CRYOABLATION TO THE AV CONDUCTION SYSTEM/Ohkawa et al.

Anatomic Effects of Cryoablation of the Atrioventricular Conduction System

SHIN-ICHIRO OHKAWA, M.D., DONALD B. HACKEL, M.D., EILEEN M. MIKAT, PH.D., JOHN J. GALLAGHER, M.D., JAMES L. COX, M.D., AND WILL C. SEALY, M.D.

SUMMARY Because of the value of cryoablation of the atrioventricular (AV) conduction system in the treatment of refractory cardiac rhythm disorders, the anatomic effects of cryoablation on the cardiac conduction system must be defined. In this report we summarize studies done on four patients who had intractable recurrent supraventricular tachyarrhythmias or refractory atrial flutter-fibrillation. They were treated by cryoablation of the AV conduction system and died 8–360 days postoperatively. Serial sections of the AV conduction system were studied. Cryoablation produced lesions that completely destroyed most of the AV node in three cases, the penetrating portion of the His bundle in all four cases, and the branching portion of the His bundle in two cases. The right bundle branch was not involved markedly in any case. The lesions were discrete and sharply delimited; the patient who died 8 days postoperatively had hemorrhage, necrosis and slight inflammatory infiltrate; patients who survived for 49–360 days showed collagen deposition. The AV nodal artery and its branches showed slight to marked intimal thickening in three cases. Small, partly organized thrombi were present just behind the tricuspid valve in two patients. We conclude that cryoablation of the AV conduction system produced discrete cardiac lesions that did not markedly damage the tricuspid valve or aorta.

A CRYOSURGICAL TECHNIQUE for ablating the atrioventricular (AV) node—His bundle has been used in patients with disabling supraventricular tachyarrhythmias unresponsive to medical management.1-3 This is an effective technique, and thus will probably become widely used. Therefore, the anatomic effects of the cryoablation procedure on the cardiac conduction system must be defined. We describe the findings in four patients who died 8–360 days after cryoablation.

Patient Population

Four deceased patients (two men and two women) with supraventricular tachyarrhythmias or atrial flutter-fibrillation with or without associated ventricular tachyarrhythmias were studied. All of them showed resistance to medical therapy and were referred to the Duke University Medical Center for surgical treatment. A brief report of the anatomic findings in one of these patients (case 4, table 1) was reported previously.3

Operative Procedures

All patients had an electrophysiologic assessment to determine the mechanism of their arrhythmias. The results of these studies have been reported.3,4 The cryosurgical technique used in this study has been described in detail elsewhere.1,3 After identification of the His bundle by observation of the electrograms generated by mapping the endocardial tissue with a handheld bipolar probe, the cryoprobe was applied three times to overlapping His bundle areas for 3 minutes each at a temperature of -50 to -60°C. After rewarming, the area was probed again and the electrograms were observed for complete AV block. All patients had implanted pacemakers.

Case 1 was treated only by cryosurgery and case 2 had concurrent coronary artery bypass grafting, encircling endocardial ventriculotomy and aneurysmectomy. Case 3 had concurrent division of the posteroseptal pathway in the crux region. Case 4 had ablation of a focus of ventricular tachycardia in the left ventricle and ablation of the His bundle region, which was contiguous to an accessory pathway.

From the Departments of Pathology, Medicine, and Surgery, Duke University Medical Center, Durham, North Carolina. Supported by USPHS grant HLB-17670.

Dr. Hackel was supported by Research Career Award HLB-K6-14188.

Address for correspondence: Donald B. Hackel, M.D., Department of Pathology, Duke University Medical Center, Durham, North Carolina 27710.

