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Topographic characteristics of the left atrial medial isthmus

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Abstract

Background: The purpose of this study was to provide detailed topography of the left atrial medial isthmus (situated between the right inferior pulmonary vein ostium and the medial part of the mitral annulus).

Methods: Two hundred human hearts (Caucasian, 22.5% females, 48.7 ± 4.9 years old) were investigated.

Results: The mean length of the medial isthmus was 42.4 ± 8.6 mm. Additionally, the medial isthmus line was divided by the oval fossa into three sections with equal mean lengths (upper: 14.2 ± 7.2 vs middle: 14.1 ± 6.1 vs lower: 14.9 ± 4.6 mm; $P > .05$). The left upper section of the atrial wall was thinner than the lower section (2.5 ± 1.1 vs 3.4 ± 1.6 mm; $P < .0001$). This study noted three separate spatial arrangements of the isthmus line. Type I (54.5%) had an oval fossa located outside the isthmus line; type II (32.5%) had an oval fossa crossed by the isthmus line, and type III (13.0%) had an oval fossa rim located tangentially to the isthmus line. In 68.5% of the examined specimens, the isthmus area had a smooth surface. Conversely, the remaining 31.5% had additional structures within its borders such as diverticula, recesses, and tissue bridges.

Conclusion: This study is the first to describe the morphometric and topographical features of the left atrial medial isthmus. Interventions within the medial isthmus line should be performed cautiously, especially when they are transected by the oval fossa (32.5%). Careful navigation of the area is also recommended due to the possibility of existent additional structures. The latter could lead to catheter entrapment during ablation procedures.

KEYWORDS
ablation, alternative isthmus, atrial fibrillation, interatrial septum, medial left atrial isthmus, septal ablation, septal isthmus

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac dysrhythmia. It is often accompanied by a wide array of complications ranging from frequent hospital admissions to increased risk of stroke and death. Structural, architectural, and/or electrophysiological abnormalities within the left atrium have been shown to trigger or perpetuate AF.[1] A common and effective treatment option for patients with AF is catheter ablation of the arrhythmogenic substrate or of the conduction pathways.[2] One of the main objectives of left AF ablation is to enable the electrical disconnection (isolation) of the pulmonary venous ostia from the remaining atrial tissue.[3] In order to improve the efficacy of the procedure and to prevent recurrence, specific ablation areas within the left atrium should be targeted since they have been shown to interrupt re-entrant circuits responsible for AF.[4] The most frequent location sought out during ablation procedures is the mitral isthmus (or left atrial or left lateral isthmus), a component of the left atrial wall located between the ostium of the left inferior pulmonary vein and the mitral valve annulus.[5] However, alternative locations are also used in the invasive treatment of AF and perimitral flutter. The most important ones include the left atrial medial isthmus, the superolateral mitral isthmus, the isthmus of the left atrial appendage, as well as the roof, the anteromedial, and anterolateral lines of the atrium.[5–7]

The left atrial medial isthmus (also known as the alternative isthmus or the septal isthmus) is an anatomical area bordering the right inferior pulmonary vein and the medial part of the mitral annulus.[8]

Furthermore, due to its close proximity with the interatrial septum, it is generally harder to access. This is especially the case during catheter septal ablation procedures for perimitral tachycardia.[9,10] In contrast to the mitral isthmus—whose anatomy has been well documented in recent years, the region of the medial isthmus remains poorly understood.[5,11]

The purpose of this study was to provide the first detailed topographic characteristics of the left atrial medial isthmus and its surrounding entities. We hope that our findings will help educate clinicians about what to expect when planning and performing procedures within this specific area of the heart.

2 | MATERIAL AND METHODS

This study was approved by the Bioethical Committee of the Jagiellonian University in Cracow, Poland (1072.6120.144.2019). The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. The methods were carried out in accordance with the approved guidelines.

