Electrical Conduction Between the Right Atrium and the Left Atrium via the Musculature of the Coronary Sinus

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Background—The purpose of this study was to determine whether the coronary sinus (CS) musculature has electrical connections to the right atrium (RA) and left atrium (LA) and forms an RA-LA connection.

Methods and Results—Six excised dog hearts were perfused in a Langendorff preparation. A 20-electrode catheter (2.4-2-mm spacing center to center) was placed along the CS. Excision of the pulmonary veins provided access to the LA, and a second 20-electrode catheter was placed along the LA endocardium opposite the CS catheter. An incision opened the CS longitudinally, and microelectrodes were inserted into the CS musculature and adjacent LA myocardium. Continuous CS musculature was visible along a 35±9-mm length of the CS beginning at the ostium. During lateral LA pacing, CS electrodes recorded double potentials, a rounded, low-frequency potential followed by a sharp potential. The rounded initial potential propagated in the lateral-to-septal direction and represented “far-field” LA activation (timing coincided with adjacent LA potentials and with action potentials recorded from microelectrodes in adjacent LA cells). The sharp potential represented CS activation (timing coincided with action potentials recorded from CS musculature). A distal LA-CS connection (earliest sharp potential in the CS during lateral LA pacing) was located 26±7 mm from the ostium. During RA pacing posterior to the CS ostium, CS electrodes recorded septal-to-lateral activation of the high-frequency potential, with slightly later activation of the rounded potential (LA activation). Incisions surrounding the CS ostium isolating the ostium from the RA had no effect on the CS musculature and LA potentials during RA pacing within the isolated segment containing the CS ostium. RA pacing outside the isolated segment delayed activation of the CS musculature until after LA activation, confirming that the RA-CS connection was located in the region of the CS ostium as well as confirming the presence of the LA-CS connection.

Conclusions—In canine hearts, the CS musculature is electrically connected to the RA and the LA and forms an RA-LA connection. (Circulation. 1998;98:1790-1795.)

Key Words: atrium ■ conduction ■ action potentials ■ arrhythmia

Several anatomic studies in human hearts and canine hearts have shown that muscle morphologically identical to atrial myocardium consistently surrounds the coronary sinus and that the coronary sinus musculature is continuous with left atrial myocardium in the proximal portion of the coronary sinus and with right atrial myocardium at the coronary sinus ostium (Figure 1). The present study was undertaken to determine in Langendorff-perfused canine hearts whether the coronary sinus musculature forms an electrical connection between the right atrium and the left atrium.

Methods

Studies were performed according to the guidelines for humane care and treatment of animals established by the National Institutes of Health and were locally monitored by the Animal Studies Subcommittee of the Department of Veterans Affairs Medical Center, Oklahoma City, Okla.

Six mongrel dogs weighing 16 to 20 kg were anesthetized with sodium pentobarbital 30 mg/kg IV and mechanically ventilated with room air. A right thoracotomy was performed, and the heart was exposed. After administration of heparin 3000 U IV, the hearts were excised and immediately submerged in iced, oxygenated (95% O2/5% CO2) modified Tyrode’s solution with the following composition (mmol/L): NaCl 117, KCl 4.1, MgCl2 0.5, CaCl2 1.35, NaHCO3 24, NaH2PO4 1.8, dextrose 5.5, and sodium pyruvate 2, plus 0.6 μmol/L albumin (to increase the stability of the Langendorff preparation) and 15 mmol/L butanedione monoxime to markedly reduce myocardial contractility.10-12

The ascending aorta of the excised canine heart was cannulated and perfused with oxygenated, warmed (37±0.5°C) modified Tyrode’s solution of the same composition as described above (pH 7.40±0.05). Perfusion was performed at a constant pressure of 90 to 100 mm Hg, and flow was kept stable at a rate of 200 to 250 mL/min. After the washout of blood, the heart was submerged in a tissue bath with warmed modified Tyrode’s solution. A previous study has shown that atrial and ventricular refractory periods and AV nodal conduction remain stable in this preparation for ≥3.5 hours.1

