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DEVICES

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Variations and angulation of the coronary sinus tributaries: Implications for left ventricular pacing

Małgorzata Mazur MD, PhD[1] | Anna Żabówka MD[1] | Filip Bolechała MD, PhD[2] | Paweł Kopacz MD[2] | Wiesława Klimek-Piotrowska MD, PhD[1] | Mateusz K. Hołda MD, PhD[1]

[1]HEART-Heart Embryology and Anatomy Research Team, Department of Anatomy, Jagiellonian University Medical College, Krakow, Poland

[2]Department of Forensic Medicine, Jagiellonian University Medical College, Krakow, Poland

Correspondence
Mateusz Hołda, MD, PhD, HEART-Heart Embryology and Anatomy Research Team, Department of Anatomy, Jagiellonian University Medical College, Kopernika 12, 31–034 Kraków, Poland.
Email: mkh@onet.eu

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Abstract

Background: Variations of the coronary sinus tributaries might result in difficulties in left ventricle electrode insertion during cardiac resynchronizing therapy. Morphometric features of tributaries, especially angulation of the coronary sinus tributaries, are crucial for coronary sinus procedures.

Methods: This study was carried out on 200 formaldehyde-fixed human hearts (22.0% females, mean age of 48.7 ± 15.6 years).

Results: The inferolateral aspect of the left ventricle was accessible from the coronary venous tree in 77.0% (in 35% from one, 29% from two, and 13.0% from three tributaries). The middle cardiac vein was present in all cases, with a diameter of 1.8 ± 0.5 mm, cannulation distance of 5.3 ± 3.2 mm, and angle of 82.0 ± 12.8°. The inferolateral vein of the left ventricle varied greatly in number: single in 63.5%, multiple in 30.5%. The ostium diameter for a single vein was 1.3 ± 0.5 mm, cannulation distance was 21.1 ± 9.8 mm, and the angle was 98.1 ± 13.5°. The left marginal vein was present in 39.5% with an ostium diameter of 0.9 ± 0.5 mm, cannulation distance of 46.0 ± 12.0 mm, and angle of 92.0 ± 13.4°. Finally, the oblique vein of the left atrium was present in 71.0% with a diameter of 1.3 ± 0.8 mm, cannulation distance of 27.2 ± 9.4 mm, and angle of 136.8 ± 16.6°.

Conclusions: This study shows the clinically relevant morphometric characteristic of coronary sinus tributaries. The middle cardiac vein is the most constant among coronary veins. However, it is usually not suitable for left ventricular pacing. The inferolateral vein of the left ventricle is highly variable in number, but its morphology makes it a suitable target for left ventricular lead placement.

KEYWORDS
cardiac resynchronization therapy, coronary veins, inferolateral vein of left ventricle, left ventricle, middle cardiac vein, oblique vein of left atrium, posterior vein of left ventricle, tortuosity

1 | INTRODUCTION

The coronary venous system is represented by the coronary sinus and its tributaries, as well as anterior and smallest cardiac veins. Through the great cardiac, middle cardiac vein (MCV), and small cardiac vein (SCV), as well as the left marginal vein (LMV), inferolateral vein of the left ventricle (ILVLV), and oblique vein of left atrium (OVLA), which are the most constant tributaries of the coronary sinus, about 60% of the venous blood of the heart comes back to the right atrium.[1]

It seems that the structures of the coronary sinus, its tributaries, and the orifice to the right atrium are well-known to the clinicians. However, high variability of the coronary venous tree represents a frequent challenge during various invasive procedures, such as radiofrequency ablation, biventricular pacing, retrograde cardioplegia administration or mitral annuloplasty.[2,3] The MCV has been considered for both placing left ventricular leads and ablation of posterior epicardial accessory pathways. The ILVLV is commonly cannulated for left ventricular pacing and veins draining the lateral wall of the left ventricle can be targeted for biventricular pacing.[4]

Cardiac resynchronization therapy is a well-established treatment for patients with left ventricular systolic dysfunction, advanced heart failure, and electrocardiographic evidence of intraventricular conduction delay. Resynchronization therapy requires the insertion of right and left ventricular leads to resynchronize ventricular contraction. To achieve successful pacing of the left ventricle, it is required to ensure proximity of the lead's tip to the left ventricular epicardium by cannulation of one of the posterolateral tributaries of the coronary sinus.[5–8] Unfortunately, up to 30-40% of the patients do not show a favorable response to the cardiac resynchronization therapy.[9] Position of successfully left ventricular pacing lead is one of the determinants of response. However, implantation procedure includes several challenging technical issues such as accessing the coronary sinus, advancing within the coronary sinus, and placement of the pacing lead on the lateral left ventricle wall.[10]

All procedures within the coronary vein tree strongly depend on the highly variable anatomy of the coronary sinus and its tributaries. Clinical experience, good manual skills, and knowledge of the coronary venous system anatomy are necessary for successful coronary sinus cannulation and reaching the desirable vein. Although coronary sinuous ostium anatomy and its influence on coronary sinuous cannulation are well-known,[11] we are still missing critical information regarding coronary sinus tributaries, such as angulations and size of tributaries, which often provide challenges for electrophysiologists.[12] Therefore, this study aimed to evaluate the clinically important aspects of coronary sinus tributaries anatomy, with special regards to types of tributaries, their ostium diameters, cannulation distances, and angles between tributary veins and the coronary sinus.

