Cryothermal Mapping and Cryoablation in the Treatment of Refractory Cardiac Arrhythmias


SUMMARY Cryoablation was applied to the treatment of 15 refractory tachyarrhythmias in 12 patients, Wolff-Parkinson-White atrioventricular reentrant tachycardia (WPW) in five patients, paroxysmal atrial fibrillation (PAF) in five patients, chronic atrial fibrillation (CAF) in one patient, paroxysmal atrial tachycardia (PAT) in two patients and paroxysmal ventricular tachycardia (PVT) in two patients. At operation the accessory pathway in four patients with left-sided WPW was located by intraluminal coronary sinus and epicardial electrographic mapping techniques. Epicardial cryothermal mapping during tachycardia terminated the arrhythmias in one patient. In three patients endocardial cryothermal mapping was necessary to abolish ventriculoatrial accessory pathway conduction. In four patients with PAF and one patient with PAT the AV node/His bundle was located by both electrographic and cryothermal mapping. In one patient with concealed WPW, one with PAT, and the patient with CAF, electrographic mapping was impossible. Cryothermal mapping accurately located the AV node/His bundle in two of these patients.

Electrographic mapping during PVT revealed earliest ventricular activation on the lateral left ventricular epicardium in one patient and on the right side of the intraventricular septum in the other. Cryothermal mapping at the point of earliest activation terminated both tachycardias. In all cases cryoablation was achieved by cooling to -65°C for 2 minutes.

In nine patients there has been no recurrence of symptomatic tachycardia during the follow-up period of 4–20 months but there were three partial failures when His bundle conduction resumed immediately, at 10 days, and at 2 months. The technique of electrographic mapping, cryothermal mapping and cryoablation has proved a simple and successful method.

WITH THE ADVENT of electrographic mapping techniques and surgical procedures have been specifically designed to eradicate cardiac arrhythmias. These techniques have been directed toward the destruction of foci of automatic tachycardias, the interruption of reentrant pathways essential to the continuation of the tachycardia or the ablation of the atrioventricular conduction tissue to prevent the ventricular expression of rapid supraventricular arrhythmias. The methods of destruction have included surgical incision, electrocautery and ligature. Recently Gallagher and colleagues introduced cryoablative techniques and in this report we confirm and extend their results. We have used a technique of cryothermal mapping not only to localize conduction tissue but also to identify irritable ventricular tissue before irreversible destruction of this tissue by cryoablation.

Patients

The clinical details of the 12 patients included in this report are summarized in table 1. They are a consecutive series of patients who underwent operation for the treatment of tachycardia between November 1977 and December 1978. All patients suffered from tachycardia that was resistant to conventional medical treatment. In the five patients with paroxysmal atrial fibrillation the frequency of attacks could not be significantly reduced by antiarrhythmic medical therapy. In one case of established atrial fibrillation with mitral valve disease, medical treatment failed to control the ventricular response or worsened existing cardiac failure and asthma. In the patient with Ebstein's anomaly and brady-tachy syndrome, antiarrhythmic drugs worsened symptomatic bradycardias and right-heart failure. Four patients presented with repetitive supraventricular tachycardia unresponsive to antiarrhythmic drug prophylaxis; two had cardiac failure. Two patients with recurrent ventricular tachycardia and syncopal spells failed to respond to a large variety of antiarrhythmic agents.

Preoperative Methods and Findings

Clinical diagnosis of the arrhythmias was achieved by 12-lead and 24-hour taped ECGs. Eleven patients underwent preoperative electrophysiologic studies to allow accurate diagnosis of each arrhythmia, based upon accepted electrophysiologic criteria. The patient with chronic atrial fibrillation was not studied preoperatively because it was felt that no further useful information could be obtained. The results of these investigations are summarized in table 1.