Received June 10, 1981; revision accepted August 24, 1981. Circulation 65, No. 6, 1982.
# Table 1. Clinical Findings

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Clinical diagnosis</th>
<th>Diagnosis of arrhythmia</th>
<th>Duration of arrhythmia</th>
<th>Medication for arrhythmia</th>
<th>Preoperative ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16</td>
<td>F</td>
<td>CM, CHF, MR</td>
<td>SVT (ECT)</td>
<td>&gt; 1 yr</td>
<td>Digitalis, propranolol</td>
<td>NSR, LAD, LVH, occ. AFI</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>M</td>
<td>OMI, HT, s/p SVBG</td>
<td>AF/AF (rapid), VT</td>
<td>1 yr 3 mos</td>
<td>Digitalis, procainamide, propranolol, quinidine</td>
<td>NSR, LAD</td>
</tr>
<tr>
<td>3</td>
<td>74</td>
<td>M</td>
<td>CHF, WPW</td>
<td>SVT (AP)</td>
<td>62 yrs</td>
<td>Aramine, digitalis, disopyramide, procainamide, propranolol, quinidine</td>
<td>WPW</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>F</td>
<td>Mitral prolapse, VT, WPW</td>
<td>SVT (AP), VT</td>
<td>15 yrs</td>
<td>Digitalis, diphenylhydantoin, disopyramide, propranolol, quinidine</td>
<td>N</td>
</tr>
</tbody>
</table>

Abbreviations: CM = cardiomyopathy; CHF = congestive heart failure; MR = mitral regurgitation; OMI = old myocardial infarction; HT = hypertension; s/p = status after operation; SVBG = saphenous vein bypass graft; VT = ventricular tachycardia; WPW = Wolff-Parkinson-White syndrome; SVT (ECT) = supraventricular tachycardia due to an ectopic atrial focus; AF = atrial fibrillation; SVT (AP) = supraventricular tachycardia due to an accessory pathway; NSR = normal sinus rhythm; LAD = left-axis deviation; LVH = left ventricular hypertrophy; occ. = occasional; N = normal; PM = pacemaker; EEV = encircling endocardial ventriculotomy; CAVB = complete atrioventricular block.

## Histopathologic Procedures

The hearts were examined by routine procedures. These included the radiographic demonstration of the coronary arteries, which had been injected with a barium sulphate–gelatin mixture. The sinoatrial node (SAN) was examined by step sections of the crista terminalis region. The AV conducting tissue was studied using the method of Lev et al., and serial sections of the AV node tissue were mounted and stained on 35-mm Mylar film as previously described. The bundle of His was divided into the penetrating and branching portion and the left bundle branch was classified into posterior and anterior regions. The right bundle branch was subdivided into three portions, designated as the first, second and third portions. The severity of the lesions in the SAN, the approaches to the SAN, the atrium and the approaches to the AV node were expressed as normal, mild, moderate and severe. Lesions in the AV conduction system were classified into five degrees: complete interruption of conducting fibers = 5, 75% destruction = 4, 50% = 3, 25% = 2, 10% = 1, and no changes = 0. Sclerosis and narrowing of coronary arteries were estimated using the modified World Health Organization classification: complete occlusion = 5, 75% stenosis of the original area = 4, 50% = 3, 25% = 2, and minimal stenosis = 1. The stenotic index was defined as the sum of the maximal value for each of the three main coronary arteries.

## Results

### Clinical Findings

The main clinical features are listed in table 1. Three of the four patients had supraventricular tachycardia and one had atrial flutter and atrial fibrillation. Two patients had combined ventricular tachyarrhythmias. Postoperative changes on ECGs showed that complete AV block was achieved just after the surgery in all four patients. The QRS morphology of induced complete AV block showed a narrow QRS (< 0.12 second) in all cases. The cause of death in three of the four patients was not directly related to cryoablation. Case 1 died suddenly in the hospital despite prolonged attempts at resuscitation. Her pacemaker was checked at that time and was functioning normally. She was discovered in ventricular fibrillation, and the probable cause of death was thought to be primary ventricular arrhythmia related to her cardiomyopathy. Cases 2 and 3 were both elderly and died of continued postoperative low cardiac output resulting in renal failure and sepsis. Case 4 died suddenly 1 year after the operation. She had occasional ventricular tachycardia postoperatively and once, while on a repeat visit to the hospital, developed ventricular fibrillation that required immediate cardioversion. She required continued antiarrhythmic agents for her recurrent ventricular tachycardia. Therefore, her death was ascribed to recurrence of the original ventricular tachycardia, which always had the same morphology. At no time did a new site of irritability develop from the site of freezing.

