Modification of atrioventricular conduction as adjunct therapy for pacemaker-treated patients with hypertrophic obstructive cardiomyopathy

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Aims Atrioventricular synchronous pacing offers symptomatic relief for patients with drug-refractory hypertrophic obstructive cardiomyopathy. Successful treatment requires complete right ventricular apical pre-excitation. Enhanced atrioventricular conduction renders this difficult in some patients. The aim of this study was to evaluate whether selective prolongation of atrioventricular conduction is a useful tool for optimization of treatment in patients with hypertrophic obstructive cardiomyopathy primarily refractory to cardiac pacing.

Methods Six patients refractory to pacemaker treatment for 3–19 months underwent radiofrequency modification of atrioventricular conduction. Patients were followed with echo-Doppler, exercise testing and clinical evaluation for 6–12 months after modification.

Results Intrinsic PQ time was significantly prolonged from $175 \pm 18$ ms to $253 \pm 22$ ms; however, one patient exhibited complete block at one month follow-up. Left ventricular outflow tract obstruction decreased from $74 \pm 17$ mmHg to $28 \pm 27$ mmHg at the 6-month follow-up. Symptomatic improvement of at least one functional class was recorded in all patients; exercise tolerance remained unchanged, however, less angina and dyspnoea were reported in everyday life.

Conclusion Radiofrequency modification of atrioventricular conduction, with persistent prolongation of the PQ interval, enhances the effects of pacing in patients with hypertrophic obstructive cardiomyopathy. This treatment enhances left ventricular outflow tract gradient reduction and improves symptoms.

Key Words: Cardiomyopathy, hypertrophic, atrioventricular synchronous pacing, atrioventricular radiofrequency conduction modification.

Introduction

Patients with hypertrophic obstructive cardiomyopathy and symptoms refractory to drug treatment are helped by atrioventricular synchronous pacing with short atrioventricular delay. PACing reduces left ventricular outflow tract obstruction more than any known medical treatment, offering symptomatic relief and increased exercise capacity[1–4]. The mechanism behind this beneficial effect is altered septal movement caused by right ventricular apical stimulation. There are two key factors behind the beneficial effects. The right ventricular stimulation site should be apical and the apical pre-excitation has to be present on exercise as well as at rest[5]. This is accomplished by programming the pacemaker atrioventricular delay so that it is shorter than the native atrioventricular conduction time. Enhanced atrioventricular nodal conduction is not uncommon in hypertrophic obstructive cardiomyopathy patients[6,7]. In such patients, the programmed atrioventricular delay may become too short to allow sufficient diastolic filling of the left ventricle.

Radiofrequency catheter ablation of the atrioventricular junction with subsequent pacemaker implantation has been developed as a therapeutic option for patients with drug-refractory atrial fibrillation[8]. Early in the history of radiofrequency ablation, selective modification of atrioventricular conduction was attempted as a method for improved rate control for patients with atrial fibrillation[9–11]. This procedure was the same as selective ablation of the fast atrioventricular pathway performed in patients with atrioventricular nodal re-entrant tachycardia[12]. The rationale to modify rather than to interrupt atrioventricular conduction was the wish to avoid potential side-effects, such as pacemaker dependency and proarrhythmias associated with complete ablation of the atrioventricular junction[13,14].

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is a useful tool for the optimization of treatment in patients with hypertrophic obstructive cardiomyopathy, primarily refractory to cardiac pacing.

Methods

Patients

Of 58 patients paced for drug-refractory hypertrophic obstructive cardiomyopathy, five were unsuccessful as regards reducing the outflow tract obstruction and subjective symptoms. The reason for pacing failure was thought to be an inability to pre-excite the apex, as judged by 2-D echocardiography or 12-lead ECG. These five patients therefore underwent modification of atrioventricular conduction. One additional patient underwent atrioventricular nodal modification immediately following a temporary cardiac pacing procedure that failed to reduce the outflow gradient. Clinical details of the six patients are given in Table 1.

Echocardiography

Echocardiographic evaluations were performed according to the standards of the American Society of Echocardiography[15] using Vingmed 750 equipment (Vingmed, Horten, Norway). A duplex probe was used, 3.25 MHz for 2-D and 2.5 MHz for Doppler. The patients were studied in the semi-lateral supine position. Continuous Doppler was used to calculate the left ventricular outflow tract obstruction, according to a modified Bernoulli equation, as previously described[16]. The filling pattern of the left ventricle was measured with pulsed Doppler with the sample volume at the tips of the mitral valve leaflets. The total mitral time velocity integral was used, together with left ventricular outflow tract gradient, to determine optimal atrioventricular delay when programming pacemakers.

