Permanent junctional reciprocating tachycardia in infants and children: effectiveness of medical and non-medical treatment

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Key words:
Children; Radiofrequency transcatheter ablation; Supraventricular tachycardia.

Background. **The aim of this study was to identify, in children affected by permanent junctional reciprocating tachycardia (PJRT), the effective treatment.**

Methods. **Seventeen children (9 males, 8 females, mean age 59 ± 62 months, median 24) affected by PJRT were referred to our Institute between the years 1987 and 2000.**

Results. **Pharmacological therapy was successfully used in 14 patients: flecainide and propranolol in 5 of them, amiodarone alone in 5 and associated with propranolol in 2, propafenone alone in 1 and in association with sotalol in 1. These drugs were given for a mean period of 54.5 ± 49.8 months with resolution of the cardiomyopathy in 7/7 patients. Treatment had been continued for 3-6 months and there were no side effects. Nine patients were treated with radiofrequency transcatheter ablation, after 78 ± 53.5 months of medical treatment, at a mean age of 150 ± 16 months. The shortest endocardial ventriculo-atrial (VA) interval during tachycardia was recorded in all cases at the coronary sinus ostium (mean value of local VA-surface RP' interval -38 ms, range -24/-55 ms). Successful ablation of the anomalous pathway was obtained at this site in all patients (mean watts delivered 26 ± 3 W, mean T° 64 ± 5°C). During the follow-up period (mean 21 ± 17 months) 2 patients with recurrences of PJRT underwent a second successful procedure.**

Conclusions. **PJRT in pediatric patients can be successfully treated with antiarrhythmic drugs, this may allow delay of the highly effective radiofrequency ablation treatment until the children have reached an adequate growth.**

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Introduction

Permanent junctional reciprocating tachycardia (PJRT) is an uncommon type of supraventricular reentry tachycardia. It is generally incessant and may result in impaired left ventricular performance due to the tachycardia-related cardiomyopathy[1-5]. This tachycardia is due to a concealed, slowly conducting accessory pathway most usually located in the right postero-septal region, even though other locations have recently been reported[6,7]. Concern exists in the literature about the effectiveness of antiarrhythmic drugs in patients affected by PJRT because this type of arrhythmia often seems to be resistant to pharmacological therapy. More recently, very good results have been reported using radiofrequency transcatheter ablation (RFTA)[8-14]. However, in pediatric populations and especially in small children, RFTA is associated with risks which are not negligible[15]. This suggests the need of an effective drug therapy in order to control PJRT until RFTA can be safely performed.

The aim of this study was to evaluate, in pediatric patients with PJRT: 1) the efficacy of antiarrhythmic drug therapy, 2) the possibility of delaying RFTA by resorting to drug therapy, and 3) the results of this combined medical and non-medical therapeutic strategy.

Methods

The study included 17 children affected by PJRT (9 males, 8 females) who were referred to our hospital between the years 1987 and 2000. The diagnosis of PJRT was based on the following criteria: 1) during tachycardia, an RP' interval longer than the

P'R interval, 2) an atrioventricular ratio of 1:1 with negative P waves in leads II-III and aVF, 3) absence of the "warming up" and "cooling down" phenomena, 4) interruption by transesophageal programmed stimulation with resumption of the tachycardia after one or a few beats. The diagnosis was electrophysiologically confirmed in 9 patients who underwent RFTA as described below. P waves were classified as positive or negative when they had a positive or negative polarity, respectively, and an amplitude ≥ 0.05 mV. A biphasic P wave was defined as one with two components of different polarity.

All patients underwent an initial evaluation that included an ECG at rest, a chest roentgenogram, a 24-hour dynamic ECG and mono- and two-dimensional echocardiograms. Transesophageal atrial pacing, performed as previously described[16,17], was used to confirm the reentry mechanism of the tachycardia as discussed above. The tachycardia was defined incessant if, during Holter monitoring, it was present in more than 90% of the recording.