### Anatomic Findings (table 2)

The average heart weight was 610 g (range 406–705 g) for the four patients. The coronary stenotic index was normal except for case 2, who had severe coronary atherosclerosis and an old myocardial infarct associated with aneurysm formation. Case 1 had congestive cardiomyopathy.

### Histologic Findings (table 2)

Histologic study of the SAN and its approaches showed moderate-to-severe necrosis and mild hemor-
rhage in case 1 and moderate-to-severe fibrosis in cases 2–4. The histologic changes in the atrium were of patchy moderate fibrosis in three cases.

In case 1, the approaches to the AV node showed hemorrhage. There was fibrinoid necrosis of the wall of the AV nodal artery (fig. 1A). The AV node (fig. 2A), the penetrating portion of the His bundle (fig. 3A) and proximal part of the branching His bundle had marked necrosis and recent hemorrhage. The middle and distal parts of the branching His bundle showed moderate changes. The left bundle branch and the right bundle branch were normal.

In case 2, the approaches to the AV node showed moderate-to-severe fibrosis. The AV nodal artery (fig. 1B) showed moderate-to-severe intimal narrowing. The AV node (fig. 2B) and the penetrating His bundle (fig. 3B) were markedly replaced by fibrosis. The bundle branches were intact (fig. 4A).

In case 3, the approaches to the AV node showed moderate fibrosis. The AV nodal artery was moderately sclerotic. The changes of the AV node included moderate-to-severe fibrosis, which continued into the proximal part of the penetrating His bundle. The remaining part of the His bundle showed moderate fibrosis. The bundle branches were intact.

In case 4, the approaches to the AV node, the AV nodal artery and the AV node itself showed only minimal changes. However, both the penetrating and branching portions of the His bundle showed marked fibrotic changes (fig. 4B). The left bundle branch showed moderate fibrosis. The initial part of the first portion of the right bundle branch showed slight fibro-

---

**Table 1. (Continued)**

<table>
<thead>
<tr>
<th>Operation</th>
<th>Result</th>
<th>Postoperative intervals to death (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryothermia, PM implant</td>
<td>CAVB, narrow QRS escape</td>
<td>8</td>
</tr>
<tr>
<td>Cryothermia, PM implant, SVBG, aneurysmectomy, EEV</td>
<td>CAVB, narrow QRS escape</td>
<td>49</td>
</tr>
<tr>
<td>Cryothermia, PM implant, division of AP</td>
<td>CAVB, narrow QRS escape</td>
<td>62</td>
</tr>
<tr>
<td>Cryothermia, PM implant, ablation VT focus</td>
<td>CAVB, narrow QRS escape</td>
<td>360</td>
</tr>
</tbody>
</table>

---

**Figure 1.** The atrioventricular (AV) nodal arteries. (A) Fibrinoid necrosis (arrows) of the vessel wall and necrosis of the surrounding AV node (N) in case 1. Hematoxylin-eosin stain; magnification × 400. (B) Marked intimal narrowing of the AV nodal artery (arrows) and fibrosis of the surrounding AV node (N) in case 2. Masson stain; magnification × 150.
**Table 2. Pathohistologic Findings**

<table>
<thead>
<tr>
<th>Case</th>
<th>Heart weight (g)</th>
<th>CSI</th>
<th>Cardiac pathology</th>
<th>Conduction system lesions*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SAN SANapp</td>
</tr>
<tr>
<td>1</td>
<td>681</td>
<td>0/15</td>
<td>Cardiomegaly, COCM, MR</td>
<td>++ to +++ Nec Hem</td>
</tr>
<tr>
<td>2</td>
<td>705</td>
<td>14</td>
<td>Cardiomegaly, CAD, s/p SBVG + aneurysmectomy, p/o pericarditis</td>
<td>++ F</td>
</tr>
<tr>
<td>3</td>
<td>648</td>
<td>5</td>
<td>Cardiomegaly, p/o pericarditis</td>
<td>++ F</td>
</tr>
<tr>
<td>4</td>
<td>406</td>
<td>3</td>
<td>p/o pericarditis</td>
<td>+++ F</td>
</tr>
</tbody>
</table>