2.1 | Study population

This study surveyed 200 autopsied human hearts. The organs belonged to Caucasian individuals (of which 22.5% were female) who were 48.7 ± 4.9 years of age. The average body mass index (BMI) of the donors was 26.8 ± 17.3 kg/m^2, and the mean heart weight was 439.0 ± 96.0 g. The hearts were collected during routine forensic medical autopsies. The leading causes of death of the studied subjects were suicide, murder, and traffic/home accidents. Donors with known severe anatomic defects, past cardiac surgeries, or vascular or cardiac pathologies discovered during autopsy (aneurysms, storage diseases, trauma) were excluded from this study.

2.2 | Dissection and measurements

Each heart, along with the proximal portions of the great vessels, was dissected from the thoracic cavity. All specimens were weighed and placed in a 10% paraformaldehyde solution for a maximum of 2 months.

Subsequently, all the hearts were opened in routine manner. In order to expose the left atrial medial isthmus and the left-sided interatrial septal region, a cut was made at the roof and at the anterior wall of the left atrium. The right atrium was opened via intercaval incision. Additional measurements were obtained with the heart held in anatomical position. Linear measurements were gathered using 0.03-mm precision electronic calipers (YT-7201; YATO, Poland). To reduce human bias, all measurements were recorded by two independent researchers. If any result differed by more than 10%, the specimen was remeasured.

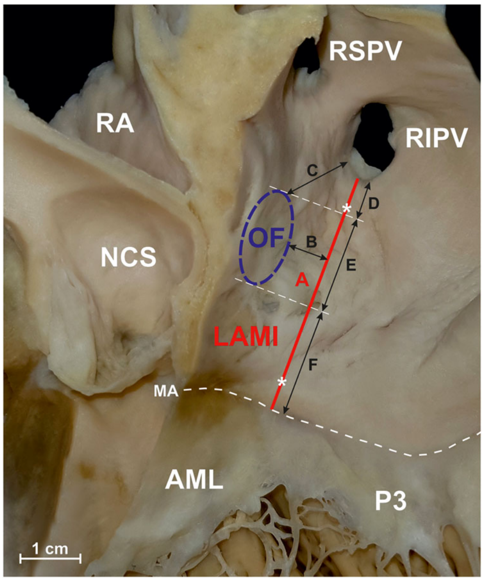

FIGURE 1 Photograph of a cadaveric heart specimen showing studied region of the left atrium. The left atrial medial isthmus (LAMI) is marked. Measurements (A-F) are described in *Material and Methods* section. Cross-section points (*) are marked, where the myocardial thickness was measured. AML = anterior mitral leaflet; MA = mitral valve annulus; NCC = noncoronary aortic sinus; OF = oval fossa; P3 = third segment of posterior mitral leaflet; RA = right atrium; RIPV = right inferior pulmonary vein [Color figure can be viewed at wileyonlinelibrary.com]

The appraisal began by identifying the left atrial medial isthmus. It was defined as the shortest, straight, endocardial line located between the inferior margin of the right inferior pulmonary vein ostium and the medial part of the mitral annulus (2-3 o'clock position of mitral annulus looking from atrial aspect). Variations in the right-sided pulmonary veins ostia were noted. The rim of the oval fossa was determined from the right atrial side and its location was marked on the left atrial side of the septum. After these initial steps, the following measurements were recorded (Figure 1):

- the length of the medial isthmus (A),
- the shortest distance between the medial isthmus line and the oval fossa rim (B) (N.B.: if the medial isthmus line crossed the oval fossa, the distance was expressed as a negative number),
- the shortest distance between the oval fossa rim and the right inferior pulmonary vein ostium (C),
- the length of the section of the medial isthmus found between the inferior margin of the right inferior pulmonary vein ostium and the superior edge of the oval fossa rim (upper sector medial isthmus length) (D),
- the length of the section of the medial isthmus found within the lines demarcated by the superior and inferior oval fossa rim (middle sector medial isthmus length) (E),

- the length of the section of the medial isthmus found between the inferior edge of the oval fossa rim and the mitral valve annulus (lower sector medial isthmus length) (F).

The left atrial medial isthmus was cut in two places: 5 mm below the inferior margin of the right inferior pulmonary vein ostium (upper point) and 5 mm above the margin of the medial part of the mitral annulus (lower point) (Figure 1). The myocardial thickness was measured at the above-mentioned locations.