Until 1988, pharmacological treatment included class I antiarrhythmic drugs and beta-blockers. After 1988, amiodarone was also used. Therapy was judged effective if the PJRT was suppressed both during the 12-lead ECG and during Holter monitoring. During successful oral treatment, all patients underwent Holter monitoring, an exercise stress test, and mono and two-dimensional echocardiography every 3-6 months in order to confirm the suppression of the arrhythmia and to assess the reversibility of the left ventricular dysfunction by the evaluation of the left ventricular shortening fraction (normal value > 30%) and of the ejection fraction (normal value using the Teicholtz method > 60%). At the end of every year of therapy, all patients were submitted to pharmacological wash-out (5 half lives of the drugs used) and studied by means of Holter monitoring and exercise stress testing in order to evaluate the persistence of the PJRT. The electrophysiological study was performed using four standard electrode catheters, in pharmacological wash-out and in general anesthesia using fentanyl and pancuronium bromide for induction and isoflurane for maintenance. Three tetrapolar or hexapolar catheters were placed in the high lateral right atrium, right ventricle (apex or outflow tract) and His bundle. A decapolar catheter was inserted into the coronary sinus. A 7F deflectable thermistor tipped catheter (Blazer, EP Technologies, San Josè, CA, USA) with a 4 mm tip, was inserted via the right femoral vein and used for mapping and ablation.

During the electrophysiological study, orthodromic reciprocating tachycardia was confirmed by demonstrating a change in the atrial activation time when a single premature ventricular extrastimulus was introduced during tachycardia at the time when the His bundle was refractory. Mapping of retrograde atrial activation was performed by recording the shortest ventriculo-atrial (VA) interval during tachycardia. The difference between the RP' interval, measured in lead II, and the local VA interval at the site of successful ablation, was calculated in every patient. Radiofrequency current was delivered from the electrode tip to the cutaneous patch electrode positioned under the left scapula under a closed-loop temperature control. The radiofrequency generator (EPT-1000 cardiac ablation controller) was set so as to achieve a temperature not higher than 70°C. RFTA was considered effective both if the tachycardia did not resume spontaneously as well as if it was not inducible by programmed stimulation 1 hour after the ablative procedure, both in basal conditions and during isoproterenol infusion. Patients were submitted to electrocardiographic monitoring for 1 day. A surface 12-lead ECG and an echocardiogram were performed 24 hours after the RFTA procedure. All patients were treated with aspirin (100 mg/day) for 3 months thereafter. Holter monitoring, exercise stress testing and echocardiographic assessment were performed every 6 months after the procedure.

Statistical analysis. The Student's t test was used to compare the tachycardia rate, at the time of the first observation, of patients < 1 year with that of patients > 1 year.

The Student's t-test and Fisher's exact test were used to analyze significant differences in age at the time of first presentation, tachycardia rate and incessant pattern of the arrhythmia between patients with and without left ventricular dysfunction.

A p value ≤ 0.05 was considered statistically significant. All values were expressed as mean ± SD.

Results

Patient characteristics. At the time of initial evaluation the age of the patients ranged from 1 day to 13 years (mean 59 ± 62 months, median 24) and the mean and median heart rates were 186 ± 33 and 180 b/min respectively. In 7 of these patients, the first episode of tachycardia occurred during the first year of life (mean age 2 ± 2 months, median 1). In these patients, the mean and median tachycardia rates, at the time of presentation, were 204 ± 27 and 210 b/min respectively, while in the other patients (mean age 98 ± 51 months, median 106), the mean tachycardia rate was 173 ± 31 b/min (p = 0.01). PJRT was incessant in 13 patients. At the time of the first evaluation, 8 patients had a reduced left ventricular function with a mean shortening fraction of 14 ± 3.5% and a mean ejection fraction of 29 ± 4% at echocardiography. Reduced left ventricular function was not statistically related neither to the age of the patients nor to the tachycardia rate and to the incessancy or otherwise of the tachycardia. Even though ventricular function was not statistically related to the age of the patients, it is important to note that the children with ventricular dysfunction had a mean age of 82 months while the patients without ventricular dysfunction had a mean age of 37 months and that 6 out of 8 patients (75%) were older than 48 months.