A 20×10-mm segment of the lateral right atrial wall was excised to provide access to the right atrial endocardium. A 20-electrode...
Simultaneous recordings from the coronary sinus and left atrial myocardium adjacent to the catheter electrodes to correlate local cellular activation with the potentials recorded from remainder of right atrium (pacing site A in Figure 3) at a cycle length of 400 ms both before and after incisions 1A and 1B. A marked delay in the timing of atrial activation at the apex of the triangle of Koch confirmed completion of the isolating incision. In step 2, the coronary sinus ostium was isolated from the remainder of the right atrium by an incision from the tricuspid annulus to the inferior vena cava (incision 2 in Figure 3). Simultaneous bipolar recordings were obtained from the coronary sinus, left atrial, and septal right atrial catheter electrodes during right atrial pacing (cycle length of 400 ms) outside the isolated segment (right atrial pacing site A in Figure 3) and during pacing inside the isolated segment (pacing site B in Figure 3).

After completion of the study, gross examination was used to measure the length of the continuous musculature within the coronary sinus and the distance between the coronary sinus ostium and the distal left atrium–coronary sinus (LA-CS) connection, defined as the location of the bipolar electrode on the coronary sinus catheter that recorded the earliest sharp potential during lateral left atrial pacing.

**Recording Methods**

Transmembrane action potentials were obtained with standard glass microelectrodes filled with 3 mol/L KCl connected to a high-impedance amplifier (model FD 223, World Precision Instruments, Inc) and filtered at 0.01 to 2000 Hz. Bipolar electrograms were filtered at 30 to 500 Hz. All signals were displayed and recorded on a computerized acquisition and analysis system (Bard Electrophysiology).

**Results**

Evidence for an LA-CS Connection

During lateral left atrial pacing, the coronary sinus catheter electrodes recorded double “atrial” potentials. The first potential was recorded sequentially from the distal to the proximal catheter electrodes, indicating a wave front propagating in the lateral to septal direction, and was low in...
frequency (far field), suggesting that it represents activation of the left atrium adjacent to the mitral annulus (Figure 4). The second potential was high in frequency and was recorded from only the region of the coronary sinus in which continuous muscular tissue was visible macroscopically, suggesting activation of coronary sinus musculature. Earliest second potential was recorded from CS 6, with later activation occurring septally and laterally, suggesting activation of coronary sinus musculature by the left atrium close to CS 6. Abbreviations as in Figure 1.

The electrograms recorded from the coronary sinus catheter during lateral left atrial pacing did not change after the longitudinal coronary sinus incision (Figure 5), indicating that the incision was not responsible for the pattern of double potentials recorded during lateral left atrial pacing.

Further evidence regarding the origin of the low-frequency and high-frequency potentials recorded from the coronary sinus catheter was provided by simultaneous recordings from the 20-electrode catheter in the left atrium and from microelectrode recordings. The initial, low-frequency (far-field) potentials recorded in the coronary sinus electrograms during lateral left atrial pacing corresponded in timing with left atrial activation recorded from left atrial catheter electrodes located directly opposite the coronary sinus electrodes (Figure 6). Transmembrane action potentials recorded from microelectrodes inserted into the left atrial myocardium coincided in timing with the adjacent bipolar left atrial potential and with the rounded initial potential in the coronary sinus electrogram (Figure 7). Action potentials recorded from microelectrodes inserted into the coronary sinus musculature coincided in timing with the second sharp potential in the adjacent coronary sinus electrogram (Figure 7). These observations suggest that the pattern of double potentials in the coronary sinus electrogram recorded during lateral left atrial pacing is explained by initial activation of the left atrial myocardium and secondary activation of the coronary sinus musculature via an LA-CS connection.