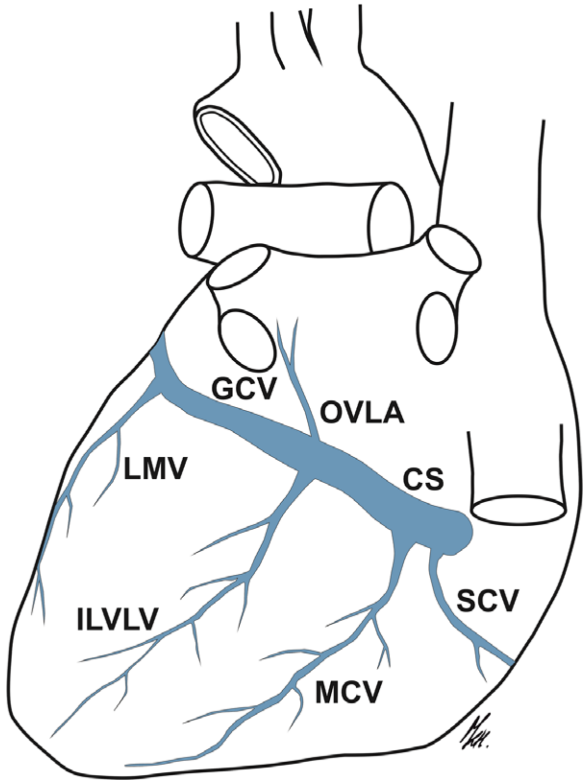

FIGURE 1 Schematic view of the coronary venous system with marked main vessels. CS = coronary sinus; GCV = great cardiac vein; LMV = left marginal vein; MCV = middle cardiac vein; OVLA = oblique vein of left atrium; ILVLV = inferolateral vein of the left ventricle; SCV = small cardiac vein [Color figure can be viewed at wileyonlinelibrary.com]

2 | MATERIAL AND METHODS

This study was approved by the Bioethical Committee of Jagiellonian University in Krakow, Poland (1072.6120.120.2018). 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

The study was carried out on 200 autopsied adult human hearts (Caucasian) of both sexes (22.0% females) aged from 17 to 93 (mean = 48.7 ± 15.6) years. The mean body mass index (BMI) of the donors was 26.6 ± 4.3 kg/m^2. Specimens were obtained during routine forensic medical autopsies from July 2013 to December 2017. Demographic data for all donors were available. The exclusion criteria included death due to heart failure, heart trauma, severe anatomical defects of the cardiovascular system, evident severe macroscopic pathologies of the heart, heart grafts, and macroscopic signs of cadaver decomposition.

2.2 | Dissection and measurements

The hearts were dissected from bodies in a routine manner together with the parts of great vessels. Hearts were washed out of blood and blood clots and weighed before preservation. After dissection, all hearts were fixed by immersion in 10% paraformaldehyde buffered solution (for a maximum of 2 months) until the time of measurement.

The coronary sinus was opened longitudinally from the coronary sinus ostium down to the great cardiac vein to allow easy observations and measurements. All descriptions and measurements were conducted in the attitudinally correct anatomical position of the heart.[13] First, the coronary sinus ostium diameter was measured. The presence of the coronary sinus tributaries (ie, MCV, SCV, LMV, ILVLV, and OVLA) was examined (Figure 1). The location of the tributary ostia in relation to the great cardiac vein/coronary sinus junction was noted. The border between the great cardiac vein and coronary sinus was assessed based on the Vieussens valve and/or the OVLA ostium presence.

The following measurements were taken for all of the above-mentioned coronary sinus tributaries:

- Ostium diameter—measured to the first point of tissue resistance;
- cannulation distance—the distance between the tributary ostium and coronary sinus ostium;
- length of the coronary vein—the distance between the coronary vein ostium and the first dichotomous division of the vessel measured along the course of the vein;
- tributary angle—angle between the axis formed by the distal 1 cm of the tributary vein and the coronary sinus/great cardiac vein axis (Figure 2).

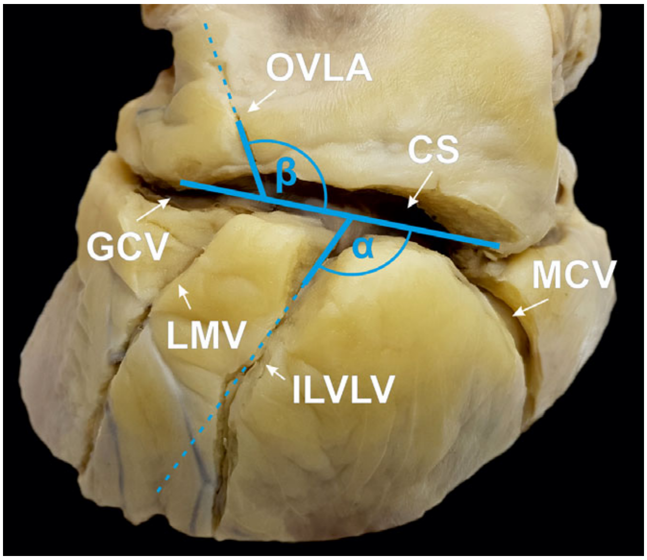

FIGURE 2 Photograph of cadaveric heart specimen. The inferolateral wall of the left ventricle is visible with dissected coronary veins. The CS axis and tributary angles are marked: α, inferolateral vein of the left ventricle (ILVLV) tributary angle; β, oblique vein of the left atrium (OVLA) tributary angle. CS = coronary sinus; GCV = greatcardiac vein; LMV = left marginal vein; MCV = middle cardiac vein [Color figure can be viewed at wileyonlinelibrary.com]

