Epicardial posteroseptal and left posterior accessory pathways (EpiPSAPs) comprise 19% of all posteroseptal and left posterior accessory pathways (APs). These APs are formed by a connection between a sleeve-like extension of the coronary sinus (CS) myocardial coat (along the middle cardiac vein, posterior cardiac vein, another coronary vein, or the neck of a CS diverticulum) and the epicardial surface of the left ventricle (CS, ventricular accessory connection). During anterograde AP conduction, endocardial mapping of the right and left ventricles identifies far-field activation (unipolar potential has a wide initial R wave), with the earliest far-field ventricular potential recorded ≥1 cm apical to the tricuspid or mitral annulus. Local endocardial activation (rapid downstroke of the unfiltered unipolar electrogram) is recorded late, reflecting activation from epicardium to endocardium. Earliest ventricular activation is recorded epicardially, from the branch of the CS containing the myocardial extension (coronary vein or neck of a CS diverticulum). Ventricular activation is preceded by a high-frequency potential, similar to an anterograde AP potential, which is generated by activation of the CS myocardial extension along the venous branch (CS myocardial extension [CSE] potential in Figure 1).

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During retrograde AP conduction, the earliest high-frequency potential (similar to a retrograde AP potential) is generated by the CS myocardial extension and is recorded from the same venous branch of the CS. This potential is followed by activation of the CS myocardium. The CS myocardial potentials propagate rapidly leftward, activating the left atrium 1 to 3 cm leftward of the vein, because of the oblique orientation of the fibers connecting the CS myocardial coat with the left atrium.

Attempts to ablate EpiPSAP conduction from the endocardium, close to the mitral annulus, by targeting the site of earliest retrograde activation generally fail to eliminate AP conduction (but often produce a septal shift in the site of
Clinical experience and recent experimental studies suggest that delivering radiofrequency current close to a CA can result in narrowing or occlusion of the artery. However, recent experimental evidence suggests that cryoablation within the CS and its branches can produce lesions in the CS and adjacent atrial or ventricular myocardium with a low risk of narrowing an adjacent artery.

The purpose of this study was to determine how often a significant branch of the distal right or left circumflex CA is located close to the ideal ablation site in the coronary vein in patients with EpiPSAP and assess the risk of injuring the CA with radiofrequency ablation as a function of the distance from the ablation site. This study also examined the efficacy and safety of cryoablation when delivered at the ideal site within the coronary venous system, close to a CA.

Methods

Study Population

Between 1989 and 2007, 716 patients were referred for catheter ablation of a posteroseptal or a left posterior AP at the University of Oklahoma Health Sciences Center. Of those, 306 (43%) had ≥1 prior failed catheter or surgical ablation procedures. An EpiPSAP (CS, ventricular connection) was identified in 240 of 716 (34%) patients, including 88 of 410 (21%) patients without prior ablation and 152 of 306 (50%) patients with prior failed ablation.

Ablation

CS angiography (balloon occlusion technique) was performed in all patients at the beginning of the procedure to define the coronary venous anatomy as well as the presence or absence of a CS diverticulum. The ideal ablation site was defined as the location within a tributary of the CS (middle cardiac vein, posterior coronary vein, small cardiac vein, or other branch) or the neck or body of a CS diverticulum recording the largest, sharpest CS myocardial extension potential on the unipolar electrogram recorded from the distal (ablation) electrode on the ablation catheter (Figure 1).