Abbreviations: CSI = coronary stenotic index; COCM = congestive cardiomyopathy; MR = mitral regurgitation; CAD = coronary artery disease; p/o = postoperative; s/p = status p/o; SVBG = saphenous vein bypass graft; SAN = sinoatrial node; SANapp = approaches to the SAN; AVNapp = approaches to the atrioventricular node; AVNart = AVN artery; HISp = penetrating portion of His bundle; HISb = branching portion of His bundle; LBp = posterior region of left bundle branch; LBa = anterior region of left bundle branch; RB1,II,III = first, second and third portions of right bundle branch; Nec = necrosis; Hem = hemorrhage; F = fibrosis; thromb = thrombus; RV = right ventricle; TV = tricuspid valve.

*N = normal; + = slight; ++ = moderate; +++ = severe. In AV conduction system: 5 = complete interruption of conduction cells; 4 = 75% destruction; 3 = 50% lesion; 2 = 25% lesion; 1 or 0 = slight to no lesion.

sis, but the remaining right bundle branch was normal (fig. 5).

Figure 6 is a summary of the conduction system lesions. In all cases, the myocardium had discrete, sharply delimited lesions (fig. 7). The pathologic changes, in addition to those of the conduction system, included a mural thrombus between the right ventricle and the tricuspid valve in cases 1 and 3 and a slight degree of hemorrhage and edema at the base of the tricuspid valve in case 1.

**Figure 2. The atrioventricular (AV) nodal (N) region. (A) Acute necrosis and granulation formation (arrow) in case 1. Hematoxylin-eosin stain; magnification × 40. (B) Marked fibrosis (arrows) and also moderate thickening of the AV nodal artery (white arrow) in case 2. Masson stain; magnification × 40.**
Table 2. (Continued)

<table>
<thead>
<tr>
<th>AVN</th>
<th>HISp</th>
<th>HISb</th>
<th>LBp</th>
<th>LBA</th>
<th>RB₁</th>
<th>RB₁₁</th>
<th>RB₁ΙΙ</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>5</td>
<td>5-3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>Mural thromb. between RV and TV, Hem and edema in the base of TV</td>
</tr>
<tr>
<td>4</td>
<td>4-5</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>F</td>
<td>Mural thromb. under TV, no accessory tract</td>
</tr>
<tr>
<td>3-4</td>
<td>5-3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>F</td>
<td>No accessory tract</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>F</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Electrophysiologic techniques have been developed that permit better interpretation and diagnosis in patients with supraventricular tachycardia, ventricular tachyarrhythmias or the preexcitation syndrome. In some cases, pharmacologic treatment or pacing to correct the abnormalities has been effective. Other patients with life-threatening and disabling arrhythmias who have not responded to these methods have been treated by surgery. For supraventricular and junctional tachyarrhythmias, surgical interruption of the bundle of His by suture ligation, cautery or dissec-

tion, followed by implantation of a permanent ventricular pacemaker, are the most frequently used procedures. Ventricular tachyarrhythmias have been treated by sympathectomy, ventricular aneurysmectomy (as in case 2), revascularization and encircling endocardial ventriculotomy. In addition, the successful application of cryosurgical techniques in the ablation of the His bundle and accessory pathways has led to the application of this technique to ablate the ectopic focus in a patient with recurrent ventricular tachycardia.

In ablating the AV node–His bundle region, tradi-

Figure 3. The penetrating portion of the His bundle (B). (A) Necrosis (arrows) in case 1. Hematoxylin-eosin stain; magnification × 40. (B) Marked fibrosis (arrows) in case 2. Masson stain; magnification × 40.
tional methods such as suture ligation, incision and cautery are all associated with the risk of inducing tricuspid regurgitation, septal defects, aneurysms and fistulas of the aortic sinus of Valsalva. To avoid these perils, cryosurgical ablation of the AV node–His bundle producing AV block was developed in 1977. Harrison et al. first used this method in 20 dogs and then in three patients with drug-resistant, life-threatening supraventricular tachycardias. Gallagher et al. reported two successful cases of cryosurgical ablation of accessory AV connections. Klein et al. reported a study of long-term follow-up in 22 patients treated by cryosurgical ablation of the AV node–His bundle in which successful AV block was achieved in 17. There was no intraoperative mortality, and significant surgical complications were not encountered.