Tortuosity of the vein was identified by the presence of ≥3 bends (defined as ≥45° change in vessel direction) along the main axis of the vein.

All linear measurements were conducted with a 0.03-mm precision electronic caliper (YATO, YT–7201, Toya SA, Wrocław Poland). Angle measurements were taken using a 1° precision circle protractor. All measurements were taken by two independent researchers to reduce human bias. If differences between results among researchers were >10%, both measurements were repeated. To simulate clinical procedures during measurements and establish tributaries lumen size, 3-, 5-, 7-, and 8-French catheters were used.

2.3 | Statistical analysis

Data were presented as: (1) mean values with the corresponding standard deviations and ranges; and/or (2) determined percentages. Shapiro-Wilk tests were used to determine if the quantitative data were normally distributed. To verify a relative homogeneity of variance, we performed Levene's tests. We also used the Student's *t*-tests and the Mann-Whitney U tests for statistical comparisons. Qualitative variables were compared using $\chi 2$ tests of proportions for categorical variables with Bonferroni corrections accounting for the multiple comparisons. Correlation coefficients were calculated to determine statistical dependences between parameters. To detect a simple correlation ($r = 0.25$), for 80% power with a 5% significance level (two-tailed; $\alpha = 0.05$; $\beta = 0.2$), the required minimal sample size was calculated to be approximately 123 cases. Statistical analyses were performed using StatSoft STATISTICA 13.1 software for Windows (StatSoft Inc., Tulsa, OK, USA). The statistical significance was set at *P* value lower than 0.05.

3 | RESULTS

The mean heart weight was 435.3 ± 95.7 g (range: 180-620 g), and the mean transverse coronary sinus ostium diameter was 9.4 ± 2.7 mm (range: 4.0-18.3 mm). The number of main tributary veins to coronary sinus/great cardiac vein within the left atrioventricular groove can be two (in 4.5% of hearts), three (in 24.0%), four (in 38.0%), five (in 29.0%), or six (in 4.5%). In addition to this, small, short, and multiple ventricular veins were identified in 16.0% of all cases. The inferolateral aspect of the left ventricle was accessible from the coronary venous tree in 77.0% (in 35% from one, in 29% from two, and in 13.0% from three tributaries). There were no veins to the inferolateral wall in the remaining 23.0%. Significant enlargement of the coronary sinus ostium diameter was detected for those coronary sinuses with six tributaries when compared to other variations ($P = 0.02$). There were no significant differences in the number of tributaries in terms of age, heart weight, the donor's BMI, or sex.

3.1 | SCV

The SCV as a coronary sinus tributary was present in 74.0% of all hearts. The mean ostium diameter for SCV was 1.1 ± 0.6 mm (range: 0.3-2.1 mm) and mean SCV length was 32.3 ± 11.9 mm (range: 7.1-54.4 mm). The SCV had a lumen >3-French in 34.5% (51/148) of all hearts with the SCV present. The mean cannulation distance for the SCV was 2.4 ± 1.9 mm (range: 0.7-8.4 mm), and the tributary angle was always acute (<90°) with a mean value of 26.3 ± 12.9° (range: 12.0-49.0°). Tortuosity of the SCV was noticed in four cases (2% of all hearts).

3.2 | MCV or inferior interventricular vein

The MCV entered the coronary sinus in all assessed specimens with a mean ostial diameter of 1.8 ± 0.5 mm (range: 0.6-3.6 mm). The MCV diameter was positively correlated with the age ($r = 0.18$, $P = 0.02$) and coronary sinus ostium diameter ($r = 0.21$, $P = 0.03$). The MCV length was 92.4 ± 26.6 mm (range: 31.6-102.7 mm). In 94.5% of all cases, the MCV lumen dimension was >3-French, in 55.0% >5-French, in 12.5% >7-French, and in 4% >8-French (Figure 3A). The mean MCV cannulation distance was 5.3 ± 3.2 mm (range: 1.5-19.0 mm). The MCV opened to the coronary sinus, forming an angle of 82.0 ± 12.8° (range: 50.0-115.0°). In 64.0% of all hearts, the MCV tributary angle was acute, in 14.5% it was <70°, and in 3% below <60°. The MCV tributary angle was independent of MCV cannulation distance but was distinctly correlated with the presence of the SCV; the MCV angle was significantly lower when the SCV was absent (85.3 ± 11.9° vs 80.9 ± 12.9°; $P = 0.03$). No other significant dependences between the presence of SMC and MCV cannulation distance or ostium diameter were found. The tortuosity of the MCV was present in 6.5% of all hearts.