Other defining features of the endocardial medial isthmus surface were noted. We documented the presence of any additional structures, such as crevices, diverticula, trabeculae, and/or tissue bridges, present within the isthmus. Also, we determined the type of coronary artery dominance supplying the inferior interventricular septum (right dominant, left dominant, or codominant).

2.3 | Statistical analysis

The data were reported as mean values with corresponding standard deviations. Student's *t*-tests and Mann-Whitney U tests were done to determine if there were any differences between sexes and measured heart parameters. The Kruskal-Wallis one-way analysis of variance with multiple comparisons was performed to find out whether there were significant differences between the three main variants of the medial isthmus. Correlation coefficients were calculated to determine statistical dependence. To detect a simple correlation ($r = 0.21$) with 80% power and a 5% significance level (two-tailed; $\alpha = 0.05$; $\beta = 0.2$), the required minimal sample size was set at approximately 176 cases. Statistical analyses were performed using StatSoft STATISTICA 13.1 software for Windows (StatSoft Inc., Tulsa, OK). Results were considered statistically significant when the *P*-value was lower than 0.05.

3 | RESULTS

All measurements obtained in this study are presented in Table 1. The mean length of the left atrial medial isthmus line was 42.4 ± 8.6 mm and was positively correlated with the age of the donor ($r = 0.31$, $P < .001$) and cardiac weight ($r = 0.25$, $P = .004$). The medial isthmus line was divided by the oval fossa into three sections with equal mean lengths (upper section: 14.2 ± 7.2 vs middle section: 14.1 ± 6.1 vs lower section: 14.9 ± 4.6 mm; $P > .05$). The length of the lower medial isthmus section correlated with the age of the donor ($r = 0.24$, $P < .001$). The left atrial wall was thinner in the upper section (the area closer to the right inferior pulmonary vein ostium) when compared to the lower section (the area closer to the mitral valve annulus) (2.5 ± 1.1 vs 3.4 ± 1.6 mm; $P < .0001$). Donor's sex had no impact on any measured parameter.

We found three distinct spatial arrangements of the left atrial medial isthmus with respect to the oval fossa. The most common variant had an oval fossa located outside the medial isthmus line (type I). This setup occurred in 54.5% of cases. In 32.5% of hearts, the oval fossa was crossed by the medial isthmus line (type II) (Figure 2) and in 13.0% of cases the oval fossa rim was located tangentially to the left atrial medial isthmus line (type III). Some significant morphometric differences were visible between these types. The length of the medial isthmus was smallest in type I (40.9 ± 7.5 mm) when compared to types II (44.2 ± 9.9 mm) and III (44.6 ± 8.8 mm) ($P = .016$). Moreover, the length of the upper section of the medial isthmus was shortest in type I (type I: 12.8 ± 5.7 vs type II: 16.6 ± 9.3 vs type III: 15.8 ± 6.7 mm, $P = .001$). Left atrial myocardial thickness in the upper point of the medial isthmus also differed between the three variants, where type I had the lowest thickness (type I: 2.2 ± 0.8 vs type II: 2.8 ± 1.1 vs type III: 3.0 ± 1.8 mm, $P = .04$).

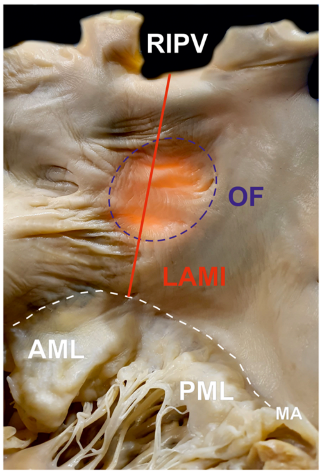

FIGURE 2 Photograph of a cadaveric heart specimen showing studied region of the left atrium with transluminated oval fossa (OF) and marked left atrial medial isthmus (LAMI). Type II of mutual OF—LAMI arrangement—the OF is crossed by the isthmus line. AML = anterior mitral leaflet; MA = mitral valve annulus; PML = posterior mitral leaflet; RIPV = right inferior pulmonary vein [Color figure can be viewed at wileyonlinelibrary.com]

In 68.5% of our specimens, the endocardial surface of the medial isthmus area was relatively smooth. In the remaining 31.5% hearts, we found additional structures located in the left atrial medial isthmus area, which are listed in Table 2 and displayed in Figure 3.