Before 1994, radiofrequency ablation was performed using a 4- or 8-mm tip electrode (without irrigation), beginning at 5 W and increasing power gradually toward 15 W (25 W with 8-mm electrode), using a temperature limit of 60°C to 70°C. The power at which AP conduction block was held constant (no further increase) for 2 minutes or until impedance rise occurred. The radiofrequency application was terminated immediately in the event of an impedance rise (≥25 Ω above the lowest value). Beginning in 1994, radiofrequency ablation was performed using an investigational irrigated electrode catheter (ThermoCool, Biosense Webster, Inc), followed by the use of the approved device after 2004. Using the irrigated electrode, the radiofrequency application was initiated at 15 W and the power was increased slowly toward 25 W, until AP conduction block was achieved (no further increase). The radiofrequency application was maintained for 2 minutes or until an impedance rise occurred (≥25 Ω). Beginning in 1994 (the last 169 patients), coronary angiography was performed before ablation, with the ablation catheter positioned at the ideal ablation site. The distance between the ablation electrode at the ideal ablation site and the closest significant artery (diameter ≥1 mm) was measured at the point in the cardiac cycle where the electrode was located closest to the artery in the right anterior oblique and left anterior oblique projections. Coronary angiography was repeated after ablation (either radiofrequency or cryoablation) in all patients when ablation was performed within the coronary venous system at a site within 5 mm of a significant CA. Intracoronary nitroglycerin was administered before contrast injection in both pre- and postablation angiography, to prevent (and exclude the diagnosis of) coronary spasm because of catheter manipulation or temperature changes.

Cryoablation was performed using an investigational 7Fr, 4-mm cryo-electrode catheter beginning in late 2002 (Freezor Focal Ablation Catheter, CryoCath Technologies, Inc), followed by the use of the approved device after 2004. Cryo-applications (−75°C for 4 minutes) were delivered at ideal sites within the coronary venous system using the 7-Fr, 4-mm or 7-Fr, 6-mm cryo-electrode, when coronary angiography revealed a significant CA within 5 mm of the ideal site.

Statistical Analysis

Data are presented as mean±SD for normally distributed continuous variables, median and interquartile range for non-normally distributed discrete variables and as percentages with 95% confidence intervals (CIs) for categorical variables. Comparison between discrete variables was performed using the Wilcoxon rank-sum test. Categorical variables were compared using χ² test. P values <0.05 were considered statistically significant.

Results

Two hundred forty patients (mean age, 31.7±15.5 years; 50% men) underwent catheter ablation for an epicardial...
posteroseptal (222) or left posterior (18) EpiPSAP between 1989 and 2007 at our institution. CS angiography identified a CS diverticulum in 51 of 240 (21%) patients. The neck of the diverticulum inserted into the middle cardiac vein (rather than the CS) in 15 of the 51 (29%) patients. A CS myocardial extension potential (similar to an AP potential) was identified in 213 of 240 (89%) patients.

Coronary Angiography Results
Coronary angiography was performed before ablation in 169 of 240 (70%) patients. Of the 169 patients, 129 (76%) had a right dominant circulation, 28 (17%) had a left dominant circulation, and 12 (7%) had a codominant circulation. The median distance between the ideal ablation site and the closest significant CA was only 2 mm (interquartile range, 1–5 mm). In 100 of 169 (59%) patients, the distance of a significant CA from the ideal ablation site was ≤2 mm (Figure 2). This distance was 3 to 5 mm in 28 (16%) patients and >5 mm in 41 (25%) patients (Table 1).

CA Injury
Of the 100 patients with a significant CA within 2 mm of the ideal ablation site, radiofrequency ablation was performed at the ideal site in only 22 patients (Table 1). Because of the risk of radiofrequency ablation close to a CA, in the remaining 78 patients, (1) radiofrequency ablation was attempted at a nonideal site, outside of the coronary venous system (at the tricuspid or mitral annulus) in 48 patients; (2) ablation was not attempted in 8 patients before the availability of cryoablation (patients were referred for surgical ablation using the epicardial approach)14; and (3) cryoablation was performed in 22 patients. For the 28 patients with a CA within 3 to 5 mm of the ideal ablation site, (1) radiofrequency ablation was performed at the ideal ablation site in 15 patients; (2) radiofrequency ablation was attempted at a nonideal site, outside of the coronary venous system in 8 patients; (3) ablation was not attempted in 1 patient; and (4) cryoablation was performed in 4 patients (Table 1). Radiofrequency ablation was performed at the ideal ablation site within the coronary venous system in all 41 patients without a significant CA located within 5 mm (mean distance, 10±3 mm; Table 1).