3.3 | Inferolateral vein of the left ventricle (ILVLV)

The ILVLV varied greatly in number. Single ILVLV was observed in 63.5% of hearts, with multiple ILVLV in 30.5% (double ILVLV in 27.0%,

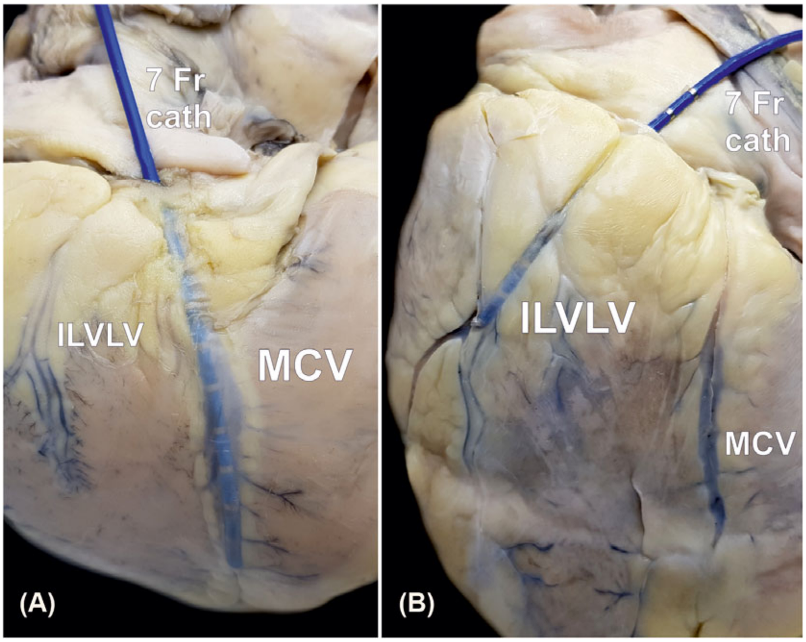

FIGURE 3 Photographs of cadaveric heart specimens. (A) The MCV with an inserted 7-French catheter into its lumen. Please note that the catheter could reach the apical region. (B) The ILVLV with an inserted 7-French catheter into its lumen. The catheter could reach only to the middle aspect of the left ventricular epicardium. ILVLV = inferolateral vein of the left ventricle; MCV = middle cardiac vein [Color figure can be viewed at wileyonlinelibrary.com]

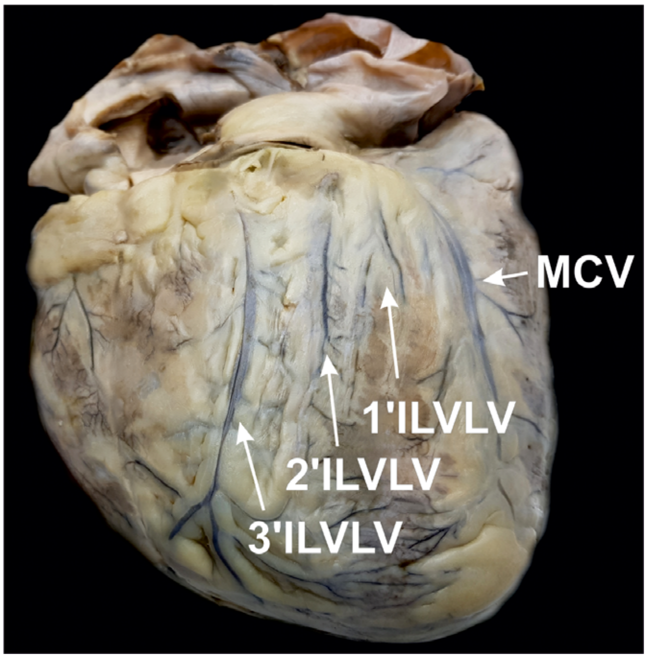

FIGURE 4 Photograph of cadaveric heart specimen. The inferolateral wall of the left ventricle is visible with a marked triple ILVLV. ILVLV = inferolateral vein of the left ventricle; MCV = middle cardiac vein [Color figure can be viewed at wileyonlinelibrary.com]

triple ILVLV in 1.0%, and single main ILVLV and small ventricular tributaries in 2.5% of all cases) (Figure 4). In 6.0% of examined hearts, the ILVLV was absent and replaced by relatively small, multiple ventricular tributaries. The mean ostium diameter for single ILVLV was 1.3 ± 0.5 mm (range: 0.5-3.3 mm) and was correlated with the donor's age ($r = 0.19$, $P = 0.01$). The length for single ILVLV was 69.2 ± 22.1 mm (range: 26.8-88.0 mm). The lumen of the single ILVLV was >3-French in 72.4% (92/127), >5-French in 11.0% (14/127), and >7-French in 4.7% (6/127) of all hearts with the single ILVLV present (Figure 3B). The cannulation distance for the single ILVLV was 21.1 ± 9.8 mm (range: 6.4-47.2 mm), and the tributary angle was 98.1 ± 13.5° (range: 60.0-145.0°), with 31.5% (40/127) of all single ILVLVs having an acute angle and in 1.6% (2/127) having an angle <70°. The tortuosity of the single ILVLV was present in eight hearts (4% of all cases).