We identified right coronary artery dominance in 86.5% of all cases, whereas left artery dominance and codominance were observed in 6.0 and 7.5% of cases, respectively. The type of coronary artery supply had no effect on the topography of the studied region. In 78.5% of all studied samples, we observed a classical pattern of right sided pulmonary venous drainage (occurring via the right superior and right inferior pulmonary vein ostium). The remaining 21.5% of hearts had modified venous circulatory routes. The most frequently observed anomaly was the presence of an additional middle right pulmonary vein (20.0%), although there were also variants, which had four independent ostia for the right-sided pulmonary veins (1.0% of cases) and other hearts, which had a single common ostium for the right-sided pulmonary veins (0.5% of cases). Regardless of the type of pulmonary venous drainage, there were no observable differences in any measured parameter.

TABLE 1 Results of obtained measurements [mm]

	Mean	SD	Min	Max	Median	Q_1	Q_3
A—Length of the left atrial medial isthmus (LAMI)	43.1	8.7	16.1	64.2	42.0	36.7	47.9
B—LAMI to oval fossa distance	1.4	6.3	−15.4	19.3	3.3	−4.3	5.8
C—Oval fossa to right inferior pulmonary vein ostium distance	15.6	5.7	2.0	50.8	15.0	12.1	17.5
D—Upper sector LAMI length	14.2	7.2	3.7	44.0	13.1	10.0	17.3
E—Middle sector LAMI length	14.1	6.1	4.1	34.6	13.9	10.0	17.6
F—Lower sector LAMI length	14.9	4.6	4.7	30.5	14.6	11.7	17.9
LAMI upper point LA myocardial thickness	2.5	1.1	0.8	11.5	2.1	1.7	2.7
LAMI Lower point LA myocardial thickness	3.4	1.6	1.0	16.0	3.2	2.5	4.2

LAMI = left atrial medial isthmus; LA = left atrial; SD = standard deviation; Q_1 and Q_3 = lower and upper quartiles.

TABLE 2 Additional structures located in the left atrial medial isthmus area and its prevalence (*N* = 200)

	Number of cases	Prevalence (%)
1—Single diverticulum	21	10.5
2—Single recess	9	4.5
3—Single bridge	7	3.5
4—Multiple diverticula	13	6.5
5—Multiple recesses	6	3.0
6—Bridge with accompanying holes	3	1.5
7—Bridge with accompanying recess	2	1.0
8—Bridge with accompanying hole	2	1.0
Total number of hearts with additional structure within the isthmus area	63	31.5

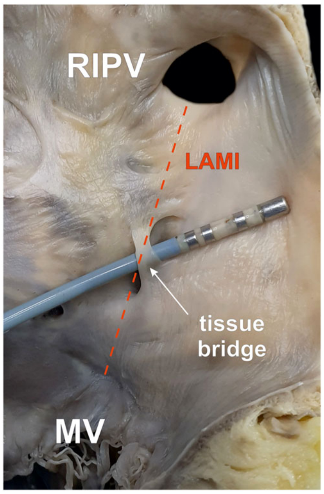

FIGURE 3 Photograph of a cadaveric heart specimen showing left atrial medial isthmus (LAMI) area. The tissue bridge is visible within the LAMI line with catheter inserted under the bridge. MV = mitral valve; RIPV = right inferior pulmonary vein [Color figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

This study is the first to provide topographical information about the left atrial medial isthmus region. Macroscopic characteristics of the medial isthmus (such as its length, shape, and location) could help determine the type of ablation technique required and improve procedural success rate.[12] Therefore, a thorough understanding of its anatomy could significantly improve clinical outcomes of ablation procedures. When comparing the left atrial medial isthmus to other left atrial lines, it was observed that the medial isthmus was the longest among all isthmuses (medial isthmus: 42.4 ± 8.6 mm vs mitral isthmus: 28.8 ± 7.0 mm vs left atrial appendage isthmus: 14.2 ± 4.8 mm; $P < .0001$). However, it was significantly shorter than the anteromedial line (49.4 ± 8.6 mm) and anterolateral line (50.1 ± 7.2 mm).[5,6] We also found that variations in the pulmonary vein ostia did not affect the morphometric features of the left atrial medial isthmus. Previous studies showed this same trend when describing the topography of the mitral isthmus (also known as left lateral isthmus) region.[5]

