 6.1 vs. 15.1 ± 4.6 mm, $p = .248$). The length of the myocardial sleeves and percentage trunk coverage were significantly greater in hearts with a single common left pulmonary vein than in both left-sided veins (Table 2; all $p < .05$). The sex of the donor did not affect any studied parameter.

4 | DISCUSSION

Atrial fibrillation is the most common sustained tachyarrhythmia seen in daily clinical practice. Arrhythmogenic foci responsible for triggering the arrhythmia are often located in the left atrium, especially in the region of the pulmonary venous ostia.[16,17] Left atrial myocardial extensions of the pulmonary veins, also known as myocardial sleeves of the pulmonary veins, were first described in 1836 by Ferdinand Raeuschel, a medical student and pupil of Jan Evangelista Purkyně.[18] These structures were largely forgotten until the end of the 20th century when it was shown that pulmonary veins were the culprit responsible for a large majority of supraventricular tachyarrhythmias.[2,19] The discovery of the arrhythmogenic role of myocardial sleeves created a new branch of electrophysiology, which pioneered new invasive techniques targeted against ectopic pulmonary vein activation. A good understanding of the morphology of myocardial sleeves continues to help explore the underlying causes of atrial fibrillation.

In our examination, the myocardial sleeves of the pulmonary veins were grossly visible in each specimen. This is consistent with reports from other studies,[20] although some authors' investigations reported that their presence was difficult to detect.[16,17] Histologically, myocardial sleeves have complex features. Ho et al.[4] showed that the walls of the distal portion of the pulmonary veins consist of a thin endothelium, an irregular medial layer of smooth muscle cells, fibrous tissue, and a thick fibrous adventitia. Arising from the left atrium and surrounding the pulmonary vein, the myocardial sleeves have varying structure, thickness, and length.[4,21] Roux et al.[13]

TABLE 2 Morphometric features of the pulmonary vein trunk and myocardial sleeves with division into groups with different pulmonary vein drainage types (mean ± *SD*)

	Left superior pulmonary vein	Left inferior pulmonary vein	Right superior pulmonary vein	Right inferior pulmonary vein	Middle right pulmonary vein	Common left pulmonary vein
Classical pulmonary vein type ($n = 90$)						
Trunk length (mm)	15.1 ± 4.6 (range: 8.0–27.0)	13.5 ± 4.0 (range: 6.1–22.3)	11.8 ± 4.0 (range: 3.8–22.0)	11.0 ± 3.7 (range: 4.0–22.2)	...	...
Myocardial sleeve length (mm)	9.4 ± 4.6 (range: 1.0–21.0)	6.6 ± 3.5 (range: 1.0–18.3)	6.0 ± 2.7 (range: 1.0–13.2)	5.0 ± 2.8 (range: 1.0–19.0)		
Myocardial sleeve coverage (%)	60.1 ± 19.4 (range: 9.6–91.0)	47.6 ± 18.3 (range: 11.6–90.7)	50.5 ± 13.9 (range: 11.3–83.8)	45.6 ± 16.2 (range: 17.3–92.1)		
Additional middle right pulmonary vein type ($n = 24$)						
Trunk length (mm)	14.8 ± 5.9 (range: 7.9–31.3) $p = .821$[a]	14.2 ± 7.2 (range: 5.9–37.7) $p = .559$[a]	11.5 ± 3.1 (range: 7.5–19.0) $p = .758$[a]	11.1 ± 3.7 (range: 6.4–23.0) $p = .887$[a]	7.8 ± 3.2 (range: 4.0–17.7)	...
Myocardial sleeve length (mm)	9.4 ± 4.9 (range: 2.8–23.5) $p = .994$[a]	6.9 ± 4.0 (range: 1.6–17.5) $p = .656$[a]	5.5 ± 2.4 (range: 2.1–10.6) $p = .404$[a]	5.2 ± 2.8 (range: 1.4–11.9) $p = .87$[a]	2.7 ± 1.1 (range: max: 1.1–5.2)	
Myocardial sleeve coverage (%)	61.4 ± 16.4 (range: 27.7–92.5) $p = .754$[a]	48.3 ± 14.9 (range: 22.9–75.3) $p = .866$[a]	46.9 ± 12.6 (range: 20.2–67.2) $p = .256$[a]	45.2 ± 16.3 (range: 17.9–89.1) $p = .918$[a]	36.0 ± 11.6 (range: 16.7–65.6)	
Common left pulmonary vein type ($n = 6$)						
Trunk length (mm)	...	...	10.5 ± 2.5 (range: 7.3–14.1) $p = .415$[b]	10.7 ± 2.2 (range: 8.9–14.4) $p = .842$[b]	...	17.4 ± 6.1 (range: 9.6–27.0)
Myocardial sleeve length (mm)			5.5 ± 2.0 (range: 3.7–9.2) $p = .664$[b]	5.1 ± 1.7 (range: 3.5–7.9) $p = .678$[b]		13.7 ± 4.4 (range: 8.1–20.3)
Myocardial sleeve coverage (%)			52.0 ± 8.0 (range: 42.1–65.1) $p = .768$[b]	46.4 ± 6.4 (range: 38.9–54.7) $p = .899$[b]		79.7 ± 4.9 (range: 73.0–84.4)