Temporary pacing and atrioventricular delay optimization

A temporary cardiac pacing procedure was performed in all patients prior to pacemaker implantation. Two quadripolar pacing catheters were placed in the right atrium and in the right ventricular apex. A dual-chamber pacemaker (APC Medical Ltd., England) was connected and atrial triggering pacing was compared to sinus rhythm. A minimum of 5 min of pacing was allowed before determining the left ventricular outflow tract gradient and mitral flow during each condition. The optimal atrioventricular delay was considered to be the one that produced the greatest reduction in the left ventricular outflow tract gradient without reducing the mitral velocity time integral. Atrioventricular delays from 30 to 120 ms were tried. When two atrioventricular delays gave the same level of reduction and a comparable mitral velocity time integral, the shortest atrioventricular delay was chosen to ensure full ventricular capture, and a maximally broadened QRS complex during exercise. The atrioventricular delay was again optimized individually the day after permanent pacemaker implantation as well as after the radiofrequency procedure.

Electrophysiological procedure

During the radiofrequency procedure, 6-French quadripolar catheters (USCI Bard) were placed in the right ventricular apical region and in the lateral part of the right atrium. All patients were in sinus rhythm during the procedure. Stimulation was performed with a 2.0 ms pulse duration at twice diastolic threshold. The

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<th>Table 1</th>
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Ami=amiodarone; Ca=calcium channel blockers; Beta=beta-blockers; LVOT reduction=left ventricular outflow tract obstruction during temporary pacing procedure in sinus rhythm and during pacing; AV delay=programmed pacemaker atrioventricular delay before and after radio-frequency modification.
atrioventricular effective refractory period was assessed at two paced cycle lengths (100 and 120 beats min\(^{-1}\)) using a single extra stimulus technique. A 7-French radiofrequency ablation catheter (Marinr, Medtronic Inc., Minneapolis, U.S.A.) with a 4-mm tip electrode was placed in the vicinity of the atrioventricular node. The proximal portion of the atrioventricular node was mapped during simultaneous recording of bipolar ECG from all four electrodes of the radiofrequency catheter, using a standard filter setting of 30–500 Hz. To conform to the criteria for radiofrequency energy application, the amplitude of the atrial ECG had to clearly exceed the ventricular in the distal bipolar recording; the His bundle ECG had to be minimal (Fig. 1). The stability of the ECG was observed for at least 30 s before applying radiofrequency energy. Catheter positions with isolated beats and larger His recordings were avoided. Using a radiofrequency generator with a rapid, closed-loop temperature monitoring system (Atakr, Medtronic Inc., U.S.A.), energy was applied with a set target temperature of 45°C for 20 s. The target temperature was increased in steps of 5°C every 20 s up to 60°C. When an accelerated nodal rhythm, or nodal extrasystoles were observed, the energy application was temporarily switched off. If the PQ interval remained unchanged during sinus rhythm, the energy application was continued during atrial stimulation at 120 beats min\(^{-1}\) during close observation of the paced PQ interval. The goal was to achieve an increase in the PQ interval of >50% or to >220 ms, that would persist for 30 min and during isoproterenol infusion.

Monitoring of clinical condition and exercise tolerance

The clinical condition of the patients was monitored at baseline and at follow-up using NYHA functional classification. All patients but one (hip arthrosis) underwent symptom-limited exercise testing on a treadmill, according to the Bruce protocol\(^{[17]}\). Ratings of perceived dyspnoea and angina, according to the Borg scale\(^{[18]}\), were given by the patients during the last 15 s of each workload.

Statistics

Values are given as mean ± standard deviation. The PQ intervals and left ventricular outflow tract gradients were compared using paired two-tailed Students’ t-test.

Results

Temporary pacing and pacemaker programming

There was a mean reduction in the left ventricular outflow tract obstruction of 21 ± 14% (Table 1) during
the temporary pacing procedure prior to pacemaker implantation. In one patient, there was no reduction in the left ventricular outflow tract gradient, but a permanent pacemaker was implanted in the light of reports of progressive reduction in the left ventricular outflow tract gradient as a result of pacemaker treatment in hypertrophic obstructive cardiomyopathy patients. After permanent pacemaker implantation, the optimal atrioventricular delay was determined to be 50 ms in all patients, according to the above described method of optimization (Table 1).

Radiofrequency ablation and capture

There was no evidence of dual atrioventricular nodal physiology in any of the six patients, of whom all underwent one radiofrequency procedure. The PQ interval during sinus rhythm prior to atrioventricular modification was 175 ± 18 ms. The modifications were achieved with 9 ± 11 (2 to 27, median 3.5) applications of radiofrequency energy and the obtained temperature of the successful application was 55 ± 6 °C (50 to 66). Thirty minutes after the final application, the PQ interval was prolonged to 253 ± 22 ms (220 to 275; P = 0.00005 vs baseline). A typical example is given in Fig. 1. During the procedure, rapidly transient atrioventricular block was observed in two patients. In one of these, the PQ interval was prolonged during the procedure from 170 to 270 ms. The following day the PQ interval had decreased to 170 ms and it was decided to allow one month of follow-up before deciding on further procedures. After the radiofrequency procedure, the optimal atrioventricular delay could be prolonged, resulting in a more satisfactory mitral flow pattern, as illustrated in Fig. 2.