Coronary angiography after ablation revealed arterial stenosis in 11 of 22 (50%; 95% CI, 28%–72%) patients who underwent radiofrequency ablation at the ideal site within 2 mm of a significant CA (Table 2; Figures 3 and 4). CA stenosis ranged from 25% in 2 patients to >50% in 9 patients, including complete occlusion in 3 patients. In 1 patient, complete occlusion was treated with balloon angioplasty. In the remaining 2 patients, complete occlusion occurred in a smaller branch, and angioplasty was not required. Of the 15 patients who underwent radiofrequency ablation at the ideal site located 3 to 5 mm from a significant CA, CA injury was detected on repeat angiography in only 1 (7%; 95% CI, 0%–32%) patient (70% stenosis). None of the 41 patients who underwent ablation at the ideal site >5 mm from a CA developed electrocardiographic or clinical evidence of CA injury (Table 2). The number of radiofrequency applications was similar between patients with (median 5 radiofrequency applications; interquartile range, 2–11) or without CA injury (median 5 radiofrequency applications; interquartile range, 2–9; P=0.81). A plot of CA injury as a function of the distance from the ablation site is shown in Figure 5.

Angiography was repeated at 6 months in 8 of the 12 patients with CA injury. All 6-month angiograms showed minimal arterial narrowing (<50% stenosis in all 8 patients tested), including the 2 patients who had had complete occlusion. Long-term follow-up in these patients is lacking, so it remains unknown whether these lesions became clinically significant or remained silent.

None of the 26 patients (0%; 95% CI, 0%–13%) who underwent cryoablation within 5 mm of a significant CA had new stenosis on angiography after ablation (Table 2).

Radiofrequency Ablation Success
When radiofrequency energy was delivered at the ideal ablation site within the coronary venous system, EpiPSAP conduction was eliminated acutely in 142 of 143 (99%; 95% CI, 96%–100%) patients, including patients with and without coronary angiography (Table 1). A median of 5 radiofrequency applications (interquartile range, 1–8) was required in this group. When radiofrequency ablation was performed at a nonideal site, EpiPSAP conduction was eliminated acutely in only 49 of 62 (79%; 95% CI, 67%–88%) patients (P<0.0001 versus radiofrequency ablation at ideal site). During a follow-up period of 3 to 6 months, EpiPSAP conduction returned in 13 patients who underwent radiofrequency ablation at the ideal site, resulting in a long-term, single procedure success rate of 90% (95% CI, 84%–95%). When ablation was performed at a nonideal site, the long-term, single procedure success was only 56% (95% CI, 43%–69%; P<0.001 versus ablation at ideal site).

Figure 2. Radiographs in the right anterior oblique (RAO; A) and left anterior oblique (LAO; B) projections during right coronary artery angiography in a patient with an epicardial posteroseptal accessory pathway. The ablation catheter is positioned at the ideal site in the middle cardiac vein (MCV). The posterolateral branch of the right coronary artery (RCA) is located within 2 mm of the proximal edge of the ablation electrode at ideal ablation site. No radiofrequency ablation was performed at that site. For size reference, note that the distal electrode of the ablation catheter is 2.5 mm in diameter.
Of the 41 radiofrequency patients who had acute failure (14 patients) or recurrence of EpiPSAP conduction at follow-up (27 patients), 21 patients underwent a second catheter ablation at our institution, which was successful in 19, whereas a third procedure was required in the other 2 patients to achieve permanent elimination of the EpiPSAP. This results in a long-term success in 137 of the 143 patients (96%; 95% CI, 91%–98%) in whom radiofrequency ablation was performed at the ideal ablation site and 48 of the 62 patients (77%; 95% CI, 65%–87%) in whom radiofrequency ablation was performed outside of the ideal ablation site.