The detailed characteristics of the patients are shown in table I.

Drug therapy. Antiarrhythmic therapy was given to 14 patients. One 13-year-old patient was initially not treated because he presented with a low-rate (130 b/min) tachycardia which was not incessant or induced by exercise. At the age of 18 years, when the PJRT became incessant and mildly symptomatic, he was submitted to RFTA. The parents of another 12-year-old patient chose to submit their son to RFTA. The remaining patient, 10 years old, was immediately submitted to RFTA because of a very poor left ventricular performance (left ventricular shortening fraction 7%).

Forty-two drug regimens were administered to 14 patients (2 ± 1 drugs for each patient). Medical therapy prevented recurrences in all cases so that PJRT was no longer present during Holter monitoring. A single drug was found to be effective in 6 patients (amiodarone in 5, propafenone in 1), while in 8 patients in whom the single drug regimen was not sufficient, a combined antiarrhythmic therapeutic regimen proved to be efficacious (5 patients treated with flecainide and propranolol, 1 with propafenone and sotalol, 2 with amiodarone and propranolol).

Normalization of the left ventricular shortening fraction was achieved in 7/7 patients with an initially poor left ventricular performance after a mean period of 5 ± 2 months of medical treatment. No significant side effect was observed in any patient during medical treatment. The mean duration of medical treatment was 54.5 ± 49.8 months. After 9 years of oral treatment, a patient (no. 7, Tables I and II) showed a progressive refractoriness to the initially successful medical regimen and, for this reason, at the age of 13, he was submitted to RFTA.

Table I. Clinical features, medical therapy and follow-up of the study population.

Patient	Sex	Age (months)	Symptoms	TR (b/min)	Incessant	LVD	SF (%)	EF (%)	Therapy		Digoxin	Follow-up (months)
									Unsuccesful	Successful		
1	F	20	HF	170	Yes	Yes	12	29	F	F+Pr	Yes	106
2	F	106	HF	160	Yes	Yes	15	31	F	F+Pr	Yes	76
3	M	1	No	200	Yes	No	36	70	–	P	Yes	149
4	M	156	Palp	130	No	No	35	70	–	–	–	60
5	F	24	No	180	Yes	No	42	79	P	P+S	No	120
6	M	112	HF	165	No	Yes	17	33	–	A	Yes	3
7	M	48	HF	220	Yes	Yes	13	29	Proc, A, F	F+Pr	Yes	108
8	F	120	HF	170	Yes	Yes	7	19	–	–	Yes	3
9	F	96	HF	180	Yes	Yes	15	31	A, F, P, S	F+Pr	Yes	42
10	M	1	No	180	Yes	No	37	75	–	A	No	20
11	F	7	No	160	Yes	No	35	70	F	F+Pr	No	2
12	F	2	HF	210	Yes	Yes	17	33	–	A	Yes	3
13	M	1	No	220	Yes	No	36	70	A	A+P	No	24
14	F	156	HF	130	No	Yes	17	33	–	A	Yes	48
15	M	1	No	220	Yes	No	41	78	P, Pr	A+Pr	Yes	2
16	M	1	No	240	Yes	No	40	77	Pr, F, P, F+Pr, S	A	Yes	2
17	M	144	Palp	220	No	No	37	75	–	–	No	2

A = amiodarone; EF = ejection fraction; F = flecainide; HF = heart failure; LVD = left ventricular dysfunction; P = propafenone; Palp = palpitations; Pr = propranolol; Proc = procainamide; S = sotalol; SF = shortening fraction; TR = tachycardia rate.

Table II. Electrocardiographic and electrophysiologic characteristics of permanent junctional reciprocating tachycardia during ablation and follow-up data.