The anatomic changes in the human cryoablated conduction system in this study are similar to those in the canine model. In case 1, who died 8 days after cryoablation of the AV conduction system, the lesion showed necrosis of myocardial cells and conduction fibers (in the approaches to the AV node, the AV node and the His bundle), polymorphonuclear leukocytic infiltration and hemorrhage (fig. 2A). In case 2, who died 49 days after the cryoablation, the entire region of the lesions was replaced by dense fibrotic connective tissue (figs. 2B and 3B). Similar fibrosis (figs. 4B and 5A) was present in case 4, who died 1 year after the cryoablation. In case 3, who died 62 days after cryoablation of the AV conduction system and had other surgical procedures in that area, the character of the lesions in the conduction system was essentially similar to that detected in case 2. The fibrotic changes in the AV node in case 3 could have been the result of the combined cryoablation procedure and surgical intervention. The marked lesions of the penetrating portion of the His bundle were similar in all four cases. In addition, marked destruction of the AV node by necrosis was found in case 1 and replacement by fibrosis was found in cases 2 and 3, in which the changes below the branching portion of the His bundle were mild and the conduction cells were spared (fig. 4A). In

Figure 4. The branching portion of the His bundle (B). (A) The surviving conduction cells in the branching His (B) and the left bundle branch (LB) in case 2. Masson stain; magnification × 40. (B) Marked fibrous replacement (arrows) in case 4. Masson stain; magnification × 40. (Reprinted with permission.)

Figure 5. The right bundle branch shows intact bifurcation (B) and the first portion of the right bundle (RB) in case 4. LB = left bundle. Masson stain; magnification × 40.
these three cases, the narrow QRS complex of junctional escape beats during complete AV block may have originated from these anatomic subjunctional areas (the middle or lower branching His), as predicted by Klein et al.8 In case 4, the changes in the AV node were only slight, and a severe lesion involved both the penetrating and branching His bundle, but the bundle branches were intact. The morphology of the QRS complex during complete AV block in case 4 showed a QRS of normal width. Thus, the anatomic changes in the AV conduction system in this study provide information concerning the correlation between the anatomic sites of lesions and the electrophysiologic findings of the ECG, which may be pertinent not only to cryoaublated cases, but perhaps also to naturally occurring conduction abnormalities.

Although the cryprobe was carefully positioned using an intraoperative electrophysiologic technique to precisely locate the AV node–His bundle, the actual location of the resulting lesions varied from case to case (fig. 6). This may be because (1) the anatomic location of the AV conduction system probably differed in detail from case to case, (2) the technique for applying the cryoprobe was not always exactly the same, and (3) there were undoubtedly temperature differences due to differences in tissue thickness and minor variations in probe temperature.

The AV nodal artery or its branches showed fibrinoid necrosis in case 1 (fig. 1A) and intimal thickening that was atheroma-like in case 2 (fig. 1B). These findings are similar to those induced by application of the cryoprobe to the myocardium and coronary arteries of canine hearts.18

The resulting necrotic or fibrotic lesions of the myocardium were homogeneous and had sharp borders of demarcation between normal and injured tissue (fig. 7), unlike the diffusely scattered lesions produced by ischemia. This could account for the lack of arrhythmogenicity in the chronic lesions.17 The existence of small, partly organized mural thrombi between the right ventricle and the tricuspid valve in cases 1 and 3, and the slight hemorrhage and edema at the base of the tricuspid valve in case 1, were of no physiologic significance. Thus, cryoablation is a relatively safe technique, as judged by the lesions described in this report and our clinical experience with its use. We have treated 41 patients by cryoablation for various severe arrhythmias. The deaths of the four patients included in this report were the only deaths, and they were apparently not primarily due to cryoablation. Three of the four deaths could be only indirectly linked to cryoablation. Patient 1 died in the early postoperative period, possibly from a ventricular arrhythmia. Patients 2 and 3 were elderly and may have died from continued low cardiac output postoperatively. In conclusion, cryoablation of the AV node–His bundle was found to be effective in inducing AV
block in patients. The lesions were discrete and did not markedly damage the tricuspid valve or aorta.

References