Evidence for a Right Atrium–Coronary Sinus Connection

When the right atrium was paced just posterior to the coronary sinus ostium, the coronary sinus electrodes recorded directly opposite the coronary sinus electrodes (Figure 6). Transmembrane action potentials recorded from microelectrodes inserted into the left atrial myocardium coincided in timing with the adjacent bipolar left atrial potential and with the rounded initial potential in the coronary sinus electrogram (Figure 7). Action potentials recorded from microelectrodes inserted into the coronary sinus musculature coincided in timing with the second sharp potential in the adjacent coronary sinus electrogram (Figure 7). These observations suggest that the pattern of double potentials in the coronary sinus electrogram recorded during lateral left atrial pacing is explained by initial activation of the left atrial myocardium and secondary activation of the coronary sinus musculature via an LA-CS connection.
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Figure 8. Comparison of coronary sinus electrograms between left atrial and right atrial pacing. A, During lateral left atrial pacing, pattern of double potentials indicates that coronary sinus musculature is activated by left atrium at a CS-LA connection close to electrode CS 5. B, When pacing right atrium, just posterior to coronary sinus ostium, coronary sinus electrodes record activation of high-frequency potential (coronary sinus musculature) beginning proximally and propagating distally. High-frequency potential is recorded before low-frequency potential representing left atrium, indicating activation of coronary sinus musculature through an RA-CS connection at coronary sinus ostium, with later activation of left atrium.

The second incision (tricuspid annulus to the anterior margin of the coronary sinus ostium and posterior margin of the coronary sinus to the inferior vena cava, incisions 1A and 1B in Figure 3) was designed to isolate the coronary sinus ostium from the right side of the interatrial septum. Evidence for this separation was obtained by pacing the right atrium below the incisions (pacing site A in Figure 3), which showed a delay in the timing of left atrial activation adjacent to the septum (tracing LA 9 in Figure 9B) and even greater delay in the timing of atrial activation along the septum on the right (tracing RAS in Figure 9B), suggesting reversal of transseptal conductance from the right-to-left direction to the left-to-right direction. This delay in timing of left atrial activation was not associated with a change in the timing or activation sequence of the high-frequency potential in the coronary sinus electrograms (Figure 9B), indicating activation of the coronary sinus musculature from the right atrium at the coronary sinus ostium. Left atrial activation in the region of the posterior mitral annulus followed activation in the region of the coronary sinus musculature, suggesting that the left atrium was activated via a CS-LA connection (arrow, Figure 9B).

The second incision (tricuspid annulus to the inferior vena cava) isolated the coronary sinus ostium from the remainder of the right atrium. Right atrial pacing outside the isolated segment (pacing site A in Figure 3) was associated with a marked further delay in activation of the septal right atrium (tracing RAS in Figure 9C), suggesting that the atrial impulse propagated around the tricuspid annulus before reaching the septal right atrium at the apex of the triangle of Koch. There was an even greater delay in the timing of left atrial activation close to the septum (tracing LA 9 in Figure 9C), suggesting right-to-left conduction across the interatrial septum and Bachmann’s bundle. The sharp potential in the coronary sinus electrograms followed the low-frequency potential (Figure 9C), indicating activation of the coronary sinus musculature by an LA-CS connection. The delay in activation of the coronary sinus musculature by this incision, preventing the paced right atrial wavefront from reaching the coronary sinus ostium, confirms location of RA-CS connection in the region of the coronary sinus ostium.

Antz et al October 27, 1998 1793
musculature of the coronary sinus and of the distance between the coronary sinus ostium and the distal LA-CS connection identified during lateral left atrial pacing. In addition, tissue swelling caused an amplitude decrease of the recorded bipolar potentials. The latter was observed primarily in potentials recorded from the 20-electrode left atrial catheter, because the swelling also pushed the catheter away from the left atrial myocardium, reducing the catheter-wall contact at selected catheter electrodes. This study was performed in canine hearts, because only an ex vivo experiment such as the canine Langendorff preparation allowed the use of microelectrode recordings to validate the catheter recordings and the use of

Figure 10. Electrograms from coronary sinus, left atrial, and septal right atrial catheters before (A) and after (B) incision 2 during right atrial pacing within isolated segment containing coronary sinus ostium (pacing site B in Figure 3). Unchanged activation of coronary sinus musculature and secondary activation of left atrium confirms RA-CS connection in region of coronary sinus ostium as well as overall RA-CS-LA connection.