The methods by which each reentrant tachycardia could be electively initiated were carefully investigated to make reasonably certain that the tachycardia could be similarly initiated at the time of surgery. During the electrophysiologic investigations the efficacy of pharmacologic and pacing techniques in the control of each patient's arrhythmia were studied. We proceeded to surgery when it had been demonstrated clinically or
Table 1. Clinical and Preoperative Investigative Details

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Symptoms</th>
<th>ECG (QRS, rhythm)</th>
<th>Preoperative electrophysiology</th>
<th>CXR</th>
<th>Angiograms</th>
<th>Previous treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>GB</td>
<td>60</td>
<td>M</td>
<td>Palpitations</td>
<td>RBBB, PAF</td>
<td>AF, AVNRT</td>
<td>Normal</td>
<td>LV normal</td>
<td>CA normal</td>
</tr>
<tr>
<td>GW</td>
<td>59</td>
<td>M</td>
<td>Palpitations</td>
<td>Normal, PAF</td>
<td>AF</td>
<td>Normal</td>
<td>LV normal</td>
<td>CA normal</td>
</tr>
<tr>
<td>JH</td>
<td>39</td>
<td>M</td>
<td>Palpitations, dizziness</td>
<td>Normal, PAF</td>
<td>AF, AFI</td>
<td>Normal</td>
<td>LV normal</td>
<td>CA normal</td>
</tr>
<tr>
<td>IU</td>
<td>55</td>
<td>F</td>
<td>Palpitations, dyspnea</td>
<td>Normal, CAF</td>
<td>—</td>
<td>LA + large heart</td>
<td>—</td>
<td>Digoxin, verapamil</td>
</tr>
<tr>
<td>RC</td>
<td>58</td>
<td>M</td>
<td>Palpitations, dizziness, dyspnea</td>
<td>RBBB, PAT sinus brady</td>
<td>ART</td>
<td>Large heart</td>
<td>Ebstain's</td>
<td>Digoxin, quinidine, disopyramide</td>
</tr>
<tr>
<td>RH</td>
<td>39</td>
<td>M</td>
<td>Palpitations, dyspnea</td>
<td>Normal, AVRT PAFi</td>
<td>AVRT, left CAP</td>
<td>Large heart</td>
<td>LV hypokinesis</td>
<td>CA normal</td>
</tr>
<tr>
<td>GG</td>
<td>48</td>
<td>M</td>
<td>Palpitations</td>
<td>Normal, AVRT</td>
<td>AVRT, left CAP</td>
<td>Normal</td>
<td>LV normal</td>
<td>CA normal</td>
</tr>
<tr>
<td>AC</td>
<td>35</td>
<td>M</td>
<td>Palpitations, dizziness</td>
<td>Type A WPW, PAF</td>
<td>AVRT, AF, left AP</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>GL</td>
<td>40</td>
<td>F</td>
<td>Palpitations</td>
<td>Normal, AVRT</td>
<td>AVRT, left CAP</td>
<td>Normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BM</td>
<td>60</td>
<td>M</td>
<td>Palpitations, dyspnea</td>
<td>Type A WPW, AVRT</td>
<td>AVRT, left AP</td>
<td>Large heart</td>
<td>LV hypokinesis</td>
<td>CA normal</td>
</tr>
<tr>
<td>VA</td>
<td>46</td>
<td>F</td>
<td>Palpitations, syncope</td>
<td>RBBB, PVT</td>
<td>RVT (RV)</td>
<td>Normal</td>
<td>Annular subaortic aneurysm, CA normal</td>
<td>—</td>
</tr>
<tr>
<td>WA</td>
<td>63</td>
<td>F</td>
<td>Palpitations, syncope, dyspnea</td>
<td>Normal, PVT</td>
<td>RVT (LV), PAT, sinus arrest</td>
<td>Large heart</td>
<td>Posterior LV aneurysm, CA normal</td>
<td>—</td>
</tr>
</tbody>
</table>

Abbreviations: RBBB = right bundle branch block; PAF = paroxysmal atrial fibrillation; CAF = chronic atrial fibrillation; PAT = paroxysmal atrial tachycardia; AVRT = atrioventricular reentrant tachycardia; PAFi = paroxysmal atrial flutter; WPW = Wolff-Parkinson-White syndrome; PVT = paroxysmal ventricular tachycardia; AF = atrial fibrillation; AVNRT = intra-AV nodal reentrant tachycardia; AFI = atrial flutter; ART = atrial reentrant tachycardia; CAP = concealed accessory pathway; RVT = reentrant ventricular tachycardia; RV = right ventricle; LV = left ventricle; LA = left atrium; CA = coronary arteries; CXR = chest x-ray.

electrophysiological that other methods were ineffective or unsuitable.