Patient	TR	P'-D_1	P'-aVL	P'-V_1	Shots	FT (min)	ECG-RP' (ms)	LVA-RP' (ms)	Recurrences	Follow-up (months)
1	140	-/+	+	+	1	30	280	-40	No	29
2	140	-/+	+	+	1	28	183	-38	No	14
3	120	-/+	+	+	5	73	360	-25	No	13
4	130	-/+	+	+	3	53	340	-35	No	27
5	130	-/+	+	+	3	63	342	-55	No	22
6	150	-/+	+	+	1	45	260	-50	No	9
7	155	-/+	+	+	3	50	280	-40	Yes (1 month)	61
8	160	-/+	+	+	3	40	280	-37	Yes (8 months)	12
9	220	-/+	+	+	5	23	140	-24	No	2

ECG-RP' = duration of the RP' interval on the standard ECG; FT = fluoroscopy time; LVA-RP' = difference between the duration of the local ventriculo-atrial interval on mapping catheter at the site of successful ablation and the ECG-RP'; TR = tachycardia rate.

In another patient, PJRT resolved completely after 48 months of medical treatment with flecainide and propranolol.

Transcatheter ablation. Nine patients underwent RFTA. Except for the 3 patients discussed above, the parents of the remaining 6 chose RFTA for their children owing to a decreased compliance to the therapy after a follow-up of 78 ± 53.5 months. The mean age of these patients at the time of RFTA was 150 ± 16 months. The shortest VA interval (mean value 274 ± 73 ms) was recorded, in 8 cases, at the coronary sinus orifice and, in 1 case, about 1 cm within the coronary sinus (Fig. 1). At surface ECG performed during tachycardia, all these patients showed biphasic P waves in lead I and positive waves in the aVL lead. The radiofrequency energy delivered at that site (mean quantity of energy 26 ± 3 W; mean temperature 64 ± 5°C) interrupted the arrhythmia in all cases with an average number of pulses of 2.8 ± 1.6 (Fig. 2). The mean value of the local VA-RP' interval was -38 ± 10 ms. Two patients respectively presented with PJRT recurrence 1 and 8 months after the apparently successful procedure and for this reason were submitted to a second one. Therefore 11 procedures were performed in 9 patients. After a mean follow-up of 21 ± 17 months all patients are free from arrhythmia. In no patient did we observe any RFTA-related complications.

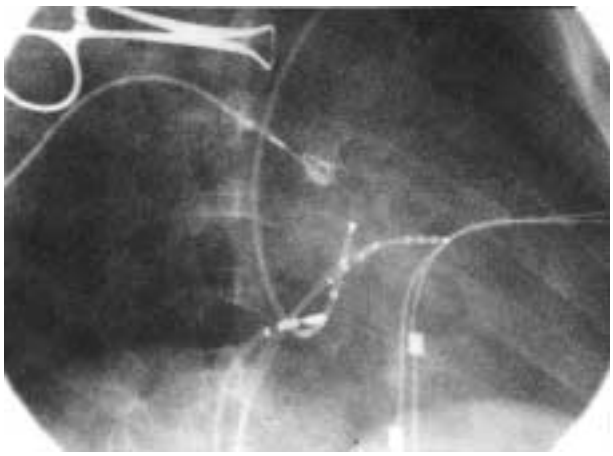

Figure 1. *Radiographic representation of the ablation site in one of the studied patients. This right anterior oblique view shows the intracardiac catheters located in the right ventricle, in the His bundle region and in the coronary sinus. The tip of the ablation catheter is placed in the right postero-septal region, just beyond the anterior rim of the coronary sinus orifice.*

Discussion

The efficacy of RFTA in patients affected by PJRT is confirmed in the literature even for young subjects[6,8-10]. This procedure, however, when performed in very small children, is not free from risks. Sudden death or minor complications render delay of the procedure until the patient has reached the body weight of 15 kg recommendable[15]. Concern exists in the literature about the role of pharmacological measures in the treatment of patients affected by PJRT. Some authors reported good results using class I and III antiarrhythmic agents, while others stressed the drug refractoriness of this arrhythmia[5,18]. In a series of 25 pediatric patients of a German multicenter study[3], complete efficacy of pharmacological therapy was reported in 6 patients whereas in 8 patients this strategy was only partly effective. In this series, PJRT was drug-refractory in 11 patients (44%). However, in this study, as in other reports, combinations of antiarrhythmic drugs were never used. In our series, we achieved good results using a combined therapeutic regimen including class I or III antiarrhythmic drugs and beta-blocking agents in 8 out of 14 patients (57%) who