Cryoablation Success
Twenty-six patients underwent cryoablation between late 2002 and 2007 because of the presence of a significant CA close to the ideal ablation site. A CS myocardial extension potential (CSE, similar to an AP potential) was recorded from the venous branch of the CS (most often the middle cardiac vein) in 25 of the 26 patients. The distance between the ideal ablation site and the closest significant CA was ≤2 mm in 22 patients and 3 to 5 mm in 4 patients. Cryoablation alone successfully eliminated AP conduction in 17 of 26 (65%; 95% CI, 44%–83%) patients (median 7 cryo-applications; interquartile range, 4–9). In 8 of the 9 remaining patients, cryoablation within the coronary venous system blocked conduction between the vein and the CS, and therefore the left atrium (median 10 cryo-applications; interquartile range, 9–21), but failed to eliminate AP conduction completely because of persistent epicardial connections between the AP and right atrium. The right atrial component of the EpiPSAP was eliminated in 7 of the 8 patients by multiple radiofrequency applications within the right atrium, away from the tricuspid annulus, at the site of earliest (far-field) retrograde atrial activation (median 8 radiofrequency applications; interquartile range, 3–9). In the eighth patient, the

Table 2. Risk of Coronary Artery Injury With Radiofrequency Ablation Versus Cryoablation at the Ideal Ablation Site as a Function of Distance From a Significant Coronary Artery

<table>
<thead>
<tr>
<th>Coronary Angiography (Distance From Artery), mm</th>
<th>No Coronary Angiography</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2</td>
<td>22</td>
<td>143</td>
</tr>
<tr>
<td>3–5</td>
<td>15</td>
<td>65</td>
</tr>
<tr>
<td>&gt;5</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>RF at ideal site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute success</td>
<td>21 (95%)</td>
<td>142</td>
</tr>
<tr>
<td>Chronic success</td>
<td>19 (86%)</td>
<td>129</td>
</tr>
<tr>
<td>RF at nonideal site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute success</td>
<td>38 (79%)</td>
<td>49</td>
</tr>
<tr>
<td>Chronic success</td>
<td>29 (60%)</td>
<td>35</td>
</tr>
<tr>
<td>Cryoablation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute success</td>
<td>14 (64%)</td>
<td>17</td>
</tr>
<tr>
<td>Chronic success</td>
<td>21 (95%)</td>
<td>25</td>
</tr>
</tbody>
</table>

RF indicates radiofrequency.

Figure 3. Radiograph in the left anterior oblique projection during right coronary artery (RCA) angiography in a patient with epicardial posteroseptal accessory pathway. A, Before radiofrequency (RF) ablation, the ablation catheter is positioned at the ideal site in the MCV (arrow), <2 mm from the posterolateral branch of the RCA. B, After RF ablation, there is a 90% stenosis of the posterolateral branch of the RCA (arrow). For size reference, note that the distal electrode of the ablation catheter is 2.5 mm in diameter.
combination of cryoablation within the coronary venous system and radiofrequency ablation in the right atrium failed to eliminate EpiPSAP conduction. In the 1 remaining patient, ablation at the posterolateral mitral annulus was required to eliminate completely EpiPSAP conduction. Thus, the overall acute success rate of cryoablation in eliminating EpiPSAP conduction was 65% (95% CI, 44%–83%) with cryoablation alone and 96% (95% CI, 80%–100%) with additional radiofrequency ablation (Table 1). The large number of cryo-applications reflects the fact that frequent recurrences of AP conduction were observed within 1 hour of the last successful cryoablation, necessitating waiting for ≤2 hours after the final successful cryoablation to ensure elimination of EpiPSAP conduction. During a follow-up period of 3 to 6 months, 5 of the 25 patients with successful cryoablation had recurrence of EpiPSAP conduction. Thus, the long-term, single procedure success rate of cryoablation (with and without additional radiofrequency ablation) was 77% (95% CI, 56%–91%).