Operative Methods

Patients were withdrawn from antiarrhythmic medical therapy at least three drug half-lives before surgery. All operations were performed via a median sternotomy. Before operative investigation vena caval and aortic cannulae were introduced to facilitate cardiopulmonary bypass if it became rapidly necessary. All mapping and ablative procedures were performed on the beating heart with or without the aid of normothermic cardiopulmonary bypass. With the exception of patient WA, neither hypothermic perfusion nor cardioplegia were used during or before cardiac electrosurgery.

In those patients undergoing His bundle section the right atrium was opened when the heart was fibrillating to avoid the complications of a possible patient foramen ovale. In three of the five patients with a left-sided accessory pathway the aorta was cross-clamped and the aortic root perfused with normothermic blood before the left atrium was opened through the interatrial groove. In patient VA, who had ventricular tachycardia, the septum below the pulmonary valve was exposed via a vertical right ventriculotomy. In patient WA, who also had ventricular tachycardia, mitral valve replacement with cardioplegia was per-
formed after ablation of the tachycardia focus but before attempted His bundle destruction.

Electrographic Mapping

The principle of electrographic mapping is now well accepted. Our technique involved the use of a tripolar mapping probe. Each pole is platinum and 1 mm in diameter and the three poles are set in araldite in a triangular pattern 2 mm apart. Three bipoles were derived by connecting each pole to the remaining two and the bipolar electrograms were amplified and passed through a band-pass filter to select frequencies of 50–700 Hz. Reference electrograms were obtained by bipolar hook electrodes anchored to the myocardium by suture. These signals were recorded simultaneously with three surface ECG leads on an Elema Mingograf at paper speeds of 100 or 250 mm/sec. The mapping probe was moved from point to point on the epicardial or endocardial surface of the heart to record signals from predetermined points in the areas of interest. At each sampling position the point at which the maximum deflection of the local electrogram crossed the baseline was timed to the nearest 5 msec in relation to a fixed reference electrogram and the surface ECG. The activation time at each point was plotted by computer at its respective planar coordinates on a computer-generated, stylized outline of the appropriate area of the heart. A stable relationship between reference electrograms and the surface ECG was required before measurements were accepted as valid.

The His bundle was located by electrographic mapping of the floor and septal region of the right atrium during sinus rhythm or atrial pacing. Epicardial localization of the atrial insertion of the accessory pathways was assisted by the use of a quadrupolar electrode catheter introduced through a stab wound in the right atrium and manipulated into the lumen of the coronary sinus. This method allowed posterior left atrial mapping without dislocating the heart. Bipolar signals from this catheter and the mapping probe were recorded during ventricular pacing or reentrant tachycardia. In patient BM the ventricular insertion was localized by left ventricular epicardial electrographic mapping during atrial pacing. In three patients (GG, GL and BM) the left atrial endocardium around the mitral valve ring was electrographically explored. In patient VA the right ventricular epicardial surface and the septal region of the right ventricular outflow tract were electrographically mapped during sinus rhythm and ventricular tachycardia. In patient WA left ventricular epicardial signals were recorded during ventricular tachycardia.

Cryothermal Mapping and Cryoablation

The cryotherapy system used was an unmodified Spembley-Amoils TCC 42 cryo-unit (fig. 1). This apparatus, which is simple to use, regulates the flow of nitrous oxide through the tip of the cryoprobe. The expansion of the gas at the tip results in cooling by the Joule-Thompson effect. This apparatus is powerful enough to freeze an iceball of 0.95 cm when the probe is immersed in water and to result in local myocardial temperatures, as measured by a thermocouple at the tip of the probe, of −65°C when the cryoprobe is placed on the myocardium. Two probes were used: a straight probe (Spembley 40 — 5H10 cryoprobe) and an angulated probe specially constructed to improve access to the posterior heart.