For the double ILVLV, the ostium diameter of the first tributary (located closer to coronary sinus ostium) was 1.0 ± 0.4 mm (range: 0.2-2.3 mm) and for the second tributary was 1.1 ± 0.6 mm (range: 0.2-3.16 mm), with no significant difference between veins ($P > 0.05$), but both were smaller than the single ILVLV ($P < 0.05$). The length of the first ILVLV was 38.1 ± 16.0 mm (range: 20.6-58.7 mm) and of the second ILVLV was 34.6 ± 12.1 mm (range: 19.8-60.5 mm). The lumen size >3-French was noted in 44.4% (24/54) for the first ILVLV and in the same percent for the second ILVLV, while >5-French was observed in 5.6% (3/54) and 13.0% (7/54), respectively. The mean cannulation distance for the first ILVLV was 16.2 ± 6.7 mm (range: 6.8-42.8 mm) and for second ILVLV was 27.5 ± 10.4 mm (range: 12.3-55.5 mm). The tributary angle for the first ILVLV was 96.3 ± 13.3° (range: 60.0-125.0°), and for a second it was 97.3 ± 11.3° (range: 70.0-125.0°) with no significant difference between veins ($P > 0.05$). No significant differences in the ILVLV morphology were found in correlation with MCV morphology (distance, diameter, or angle).

3.4 | Left marginal vein (LMV) or left lateral vein

The LMV was present in 39.5% of all cases. It was either a coronary sinus tributary in 21.5% (17/79), or it entered into the great cardiac vein in 78.5% (62/79). In 7.5% of all hearts, when the LMV was absent, we were able to see small ventricular venous tributaries. The mean LMV ostium diameter was 0.9 ± 0.5 mm (range: 0.1-2.24 mm). The LMV, which opened into the coronary sinus, had significantly bigger ostium diameter than the great cardiac vein tributary (1.2 ± 0.4 mm vs 0.8 ± 0.5 mm, $P = 0.005$). The mean LMV length was 65.8 ± 22.7 mm (range: 23.1-82.9 mm). Among all the cases with an LMV present, the

LMV had a lumen >3-French in 36.7% (29/79) and >5-French in 7.6% (6/79). The mean cannulation distance was 46.0 ± 12.0 mm (range: 27.2-83.0 mm), and it was significantly greater for males than females (46.9 ± 12.7 mm vs 42.8 ± 8.8 mm, $P = 0.04$). The LMV mean tributary angle was 92.0 ± 13.4° (range: 50-130°), and it was acute in 59.5% (47/79); in 5.1% (4/79) an angle was <70°. The tortuosity of the LMV was noticed in five cases (2.5% of all hearts).

3.5 | OVLA or vein of Marshall

The OVLA was present in 71.0% of all hearts, with a mean ostium diameter of 1.3 ± 0.8 mm (range: 0.3-7.5 mm). The length of the OVLA was 21.4 ± 9.3 mm (range: 5.7-48.9 mm). The OVLA had a lumen >3-French in 58.5% (83/142) of all hearts with OVLA present, and >5-French in 15.5% (22/142). The mean cannulation distance was 27.2 ± 9.4 mm (range: 2.6-53.7 mm). The mean tributary angle for the OVLA was 136.8 ± 16.6° (range: 87.0-161°) and had an acute angle in only one case. No tortuosity of the OVLA was observed.

4 | DISCUSSION

Cardiac resynchronization therapy is a commonly used treatment method for patients with chronic heart insufficiency that results in lowering mortality among them.[14] Suitable placement of the left ventricular lead in a coronary sinus tributary is required for successful resynchronization.[7,15–18] Also, other procedures involve the coronary sinus cannulation; however, none of them requires such high accuracy in knowing the morphology of the coronary venous tree. Clinicians are challenged by the high variability of the coronary sinus and its tributaries, and for this reason knowledge of their nature appears to be important. Several factors might be responsible for unsuccessful tributary cannulation including: (1) the inability of coronary sinus ostium localization in the right atrium; (2) the presence of an obstructive Thebesian valve in the coronary sinus ostium; (3) presence and morphology of the Vieussens valve; (4) presence of other venous valves within the coronary sinus tributaries; and (5) size and angulation of the tributary.[11,19–21] Moreover, clinicians and researchers are challenged not only by the variability of the coronary venous system morphology, but also different nomenclatures, which often brings unnecessary confusion and causes serious difficulties in a direct comparison between the results of different anatomical and clinical studies.[7,22] In this study, we have used previously proposed, attitudinally correct terminology for cardiac veins.[13] The most prominent difference in relation to commonly used, wrong terminology is change of the name of the vein located on the inferolateral wall of the left ventricle from the "posterior vein of the left ventricle" to the ILVLV. The MCV could be also called inferior interventricular vein to highlight its location. The simple classification and terminology presented in the current study should be used in all future studies, as well as in clinical practice to avoid misunderstanding and ensure comparability between studies.