Discussion

The main finding of this study is that radiofrequency energy delivered within coronary veins or the neck of CS diverticula in close proximity to a CA is associated with a high risk of CA injury. This is extremely important considering that most patients undergoing ablation of an EpiPSAP are young (average age, 31 years in our cohort). Moreover, ablation within the coronary venous system may lead to disastrous complications, including lethal arrhythmias. Therefore, radiofrequency ablation within <5 mm of a significant CA should be considered carefully or avoided. The orientation of the ablation catheter may be an important determinant of the likelihood of CA injury. Based on our experience, delivering radiofrequency energy with the electrode oriented perpendicular to a CA (where the electrode in the vein compresses the artery) seems to carry a higher risk of CA injury compared with an electrode oriented parallel to an artery (Figure 4).

Our results highlight the value of coronary angiography when ablation anywhere within the coronary venous system is contemplated. We found that it was often safer to perform ablation relatively deep in the middle cardiac vein (or other vein) than within the CS or just inside the vein, because of the frequent proximity of the posterolateral branch of the right CA to the CS (Figure 4). The risk of injuring a CA, as a function of the distance from the CA, represents a continuum, rather than an all-or-none phenomenon. The risk diminishes significantly for distances >2 mm and is negligible for distances >5 mm. Although the stenosis often seems to regress at 6 months, experimental studies have shown that the media, and frequently the intima, of the artery are destroyed and therefore the ability of the artery to dilate may be compromised.

Targeting ablation of an EpiPSAP outside the coronary venous system is associated with a significantly lower success rate compared with ablation within the coronary venous system (middle cardiac vein, posterior coronary vein, other coronary vein, or the neck of a CS diverticulum). This is because of the unique anatomy of the EpiPSAP, which represents an anatomic and electric connection between an extension of the CS myocardial coat (along a coronary vein) and the epicardial surface of the left ventricle. This places the entire CS myocardial coat within the connection between the left atrium and ventricle. Although a typical atrioventricular AP connects the atrium and ventricle at the level of the tricuspid or mitral annulus, allowing successful ablation from the endocardium, the extensive connections between the CS myocardial coat and the left atrium, compounded by the oblique course of the CS myocardial fibers and the absence of a clear endocardial location for the ventricular insertion of the AP, lead to frequent ablation failure of EpiPSAP from the endocardial aspect at the mitral annulus. Radiofrequency ablation of an EpiPSAP should be ideally attempted within the coronary vein or neck of a diverticulum, where the connecting fibers are narrowest. Cryoablation is the preferred option when a significant CA is located close to the ideal ablation site. Surgical ablation, using the epicardial approach described by Guiraudon et al., is another treatment option for these patients.

Figure 4. Right coronary artery (RCA) angiography (left anterior oblique projection) in a patient with an epicardial posteroseptal accessory pathway, showing the posterolateral branch of the RCA coursing directly behind the coronary sinus (CS). Ablation was performed deep in the middle cardiac vein, far from the posterolateral branch of the RCA, but close (<2 mm) to a small artery running parallel to the ablation electrode. A, Before radiofrequency ablation, the ablation electrode is positioned at the ideal site, deep in the middle cardiac vein (arrow), <2 mm from a small branch of the distal RCA. B, Angiography before ablation, showing the small arterial branch. C, After radiofrequency ablation, there is no change in the small arterial branch that was oriented parallel to the ablation electrode. For size reference, note that the distal electrode of the ablation catheter is 2.5 mm in diameter.