[a]Additional middle right pulmonary vein-type versus classical pulmonary vein type.

[b]Common left pulmonary vein-type versus classical pulmonary vein type.

TABLE 3 Comparison of the results of previous studies on pulmonary veins myocardial sleeves length (classical confluence type)

Study (year)	Nathan et al. (1966)	Saito et al. (2000)	Tagawa et al. (2001)	Kholova et al. (2003)	Hassink et al. (2003)	Roux et al. (2004)	Current study (2020)
Material	Macroscopic examination; formalin fixation	Macroscopic examination; formalin fixation	Macroscopic examination; 10% formalin fixation	Histological examination; formalin fixation and tissue processing	Histological examination; 10% formalin fixation and tissue processing	Histological examination; 4% formalin fixation and tissue processing	Macroscopic examination; fresh, nonpreserved tissue
Data type	Mean (min–max)	Mean ± *SD*	Mean ± *SD*	Mean ± *SD*	Mean ± *SD*	Mean (min–max)	Mean ± *SD*
Non-AF individuals (*N*)	16	15	10	27	14	10	90
Pulmonary vein myocardial sleeves length (mm)							
Left superior	18.0 (8.0–24.0)	14.3 ± 7.5	8.7 ± 4.4	**7.2 ± 6.5***	**8.8 ± 3.6***	22.2 (9.0–38.0)	9.4 ± 4.6
Left inferior	10.0 (1.0–19.0)	9.3 ± 4.6	**3.3 ± 2.8***	7.6 ± 9.0	8.3 ± 6.6	15.3 (9.0–30.0)	6.6 ± 3.5
Right superior	13.0 (5.0–25.0)	12.6 ± 6.6	5.1 ± 3.9	8.2 ± 9.7	10.4 ± 8.7	18.2 (12.0–31.0)	6.0 ± 2.7
Right inferior	8.0 (1.0–17.0)	5.8 ± 3.6	**1.7 ± 1.9***	10.1 ± 8.3	7.2 ± 4.9	12.3 (7.0–25.0)	5.0 ± 2.8
AF individuals (*N*)	...	19	11	16	6	...	...
Pulmonary vein myocardial sleeves length (mm)							
Left superior	...	14.8 ± 6.0	8.4 ± 2.8	**13.1 ± 10.0***	**15.1 ± 3.8***	...	...
Left inferior	...	6.6 ± 4.3	**7.3 ± 4.6***	7.1 ± 7.9	8.9 ± 1.8	...	...
Right superior	...	11.8 ± 4.9	6.5 ± 3.5	14.8 ± 13.8	10.2 ± 6.4	...	...
Right inferior	...	6.0 ± 4.5	**5.7 ± 2.4***	9.8 ± 10.3	7.2 ± 2.4	...	...

Note: Statistically significant values are given in bold.

Abbreviation: AF, atrial fibrillation.

*Statistically significant difference (non-AF vs. AF patients), $p < .05$.

indicated that there are two distinct layers of muscular cells at the base of the venoatrial junction: a circulatory external layer and a longitudinal internal layer. The myocardial bundles of the sleeves are arranged circularly, longitudinally, and obliquely and are vastly interconnected with each other.[4] The myocardial layer is usually thickest at the venoatrial junction (with an average thickness of 1.1 mm) and it thins out along the course of the pulmonary vein trunk until it disappears.[4] Interestingly, it does not extend over the tributaries of the pulmonary vein trunk, ending before the most distal tributary joins the trunk.[3]