Among all coronary sinus tributaries, the MCV is the most constant vessel (present in 100%) with a reasonable size (1.8 ± 0.5 mm, 94.5% lumen dimension >3-French). Hence, it may be found to be very reliable for catheter manipulations, but not for all cardiac procedures. On the other hand, the MCV forming the inconvenient cannulation angle of 82.0 ± 12.8° (acute angle in 64.0%), which together with the relatively short cannulation distance (5.3 ± 3.2 mm) and the presence of MCV valve located in the MCV ostium (in 3% near occlusive valve) may significantly impede entry with a catheter to the MCV.[20] Nevertheless, the MCV is not considered to be an optimal pacing site during cardiac resynchronization therapy as it runs in the interventricular groove toward the ventricular apex.[15,23] The midlateral left ventricle could be accessible from the MCV in only about 20% of the hearts. Thus, the MCV is usually not a suitable target for left ventricular lead placement.[20]

During resynchronization therapy, it is important to identify a proper stimulation center (ie, a place with the latest possible activation moment of the left chamber). This is one of the key elements in ensuring proper cardiac resynchronization therapy response. Most frequently, the suitable place would be localized on the lateral or inferolateral wall of the left ventricle, with proper distance from the apical segment. Targeting the left ventricular lead to the area of maximal delay is, however, significantly limited by the coronary venous anatomy.[24,25] Large clinical studies exploring the optimal placement of electrodes in the left chamber confirmed worse medical prognosis for cases in which the electrode is placed in the apical position. Such positioning was directly correlated with higher risk of heart failure exacerbation or death in comparison to parabasic or intermediary placement (MADIT-CRT) or other placement types (REVERSE).[26,27] In the large postmortem study performed by Noheria et al, it was found that the ILVLV and the anterior interventricular vein are suitable for stimulation of the middle segment of lateral left ventricle wall in 92% and 86% of all cases, respectively.[20] Our study shows that the middle aspect of the inferolateral left ventricle wall is accessible from the coronary venous tree in 77.0%, mainly via the ILVLV and LMV.

The ILVLV highly varied in number and morphology. The single ILVLV, which is present in 63.5% has a relatively large lumen (>3-French in 72.4%) and convenient, obtuse tributary angle (98.1 ± 13.5°). When the ILVLV is multiplied (in 30.5%), its lumen is slightly reduced in comparison with the single ILVLV (>3-French in 44.4%), and the tributary angle remains obtuse in most cases. The morphometric characteristics of the ILVLV make this vein a suitable target for left ventricular lead placement. It is considered as a convenient cannulation target in about 35-45% of all cases.[28,29] Angiographic study of the coronary sinus anatomy revealed that the absence of the ILVLV limits the ability of left ventricle endovenous pacing. Moreover, it was found that the diameter of the vein smaller than 2 mm and its tortuosity might complicate lead insertion. It was also observed that higher tributaries number results in their reduced accessibility for pacing lead insertion.[30]

The second commonly used coronary sinuous tributary is the LMV, which is present in only about 40% of hearts. However, the location of the LMV makes this vein the perfect place for left ventricular lead implantation; the relatively small vein lumen (>3-French in only 36.7%) and tributary angle, which is acute in 59.5%, may pose some difficulties in the LMV cannulation. Moreover, the LMV was observed significantly less frequently in patients with a previous history of myocardial infarction, which might hamper optimal left ventricular lead positioning in such patients.[31]

The preimplantation knowledge of the coronary venous anatomy might help to precisely define the place of lead placement for cardiac resynchronization therapy and, thus, increase the efficiency and safety of this procedure. The retrograde venography performed in at least two different views remains the basic technique for coronary venous tree visualizations. More sophisticated techniques include multislice computed tomography angiography, as well as magnetic resonance, where the anatomy of the coronary sinus and its tributaries can be evaluated in detail and three-dimensionally reconstructed.[31,32]

A challenge associated with resynchronization therapy is the fact that a significant number of patients do not notice clinical health improvement after leads insertion. Unfortunately, this also translates into the lack of improvement in life expectancy.[33] For this reason, large hopes are placed on every innovation in the construction of left ventricle electrodes. A full spectrum of vein cannulation catheters has been developed to gain an advantage in finding optimal electrode placement spot, as well as facilitating the electrode insertion process. Catheters of various size, length, flexibility, bending, and curvature have been proposed to address the challenge of nuances in individual cardiac anatomical differences. Significant advances include reducing the diameter of the electrodes to achieve accessibility to smaller coronary veins, and the new quadripolar left ventricular electrode, which makes it possible to stimulate the left chamber from the distal or proximal part of the electrode, while also applying a multipoint stimulation of the left ventricle using one electrode only. However, the distance from the catheter tip to the most proximal electrode of the quadripolar leads ranges from 40 to 60 mm. In light of these study results we can conclude that SCV and OLVA are usually not suitable (too short) for such quadripolar leads implantations.