Figure 5. Risk of coronary artery injury with radiofrequency ablation as a function of the distance from the ablation site. Note that no coronary artery injury was observed when the distance from the ablation site was >5 mm (dotted line).
Our results suggest that cryoablation is safe, as supported by the absence of CA narrowing, despite the close proximity of cryo-applications to a significant CA. Given that CA stenosis has been reported with epicardial cryoablation, both clinically and in experimental models, the risk of CA stenosis with cryoablation close to a CA, although significantly smaller compared with radiofrequency ablation, may not be zero. However, based on recent experimental data, the probability of vascular damage is inversely proportional to vessel diameter, with no evidence of vascular damage in vessels with diameters >0.7 mm. Cryoablation (alone or in combination with radiofrequency applications at endocardial sites) is associated with a reasonable acute success rate and should be considered when coronary angiography shows a significant CA located close to the ideal ablation site, although the long-term success rate of cryoablation is less optimal than radiofrequency ablation. Notwithstanding this limitation, the significantly better safety of cryoablation in our cohort may have been underestimated because of the use of 4- and 6-mm tip cryo-electrodes. In our subsequent experience, the acute success rate is somewhat improved with advances in cryo-electrode technologies (use of 8-mm tip cryo-electrodes), but the recurrence rate remains higher with cryoablation than with radiofrequency ablation. Notwithstanding this limitation, the significantly better safety profile of cryoablation compared with radiofrequency ablation makes it the treatment of choice for ablation of EpiPSAP located in close proximity to a CA, to avoid CA injury.

These results are consistent with recent experimental data, which suggested that cryoablation within 2 mm of a CA was not associated with CA narrowing, despite producing a similar incidence of necrosis of the media of the artery as radiofrequency ablation. The type of medial necrosis is different between radiofrequency ablation and cryoablation. Radiofrequency ablation causes coagulation necrosis, destroying the architecture of the vessel, whereas the medial necrosis produced by cryoablation is associated with fibroblast infiltration and relatively preserved architecture. The exact mechanism of CA narrowing produced by radiofrequency ablation has not been elucidated. Spasm is unlikely because the narrowing occurred despite the presence of intracoronary nitroglycerin. It is possible that heat-induced shrinkage of collagen fibers associated with radiofrequency energy application is responsible for the CA narrowing. Cryoablation was not associated with late intimal proliferation or narrowing of the coronary arteries ≤6 months post ablation in a recent experimental study in young pigs. The clinical implication for this observation is that cryoablation can be safely used in both children and adults with little or no risk of acute or chronic injury to the coronary arteries.

Conclusions

The risk of injuring a CA with radiofrequency ablation delivered within a coronary vein is inversely related to the distance of the artery from the ablation site, with high (50%) risk of CA injury for radiofrequency ablation within 2 mm of the artery. Cryoablation is a safe and reasonably effective alternative when a significant CA is located close to the ideal ablation site.

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Disclosures

None.

References

CLINICAL PERSPECTIVE

Epicardial posteroseptal and left posterior accessory pathways comprise 19% of all posteroseptal and left posterior accessory pathways. Attempts to ablate epicardial posteroseptal accessory pathway conduction from the endocardium often fail, as the ideal ablation site is located within the coronary venous system (coronary vein or neck of a coronary sinus diverticulum). However, in some patients, branches of the distal right coronary artery or left circumflex coronary artery course between the vein and the ventricle, just below the coronary sinus, adjacent to the ideal ablation site. In this study of 240 patients who underwent ablation of an epicardial posteroseptal accessory pathway at our institution, we show that the risk of coronary artery injury with radiofrequency ablation within the coronary venous system is inversely related to the distance of the artery from the ablation site. Radiofrequency ablation within 2 mm of the artery is associated with a high risk of coronary artery injury, whereas ablation at a distance >5 mm from the artery is safe. Cryoablation is a safe and reasonably effective (albeit less effective than radiofrequency ablation) alternative when a significant coronary artery is located close to the ideal ablation site. With the increasing number of cardiologists performing catheter ablation, it is important to recognize the potential risk of radiofrequency ablation within the coronary venous system, which can lead to serious complications, including permanent coronary artery injury. Our results highlight the value of coronary angiography when ablation anywhere within the coronary venous system is contemplated, to guide further ablation strategy.
Risk of Coronary Artery Injury With Radiofrequency Ablation and Cryoablation of Epicardial Posteroseptal Accessory Pathways Within the Coronary Venous System
Stavros Stavrakis, Warren M. Jackman, Hiroshi Nakagawa, Yingxian Sun, Qingke Xu, Karen J. Beckman, Deborah Lockwood, Benjamin J. Scherlag, Ralph Lazzara and Sunny S. Po

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