Reduction of the myocardial temperature to between 0°C and −10°C for 15–30 seconds results in reversible inactivation of electrically active tissue. Cryothermal mapping is based on this principle. During an appropriate rhythm the effect on that rhythm of freezing electrically active tissue can be assessed without producing permanent damage. The accuracy of electrographic mapping was validated in this relatively harmless way before attempting cryoablation. To achieve cryoablation the probe was reapplied and the temperature at the tip of the cryoprobe was reduced to −65°C for 2 minutes. This procedure was repeated at several closely adjacent areas. Both cryothermal mapping and cryoablation were performed on the beating heart and to facilitate fixation of the probe tip before freezing a small nick was made with a knife in the epicardium or endocardium. This tiny incision served as a guide to the area that had been frozen. At the conclusion of any freezing procedure, when the interface between probe and tissue had thawed sufficiently the cryoprobe was removed without causing further damage.
Results and Follow-up

His Bundle Ablation

In patients who underwent His bundle ablation, cryothermal mapping was performed by applying the cryoprobe to areas from which the largest His bundle deflections were recorded. Figure 2 illustrates the response to cooling to between 0°C and −10°C in an area closely adjacent to the His bundle producing first-degree atroventricular (AV) block. Freezing an area closer to the AV node/His bundle produced complete AV block (fig. 3). Cryoablation after combined electrographic and cryothermal mapping was performed at five operations (table 2). At reoperation on patient RH, no His bundle deflection could be obtained, and in patient IU the His deflection was obscured by atrial fibrillation electrograms. In these two cases only cryothermal mapping allowed localization of the AV node/His bundle. In patient WA, after cardioplegia, the atria were inexcitable and cryoabla-
tion of the AV conduction system was performed blindly.

Cryoablation of the His bundle was successful in four of seven patients. In patient RH conduction resumed 10 days after operation. Incessant supraventricular tachycardia immediately recurred and the patient was submitted to reoperation during which AV block was achieved and has persisted for 12 months. Of these five patients, four, who have now been followed for an average of 16 months, are free of symptomatic palpitations and remain in complete AV block. In patient IU, who has chronic atrial fibrillation, AV block persisted for 2 months before conduction resumed. However, the previously uncontrolled ventricular response now never exceeds 110 beats/min and with regular digoxin treatment the mean heart rate is usually 70–85 beats/min. In Patient WA, in whom blind cryoablation of the His bundle was unsuccessful, the ventricular rate during atrial tachycardia is controlled by verapamil and digoxin.

### Accessory Pathway Ablation

Epicardial cryothermal mapping was performed in four patients with accessory pathways. The cryoprobe was placed in the region of the tip of the indwelling coronary sinus catheter, resulting in block of accessory pathway conduction in patient AC. In this patient the accessory pathway was cryoablated from the epicardial surface and cardiopulmonary bypass was not required. In the three other patients endocardial cryothermal mapping was performed at points on the atrial side of the mitral valve ring previously identified by electrographic mapping. This resulted in accessory pathway block (fig. 4) in all three cases. Profound cooling of these and adjacent areas was then performed. Initiation of tachycardia was not possible after this procedure in any of these four patients. These patients have been followed up for an average of 11 months without recurrence of symptomatic tachycardias and none requires additional antiarrhythmic therapy.
Ventricular Tachycardia Focus Ablation

During established ventricular tachycardia cryothermal mapping over the earliest areas of epicardial activation resulted in the termination of tachycardia in patient WA. In patient VA, the earliest epicardial activation occurred 25 msec after the onset of the tachycardia QRS complex, and cryothermal mapping at this point had no effect. Cryothermal mapping of the right ventricular septal surface, where electrical activation was coincident with the onset of the QRS complex, resulted in irregularity and termination of the tachycardia (fig. 5). Full cryoablation was performed at the sites identified by cryothermal mapping. Attempts to reinitiate tachycardia were unsuccessful after cryoablation. Ventricular tachycardia has not recurred in either case and antiarrhythmic therapy has not been required. A single episode of ventricular fibrillation occurred in patient VA 6 hours after operation and was successfully treated by DC conversion. Occasional ventricular ectopic depolarizations are observed in both patients, who have been followed for 10 and 14 months.

Discussion

As in other reported cases and series of tachyarrhythmias treated by surgery, the indication for surgery in all our patients was a lack of response to medical therapy in terms of reduction of frequency or duration of symptomatic arrhythmias. In addition, pacing methods to control the tachyarrhythmias were either inappropriate, as in those patients with paroxysmal atrial fibrillation, or ineffective in those patients with reentrant tachycardias, in four of whom (RH, GL, BM and WA) the tachycardia was almost incessant. During preoperative electrophysiologic studies, particular attention was paid to the ability of stimulation techniques to reliably initiate reentrant tachycardia in patients with accessory pathways or ventricular tachycardia. This is important for the success of intraoperative electrophysiographic and cryothermal mapping, particularly in those patients with ectopic ventricular foci, the only abnormal expression of which may be the tachycardia itself.