The current study has several limitations. First, the main limitation of this study was the use of formaldehyde-fixed postmortem specimens, which might give a bias in the measurements. However, previous studies have shown that the measurements after fixation in 10% paraformaldehyde, especially those associated with the vessel diameters and angle dimensions, are similar to those before fixation and can be considered nonsignificant.[34] Nevertheless, reported in this study dimensions of the coronary veins' ostia may be considered to be lower when compared to everyday clinical practice. These discrepancies could be explained by: (1) shrinkage of the tissue under the influence of fixation; (2) collapse of the veins which are not filled with blood; (3) the measurement technique used in this study, where the measurements were performed to the first point of the tissue resistance and, thus, the potential extensibility of veins was not addressed in our study. An ex vivo study should be performed to investigate whether the coronary sinus tributaries are stretchable and what is the largest left ventricular lead that can be accommodated inside the vein without its dissection or significant damage. Moreover, studies performed based on the autopsied material might not directly correlate to the physiology of tissues in vivo. Therefore, we cannot say anything about behavior and dimension changes of the coronary venous tree within the cardiac cycle. Despite these limitations, we believe that they do not impede our morphological analysis.

5 | CONCLUSION

This study shows the clinically relevant morphometric characteristic of coronary sinus tributaries. The MCV is the most constant among coronary veins. However, the MCV is usually not suitable for left ventricular pacing. The ILVLV is highly variable in number, but its morphology (relatively large lumen and convenient, obtuse tributary angle) makes it a suitable target for left ventricular lead placement. The LMV is present only in 40% and has less convenient cannulation conditions than the ILVLV. The significant technological innovations made for left chamber electrodes or catheters gives hope for greater manipulation within the coronary sinus and for finding an optimal spot for stimulation. Our results may be also used in the development of new generations of leads and tools to place leads effectively.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

COMPLIANCE WITH ETHICAL STANDARDS

a. Disclosure of potential conflicts of interest: The authors declare that they have no conflict of interest.

b. Funding: none.

c. Research involving Human Participants: This study was approved by the Bioethical Committee of Jagiellonian University in Cracow, Poland (1072.6120.120.2018). The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

d. Informed consent: In our study we personally collected hearts only from deceased person who did not express objection, when alive, and if family did not express objection. In accordance with Polish Law our Bioethical Committee waived the need for written or verbal informed consent. We are extremely grateful to the individuals (and their families) who donated their bodies to science.

AUTHOR CONTRIBUTIONS

Małgorzata Mazur contributed to the Concept and design, data analysis/interpretation, drafting article, critical revision of article, and approval of the article. Anna Żabówka also contributed to the concept/design, data collection, data analysis/interpretation, drafting article, critical revision of article, approval of the article. Filip Bolechała, Paweł Kopacz, Wiesława Klimek-Piotrowska, and Paweł Kopacz all worked on the concept/design, data collection, critical revision of article, approval of the article. Wiesława Klimek-Piotrowska contributed to the concept/design, critical revision of article, approval of the article. Mateusz K. Hołda worked on the concept/design, data collection, data analysis/interpretation, statistics, drafting article, critical revision of article, approval of article.