At the one month follow-up, this patient had complete atrioventricular block, which thereafter persisted. Five patients exhibited 1:1 atrioventricular conduction at the 6–12 month follow-up (Fig. 3). The QRS width after the radiofrequency procedure increased significantly, indicating more complete ventricular capture in all but one patient (Fig. 4).
Left ventricular outflow tract gradient reduction

Five patients were paced permanently for 3 to 19 months prior to radiofrequency ablation. During this period, there was a slight decrease of the left ventricular outflow tract gradient from $91 \pm 11$ mmHg at baseline, before permanent pacemaker implantation, to $74 \pm 17$ mmHg ($P=0.02$, Fig. 5) prior to radiofrequency procedure. After radiofrequency modification, the left ventricular outflow tract gradient decreased significantly (Fig. 5).

Clinical condition and exercise tolerance

During the pacing period prior to the radiofrequency procedure, one patient improved from NYHA III to II, while the condition of the remaining four patients was unchanged. One month after atrophicventricular nodal modification, the functional class had improved in five and after 3 months in all patients. The functional class has thereafter remained unchanged in all patients (Fig. 6). Exercise tolerance improved in one and was unchanged in four of the patients in whom it was assessed. At a submaximal workload, the rate of dyspnoea and general exhaustion was lower in all patients following the radiofrequency procedure (Fig. 7). All patients had improved as regards angina and dyspnoea during everyday life.

Discussion

In this study, six hypertrophic obstructive cardiomyopathy patients refractory to atrophicventricular synchronous pacing with short atrophicventricular delay, underwent radiofrequency catheter modification of the atrophicventricular conduction in order to increase the spontaneous PQ interval and facilitate intraventricular apical pre-excitation. This enabled programming of...

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**Figure 4** QRS width during pacing with optimal AV delay before and 6 months after radiofrequency procedure at comparable heart rates. **$P<0.01$.**

**Figure 5** Left ventricular outflow tract gradient (LVOT) prior to pacemaker implantation, after 3 to 19 months of pacing prior to radiofrequency modification and 6-12 months after the procedure. *$P<0.05$; ***$P<0.001$; ns = not significant.
atrioventricular delays long enough to allow adequate ventricular filling, without loss of apical pre-excitation. The left ventricular outflow tract obstruction decreased significantly following the procedure and all patients improved their functional capacity.

Response to pacing

There are several reports on the beneficial effects of atrioventricular synchronous pacing with short atrioventricular delays in patients with hypertrophic obstructive cardiomyopathy. All studies do, however, contain a small number of refractory patients[1–4]. Temporary pacing has been a tool to predict the extent to which permanent pacing may influence left ventricular outflow tract obstruction[3,4]. The correlation between the pre-implant reduction of the left ventricular outflow tract gradient during temporary pacing and the subsequent left ventricular outflow tract gradient reduction and clinical improvement is, however, variable[3,4]. This may be explained by a difference in the position between the temporary and permanent pacing electrodes. Another possibility is that the beneficial effect of pacing may appear gradually in patients with little or no acute effect.

In the present series of six patients, the reduction of left ventricular outflow tract gradient during the temporary procedure was only 21 ± 14% (0–38 mmHg). This is less than reported by other investigators[1–4] and also less than the average reduction (55 ± 18%) in our total series of 58 patients. Thus, the modest reduction of the left ventricular outflow tract gradient during the temporary procedure indicated the failure of long-term pacing.

One explanation for pacing refractoriness is failure to obtain apical pre-excitation of the intraventricular septum. Too short an atrioventricular delay may result in compromised ventricular filling due to the loss of the atrial contribution. Thus, the native PQ time must be increased to allow paced apical pre-excitation with preserved filling time. Medical therapy with this aim often results in unwanted side effects.

Radiofrequency ablation of the atrioventricular junction has been successfully applied in hypertrophic obstructive cardiomyopathy patients with chronic or paroxysmal atrial fibrillation[3,4,19]. In order to avoid potential side effects of induction of complete atrioventricular block, such as pacemaker dependency and pro-arrhythmic events[13,14], we tested the feasibility and long-term results of atrioventricular nodal modification rather than ablation. To our knowledge, this is the first report of such a procedure for the present purpose. Besides some reports on selective prolongation of atrioventricular conduction in patients with atrial fibrillation and poor rate control[19–21] the feasibility of this method in patients without dual atrioventricular nodal physiology is largely untested.

Symptomatic improvement after radiofrequency ablation

All patients improved by at least one functional class following the initial 3 months of pacing after radiofrequency ablation. This improvement was not reflected in an increased exercise tolerance, but all patients reported fewer symptoms of tiredness and chest pain during submaximal work levels and in everyday life. Thus, the procedure was successful, at least in terms of subjective feelings of wellbeing. The evaluation is, to some extent, limited by the small number of patients and a relatively short period of follow-up.

Unwanted side effects and complications were limited to complete atrioventricular block and in one patient. Since late development of complete atrioventricular block has been described in patients who have undergone ‘fast’ pathway ablation[21] the long-term incidence of this complication remains to be established.

Conclusion

Radiofrequency modification of the atrioventricular conduction, with persistent prolongation of the PQ interval, enhances the effects of pacing in patients with hypertrophic obstructive cardiomyopathy giving further left ventricular outflow tract gradient reduction and improvement in symptoms.

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References