We also observed that the configuration between the medial isthmus and the true interatrial septum (defined as the floor of the oval fossa and its immediate muscular inferoanterior rim) could have clinical implications.[13] Three different types of spatial arrangements were observed: type I (found in 54.5% of all cases) had an oval fossa located outside the medial isthmus line; type II (32.5% of all cases) had an oval fossa crossed by the medial isthmus line, and type III (13.0%) had an oval fossa rim located tangentially to the medial isthmus line. Among these three broad categories, the first type had the most convenient setup for future interventions, since the medial isthmus line was located far away from the true interatrial septum. Therefore, transseptal access would pose minimal risk of injury to surrounding septal structures. In the remaining types (types II and III) access to the medial isthmus line via the transseptal puncture would be hindered and would need to be achieved via alternative approaches.

Our results also showed that an intersecting oval fossa had a significant impact on the length of the medial isthmus (which was lower in type I when compared to types II and III) and on myocardial thickness within the upper sector of the medial isthmus (which was thinner in type I when compared to types II and III). These findings suggest that procedures may be more difficult in type II and type III arrangements since the ablation success rate is inversely proportional to line length and tissue thickness.[14–16]

In normal cardiac anatomy, when observing the heart from the epicardial side, the left atrial medial isthmus is usually crossed by two main coronary vessels: the coronary sinus and the right coronary artery. In our study, investigated region was crossed by the coronary sinus in all, even though right coronary supply was present in only 94.0% of hearts (when right artery dominance and codominance were considered together).

It has been proposed that differing configurations of blood vessels within the isthmus line could complicate ablation procedures via different mechanisms.[11,17] For instance, in anomalous variations, the intramural blood flow (especially within the coronary sinus) could act as an epicardial "heat-sink." More specifically, these vessels could remove heat from the ablation site via convective cooling, all the while reducing the efficacy of isthmus ablation.[18] It was proven that veins with a diameter >5.9 mm (which were almost always found within the coronary sinus in the left atrial medial isthmus line) were a strong predictor for a mandatory epicardial ablation.[19] Furthermore, it has been suggested that myocardial sleeves around the coronary sinus could act as an epicardial connection, with the potential to bridge the lesion line and act as a proarrhythmogenic.[20] In such cases, higher ablation energy would be required to achieve isthmus block. At the same time, the close proximity of the right coronary artery would warrant the use of lower radiofrequency energy, in order to avoid several complications, such as arterial injury, thrombosis, or spasm, which could lead to myocardial infarction.[21] With these limitations in mind, the most unwanted arrangement of vessels would be one where the coronary artery would be interposed between the coronary sinus and isthmus line, as it could be a predictor of an unsuccessful linear ablation during endocardial and epicardial ablation.[22] Nevertheless, there have still been no studies focusing on the mutual relationships of the coronary blood vessels within this region. Further research on this topic is highly in need.

Successful ablations would not only be affected by the dimensions and location of blood vessels within its area, but also by the presence of additional endocardial structures.[5] Crevices, recesses, diverticula, and tissue bridges were often found within the region of the medial isthmus (approximately one-third of cases).[23] These unwanted embryological remnants of the primitive atrium could significantly hinder endocardial ablation procedures or entrap the tip of the ablation catheter.[24] The presence of deep recesses or diverticula could lead to the loss of direct catheter contact with the atrial tissue. Moreover, the space in-between the tissue bridges and the proper atrial wall could negatively influence the isthmus ablation procedure, as more energy would be required for complete isthmus block. At the same time, high radiofrequency energy would be contraindicated in this area, since it could damage the very thin tissue inside the floor of the diverticula and lead to cardiac tamponade. Interestingly, the prevalence of additional endocardial structures within the isthmus region of the left atrial medial isthmus was similar to that of the mitral isthmus region (where crevices, diverticula, intertrabecular recesses, or trabecular bridges were seen in 34.5% of cases).[5]