ORCID

Mateusz K. Hołda MD, PhD
https://orcid.org/0000-0001-5754-594X

REFERENCES

1. Mazur M, Hołda M, Koziej M, et al. Morphology of tributaries of coronary sinus in humans—corrosion casting study. *Folia Med Cracov*. 2015;55:5-13.
2. von Lüdinghausen M. Clinical anatomy of cardiac veins, Vv. cardiacae. *Surg Radiol Anat*. 1987;9:159-168.
3. Ortale JR, Gabriel EA, Iost C, Márquez CQ. The anatomy of the coronary sinus and its tributaries. *Surg Radiol Anat*. 2001;23:15-21.
4. Habib A, Lachman N, Christensen KN, Asirvatham SJ. The anatomy of the coronary sinus venous system for the cardiac electrophysiologist. *Europace*. 2009;11:v15-v21.
5. Becker M, Hoffmann R, Schmitz F, et al. Relation of optimal lead positioning as defined by three-dimensional echocardiography to long-term benefit of cardiac resynchronization. *Am J Cardiol*. 2007;100:1671-1676.
6. Gold MR, Auricchio A, Hummel JD, et al. Comparison of stimulation sites within left ventricular veins on the acute hemodynamic effects of cardiac resynchronization therapy. *Hear Rhythm*. 2005;2:376-381.
7. Saremi F, Muresian H, Sánchez-Quintana D. Coronary veins: Comprehensive CT-anatomic classification and review of variants and clinical implications. *Radio Graphics*. 2012;32:E1-E32.
8. Stirbys P. Cardiac resynchronization therapy with special focus on patency of coronary sinus and its branches: Conceptual viewpoint and semi-theoretical considerations on lead-induced obstruction. *Med*. 2006;42:273-277.
9. Bleeker GB, Bax JJ, Fung JW, et al. Clinical versus echocardiographic parameters to assess response to cardiac resynchronization therapy. *Am J Cardiol*. 2006;97:260-263.
10. Morgan JM, Delgado V. Lead positioning for cardiac resynchronization therapy: Techniques and priorities. *Europace*. 2009;11:v22-v28.
11. Hołda MK, Klimek-Piotrowska W, Koziej M, Mazur M. Anatomical variations of the coronary sinus valve (Thebesian valve): Implications for electrocardiological procedures. *Europace*. 2015;17:921-927.
12. Debruyne P, Geelen P, Janssens L, Brugada P. Useful tip to improve electrode positioning in markedly angulated coronary sinus tributaries. *J Cardiovasc Electrophysiol*. 2003;14:415-416.
13. Anderson RH, Mori S. How can we best describe the cardiac components? *J Cardiovasc Electrophysiol*. 2016;27:972-975.
14. Brignole M, Auricchio A, Baron-Esquivias G, et al. 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: The Task Force on Cardiac Pacing and Resynchronization Therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association. *Eur Heart J*. 2013;34:2281-2329.
15. Blendea D, Altman RK, Singh JP. Procedural aspects of lead positioning for cardiac resynchronization therapy. *J Innov Card Rhythm Manag*. 2011;2:165-171.
16. Van de Veire NR, Marsan NA, Schuijf JD, et al. Noninvasive imaging of cardiac venous anatomy with 64-slice multi-slice computed tomography and noninvasive assessment of left ventricular dyssynchrony by 3-dimensional tissue synchronization imaging in patients with heart failure scheduled for cardiac resynchronization technique. *Am J Cardiol*. 2008;101:1023-1029.
17. Gutleben K-J, Nölker G, Ritscher G, et al. Three-dimensional coronary sinus reconstruction-guided left ventricular lead implantation based on intraprocedural rotational angiography: A novel imaging modality in cardiac resynchronization device implantation. *Europace*. 2011;13:675-682.
18. Niazi I, Ryu K, Hood R, Choudhuri I, Akhtar M. Three-dimensional electroanatomic mapping of the coronary veins during cardiac resynchronization therapy implant: Feasibility and possible applications. *J Interv Card Electrophysiol*. 2014;41:147-153.
19. Karaca M, Bilge O, Hakan Dinckal M, Ucerler H. The anatomic barriers in the coronary sinus: Implications for clinical procedures. *J Interv Card Electrophysiol*. 2005;14:89-94.
20. Noheria A, DeSimone CV, Lachman N, et al. Anatomy of the coronary sinus and epicardial coronary venous system in 620 hearts: An electrophysiology perspective. *J Cardiovasc Electrophysiol*. 2013;24:1-6.
21. Corcoran SJ, Lawrence C, McGuire MA. The valve of Vieussens: An important cause of difficulty in advancing catheters into the cardiac veins. *J Cardiovasc Electrophysiol*. 1999;10:804-808.
22. Ho SY, Sánchez-Quintana D, Becker AE. A review of the coronary venous system: A road less travelled. *Heart Rhythm*. 2004;1:107-112.
23. Khan FZ, Virdee MS, Fynn SP, Dutka DP. Left ventricular lead placement in cardiac resynchronization therapy: Where and how? *Europace*. 2009;11:554-561.
24. Vassallo JA, Cassidy DM, Miller JM, Buxton AE, Marchlinski FE, Josephson ME. Left ventricular endocardial activation during right ventricular pacing: Effect of underlying heart disease. *J Am Coll Cardiol*. 1986;7:1228-1233.
25. Rodriguez L-M, Timmermans C, Nabar A, Beatty G, Wellens HJJ. Variable patterns of septal activation in patients with left bundle branch block and heart failure. *J Cardiovasc Electrophysiol*. 2003;14:135-141.
26. Singh JP, Klein HU, Huang DT, et al. Left ventricular lead position and clinical outcome in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT) Trial. *Circulation*. 2011;123:1159-1166.
27. Thebault C, Donal E, Meunier C, et al. Sites of left and right ventricular lead implantation and response to cardiac resynchronization therapy observations from the REVERSE trial. *Eur Heart J*. 2012;33:2662-2671.
28. Molhoek SG, Bax JJ, van Erven L, et al. Effectiveness of resynchronization therapy in patients with end-stage heart failure. *Am J Cardiol*. 2002;90:379-383.
29. Yaminisharif A, Virdee MS, Gopalan D, et al. Characterization of suitability of coronary venous anatomy for targeting left ventricular lead placement in patients undergoing cardiac resynchronization therapy. *J Tehran Heart Cent*. 2012;7:10-14.
30. Gilard M, Mansourati J, Etienne Y, et al. Angiographic anatomy of the coronary sinus and its tributaries. *Pacing Clin Electrophysiol*. 1998;21:2280-2284.
31. Van de Veire NR, Schuijf JD, De Sutter J, et al. Non-invasive visualization of the cardiac venous system in coronary artery disease patients using 64-slice computed tomography. *J Am Coll Cardiol*. 2006;48:1832-1838.
32. Younger JF, Plein S, Crean A, Ball SG, Greenwood JP. Visualization of coronary venous anatomy by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2009;11:26.

33. Ypenburg C, van Bommel RJ, Borleffs CJ, et al. Long-term prognosis after cardiac resynchronization therapy is related to the extent of left ventricular reverse remodeling at midterm follow-up. *J Am Coll Cardiol*. 2009;53:483-490.

34. Holda MK, Klimek-Piotrowska W, Koziej M, Piatek K, Holda J. Influence of different fixation protocols on the preservation and dimensions of cardiac tissue. *J Anat*. 2016;229:334-340.

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