Discussion

Recent studies suggesting that propagation of impulses between the left and right atria plays an important role in sustaining atrial fibrillation combined with the development of atrial compartmentalization procedures to eliminate atrial fibrillation have led to a renewed interest in identifying RA-LA connections. Bachmann’s bundle and the interatrial septum (region of the fossa ovalis) are well-established interatrial electrical connections. The possibility that the coronary sinus musculature forms another RA-LA connection is supported by surgical reports showing that complete isolation of the left atrium in dogs and successful elimination of atrial fibrillation have led to a renewed interest in identifying RA-LA connections. Bachmann’s bundle and the interatrial septum (region of the fossa ovalis) are well-established interatrial electrical connections.

Clinical Implications

The electrical activity of the coronary sinus musculature and its connection with the right and left atria may have multiple implications for the generation of atrial arrhythmias. Already mentioned is the potential role of the additional RA-LA connection in the maintenance of atrial fibrillation and the requirement to interrupt this connection in the surgical maze procedure. The coronary sinus musculature may also form part of the atrial end of the slow AV nodal pathway in some patients with AV nodal reentrant tachycardia. We studied 12 patients in whom slow pathway conduction was attenuated or eliminated by ablation of the posterior or posterolateral mitral annulus (4 patients) or by ablation within the coronary sinus >10 mm from the ostium (8 patients). In patients with so-called epicardial “posteroseptal” accessory pathways requiring ablation from the proximal portion of the coronary sinus or the orifice of the middle cardiac vein, the coronary sinus musculature may form the atrial connection of these pathways. Finally, we have seen a small number of patients in whom focal atrial tachycardia appeared to originate within the coronary sinus musculature or within the proximal portion of the middle cardiac vein. This study also has implications regarding the interpretation of electrograms recorded from the coronary sinus. Potentials from both the coronary sinus musculature and the adjacent left atrium are recorded and may simulate accessory pathway potentials.

Study Limitations

Tissue swelling in the Langendorff preparation may have led to a slight overestimation of the length of the visible coronary sinus musculature and of the distance between the coronary sinus ostium and the distal LA-CS connection identified during lateral left atrial pacing. In addition, tissue swelling caused an amplitude decrease of the recorded bipolar potentials. The latter was observed primarily in potentials recorded from the 20-electrode left atrial catheter, because the swelling also pushed the catheter away from the left atrial myocardium, reducing the catheter-wall contact at selected catheter electrodes. This study was performed in canine hearts, because only an ex vivo experiment such as the canine Langendorff preparation allowed the use of microelectrode recordings to validate the catheter recordings and the use of
incisions surrounding the coronary sinus ostium to study the electrical connection between the right atrium and the coronary sinus musculature. Although morphological and histological studies suggest that the coronary sinus musculature and its left atrial and right atrial connections appear to be similar in canine and human hearts, further studies are warranted to confirm the electrophysiological findings in the human heart in vivo.

Conclusions
In canine hearts, electrical activation can propagate along coronary sinus musculature, extending $35 \pm 9$ mm from the coronary sinus ostium. The coronary sinus musculature is electrically connected to the right atrium (via the coronary sinus ostium) as well as to the left atrium (distal LA-CS connection located $26 \pm 7$ mm from the ostium), forming an electrical RA-LA connection. This RA-LA electrical bridge may form part of the reentrant circuit in so-called epicardial “posteroseptal” accessory pathways and in AV nodal reentrant tachycardia and may help to sustain atrial fibrillation.

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References
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