Finally, it is highly probable that surrounding cardiac and extracardiac structures could be damaged during ablations along the left atrial medial isthmus. In particular, the AV node would be principally vulnerable. Located on the right-sided aspect of the interatrial septum, it could even be damaged during interventions involving the left-sided aspect of the interventricular septum.[25,26] At its mitral valve annulus end, the left atrial medial isthmus line may cross atrioventricular node area, where ablations should be performed carefully, especially in the case of very thin base of interatrial septum. The isthmus line will reach the atrioventricular node close proximity in hearts with type II and III of oval fossa—isthmus line arrangement (45.5% of all cases), but this will be rarely seen for hearts, where the oval fossa is located outside the medial isthmus line (type I: 54.5% of all cases). Any damage to the left atrium or esophagus could also lead to life-threatening complications such as esophageal injury, atrioesophageal fistula, and paraesophageal vagal nerve damage. Fortunately, the esophagus is located closer to the left-sided pulmonary veins and would not be in harm's way. In most cases, both the right superior and the right inferior pulmonary veins are located at a safe distance away from the esophagus (28.6 ± 8.2 and 28.3 ± 8.4 mm, respectively).[27] Another important structure susceptible to damage during ablation procedures would be the right phrenic nerve, overlying the right aspect of the right atrial wall. Fortunately, the minimal distance between it and the right inferior pulmonary vein ostium is about 8.0 mm.[28]

This study had several limitations. First, all measurements were taken from autopsied heart specimens after formaldehyde fixation, which could have potentially affected the size and shape of the tissue. However, other studies have shown that the use of 10% paraformaldehyde in cardiac tissue preservation did not cause significant changes in atrial tissue dimensions.[29] A second limitation of this study was that measurements were performed postmortem and, thus, were not a representation of the physiology of tissues in vivo. Therefore, our findings cannot infer much about the natural dimension changes of the studied area within the cardiac cycle. Moreover, we did not investigate the distances and configurations of several important heart structures that lie near the isthmus. Therefore, future studies should explore the interconnections between structures such as the AV node or the coronary sinus and the isthmus, and whether they have any clinical relevance. An additional limitation was that we studied hearts from patients who did not suffer from AF; instead our samples represented normal cardiac anatomy. Hypothetically, the dimensions of the left atrial medial isthmus would be significantly larger in patients with a remodeled left atrium due to their respective tachyarrhythmias. Last, this study included Caucasian subjects only. Despite these limitations, we believe that they do not interfere with our morphological analysis of the relationships between individual heart structures and their relative dimensions.

5 | CONCLUSION

This study presented the first complex morphometric and topographical description of the left atrial posteroseptal region. Three variants of the position of the oval fossa and the left atrial medial isthmus line were distinguished, and each type showed significant differences in isthmus parameters. In 32.5% of hearts, when the oval fossa was crossed by the medial isthmus line (the medial isthmus line overlapped the true interatrial septum), interventions within this configuration have been deemed difficult and dangerous. Although the studied specimens had anatomical variations in the right-sided pulmonary veins and in their coronary artery dominance, the size of the left atrial medial isthmus did not vary considerably. In 31.5% of cases, the left atrial medial isthmus line had additional structures found within it, which increased the risk of catheter entrapment and procedural complications.

AUTHOR CONTRIBUTIONS

Concept/design, performing measurements, data analysis/interpretation, drafting article, approval of article: Katarzyna Piątek-Koziej and Jakub Hołda. Collecting material, critical revision of article, and approval of the article: Filip Bolechała and Paweł Kopacz. Concept/design, data analysis/interpretation, statistics, approval of article: Mateusz Koziej. Performing measurements, data analysis/interpretation, and approval of the article: Marcin Chłosta. Performing measurements, data analysis/interpretation, drafting article, and approval of the article: Kamil Tyrak. Data analysis/interpretation, drafting article, critical revision of article, and approval of the article: Katarzyna A. Jasińska. Concept/design, data analysis/interpretation, drafting article, critical revision of article, and approval of the article: Mateusz K. Hołda.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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