The circumferential thickness of the myocardial layer is not uniform and structural variations exist between specimens. Moreover, throughout the course of the pulmonary vein trunk and at the venoatrial junction, visible gaps in the histological architecture can be observed which are filled by fibrous connective tissue. Several electrophysiological studies have shown that myocardial sleeves have common features with the sinoatrial node pacemaker cells, but they also have unique properties that predispose them to spontaneous electrical activity.[8] The myocardial cells house dense nerve fibers and ganglions of the autonomic nervous system. Different populations of specialized cells, such as telocytes, have also been reported within these anatomical structures.[22]

The macroscopic and microscopic traits of the area of the pulmonary venous trunk make it an extremely frequent arrhythmogenic site that facilitates electrical reentry and enhances automaticity.[1] Moreover, numerous studies have reported that patients with atrial fibrillation have altered the structure and function of myocardial sleeves compared with nonarrhythmic patients.[14,15,23,24] The length of myocardial sleeves is one of the main factors which may play a significant role in the initiation and sustenance of atrial fibrillation.[15] Therefore, it should come as no surprise that the superior pulmonary veins, which have significantly longer muscular sleeves, have been reported to be more arrhythmogenic than the inferior pulmonary veins.[4]

A thorough review of previous morphometrical studies reveals large discrepancies in the reported length of the sleeves of the pulmonary veins (Table 3). Such incongruencies are most likely due to small sample sizes and different approaches in tissue processing and collecting measurements. Formaldehyde fixation and histological processing significantly affect tissue dimensions, causing considerable shrinkage of samples.[25,26] The current study was unique because it analyzed a much larger group of specimens (almost twice the combined amount of all previously studied hearts). Furthermore, the measurements were made on fresh, nonpreserved autopsied material, allowing for a more truthful portrayal of their actual physiologic characteristics.

Although previous studies disagreed about the length of the myocardial sleeves, most have reported common observations about this anatomical area. Generally, superior pulmonary veins possessed the longest sleeves, while the left superior pulmonary vein had the largest myocardial coverage.[4,13,15,20] The study by Haissaguerre et al.[2] mapped the location of foci responsible for initiating atrial fibrillation and reported that the majority were located in the left superior pulmonary vein. This finding could explain the probable relationship between the length of the myocardial sleeves and their arrhythmogenic potential.[2] Several small studies contrasted the morphology of myocardial sleeves of pulmonary veins of patients with and without atrial fibrillation,[14–16,20] although they reported no definite results. So far, only two studies have demonstrated that patients with atrial fibrillation had significantly longer myocardial sleeves in the left superior pulmonary vein than patients that did not (Table 3).[14,16]

The current study uniquely provided characteristics of myocardial sleeves based on different pulmonary venous drainage patterns (Table 2). The classical pulmonary venous pattern (with two right and two left pulmonary veins) is present in about 70% of the population, 20% of the population has a heart with an additional middle right pulmonary vein and 4.5% of the population has a single common ostium for the left superior and the left inferior pulmonary vein.[3] Some studies have shown that patients with variations in pulmonary venous ostia had higher instances of atrial fibrillation than patients with a classical pulmonary drainage pattern. Therefore, it would be beneficial to have as much information about the characteristics of myocardial sleeves in patients with the most common anatomical variants.[27–29] The explanation why the myocardial sleeves over the single common trunk for the left superior and the left inferior pulmonary vein are the longest may be derived from fact, that in this variant of the pulmonary venous drainage incorporation of the left-sided pulmonary veins to the left atrium wall is terminated more proximally to the lung hilum and thus the structure of the vein trunk belongs to the atrium, not to the venous vasculature.

This study had some limitations. The main one pertains to the fact that it only considered hearts with no known atrial fibrillation. The second limitation was that the measurements were performed postmortem. Consequently, these did not fully represent the physiology of tissues in vivo, and could not have taken into account the dimensional changes of the cardiac cycle. Nevertheless, we believe that these drawbacks did not significantly impede our morphological analysis of the myocardial sleeves of the pulmonary veins.

5 | CONCLUSION

The myocardial sleeves of the pulmonary veins are highly variable structures. Although they can be observed macroscopically, their length and coverage of the main pulmonary vein trunk can vary tremendously. This study demonstrated that in hearts with classical venous drainage (two right and two left pulmonary veins), the left superior pulmonary vein had the longest myocardial sleeves and the greatest trunk coverage. A comparison of individual veins revealed no significant differences between hearts with classical venous drainage and those with nonclassical venous drainage. Nevertheless, when present, the additional middle right pulmonary vein had the shortest sleeves, while the left common pulmonary vein had the longest sleeves with an average coverage greater than three-quarters of the length of the pulmonary vein trunk.

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