The use of specific surgical procedures to abolish or ameliorate resistant cardiac tachyarrhythmias is becoming an established therapeutic approach. Interruption of the bundle of His has been used in two situations: to control the ventricular rate in arrhythmias entirely confined to the atrial myocardium or AV node and to interrupt the tachycardia circuit in those patients with a reentrant mechanism involving the His bundle and an accessory pathway. However, in this latter situation a better alternative is direct ablation of the accessory pathway itself. This is particularly important in patients with short accessory pathways.

Figure 4. The effect of cooling to between 0°C and -10°C in the region of an accessory pathway. Reentrant atrioventricular (AV) tachycardia terminates by block in the accessory pathway. Complete retrograde AV block is present during ventricular pacing. A' = retrograde atrial depolarization. Paper speed is 25 mm/sec.

Figure 5. Termination of ventricular tachycardia by cryothermal mapping. I and III are surface ECG leads. V ref = ventricular reference electrogram.
pathway refractory periods that suffer from rapid atrial arrhythmias with a high conduction rate to the ventricles over the accessory pathway.5, 6, 10, 12, 16, 20-22

The surgical approach to ventricular tachycardias has, in part, been determined by the underlying pathologic process. For example, coronary artery bypass grafting23, 24 resection of a ventricular aneurysm25, 26 or combinations of these techniques have been successful in some patients suffering from coronary artery disease and its sequelae. More specific techniques have included simple ventriculotomy,7, 8 division of the bundle branches where reentry is thought to involve these structures,27 and more recently, an “encircling ventriculotomy.”28 Similarly specific ablative techniques have been applied to atrial tachyarrhythmias.29, 30

A new technique for the destruction of normal and abnormal conduction pathways9, 10 and excitable fog11 was recently described. This method uses hypothermic injury achieved by the application of a cryoprobe containing expanding nitrous oxide. This method has several advantages over other surgical techniques, as summarized by Harrison et al.8 In particular, by cooling to only −10°C, reversible damage may be achieved in areas considered relevant to the expression of the tachyarrhythmia. This principle is embodied in the technique of cryothermal mapping.9, 31

For surgery to be effective in the treatment of tachyarrhythmias, accurate definition of the location and mechanism of the tachycardia is essential. In patients with reentrant arrhythmias, this is accomplished in part by detailed preoperative electrophysiologic studies.5, 17 More precise information must be obtained by intraoperative epicardial or endocardial mapping. These conventional electrographic mapping procedures may be complemented by specific cryothermal mapping, with the aim of achieving a temporary therapeutic result. The use of cryothermal mapping during regular tachycardia offers an immediate confirmation that the maneuver is relevant to the abolition of the tachycardia. Permanent damage to the relevant areas may then be achieved by more profound cooling. In three operations performed for His bundle section, electrographic mapping was not possible. Cryothermal mapping alone was successful in localizing the AV node/His bundle in two of these patients.

Except for patient WA, who had cardioplegic solution before mitral valve replacement and attempted His bundle section, all operations were performed using perfusion techniques that were least likely to interfere with the electrical activity of the heart. Hypothermic perfusion or topical hypothermia other than that caused by the cryoprobe were avoided.

Cardiopulmonary bypass facilities were on standby at all operations for two reasons: first, in the case of rapid hemodynamic deterioration either secondary to an arrhythmia or to manipulation of the heart during mapping; and second, if it was necessary to open the heart to successfully locate and ablate the tachycardia. In two patients epicardial ablation was achieved without recourse to extracorporeal bypass. In patient AC the accessory pathway was located and effectively damaged without opening the left atrium, and in the patient WA the ventricular focus was situated in a "paper-thin" area of a left ventricular aneurysm, and epicardial freezing probably resulted in full-thickness damage in this area. However, it must be emphasized that exclusively epicardial cryothermal mapping was unsuccessful in four patients, excluding those undergoing His bundle ablation, and endocardial exploration may be necessary in most cases.

The combined application of electrographic mapping and cryothermal mapping and ablation is successful in controlling otherwise resistant arrhythmias. The procedure was without mortality or significant morbidity and during follow-up no patient has developed murmurs or other physical signs suggesting major structural damage. Only two patients currently require antiarrhythmic therapy.

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