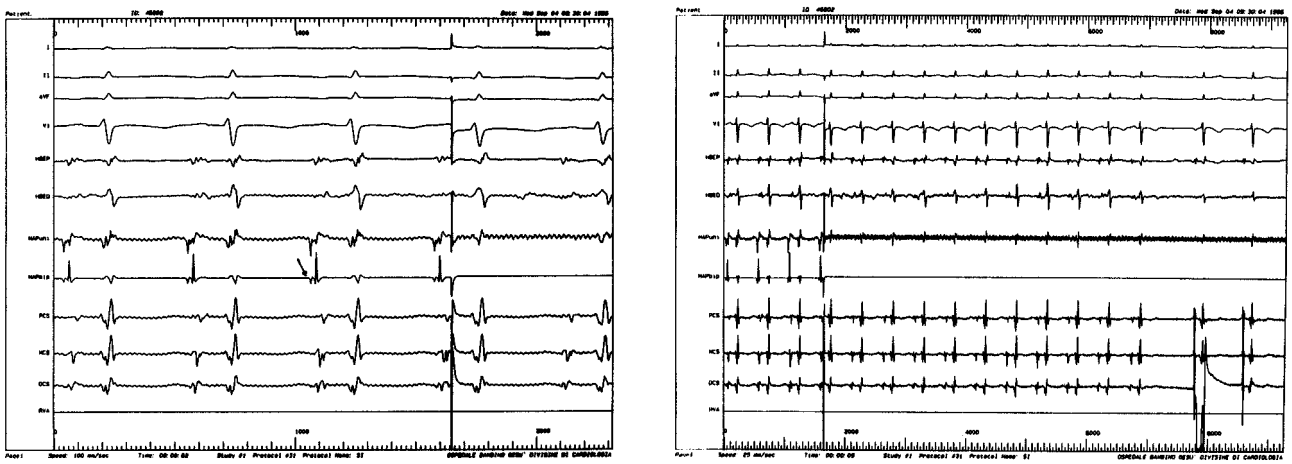

Figure 2. *Electrophysiologic recordings during transcatheter radiofrequency ablation of permanent junctional reciprocating tachycardia in one patient (no. 5, Tables I and II). In the recording, a probable accessory pathway potential* (arrow) *is clearly visible on the* left panel *(this was the only case in which this type of potential has been recorded). The recording on the* right panel *shows conversion to sinus rhythm within 5 s of the delivery of radiofrequency energy. DCS = distal coronary sinus; HBED = distal His bundle potential; HBEP = proximal His bundle potential; MAP bip = bipolar mapping catheter; MAP uni = unipolar mapping catheter; MCS = middle coronary sinus; PCS = proximal coronary sinus.*

were refractory to a class I or class III drug alone. Thus, suppression of the arrhythmia was achieved in 14/14 patients treated with medical therapy. Besides, this strategy completely resolved secondary left ventricular dysfunction in 7/7 patients. Beta-blocking agents not only enhance the pharmacological effects of flecainide and amiodarone, as already reported[19-23], but also reduce the most important causes of the induction of PJRT: the sudden acceleration of the sinus rhythm and the premature ventricular beats. Moreover, it is important to note that at the beginning of our experience, we used class IC and beta-blocking drugs in patients with reduced left ventricular function too. This seems to suggest that, in the subgroup of pediatric patients with tachycardiomyopathy, the beneficial effect of these drugs in restoring sinus rhythm outdoes their negative inotropic effect. With regard to this, however, it is very important to bear the potential proarrhythmic effect of class I antiarrhythmic drugs in mind[24]. When we started using amiodarone, this drug was chosen to treat patients with ventricular dysfunction or patients < 12 months of age who are those who present with less side effects[25]. Regarding the efficacy and the safety of ablative therapy in PJRT, the literature reports a high success rate for the elimination of the arrhythmogenic substrate of PJRT and no significant complications. The reported arrhythmia recurrence rate after an apparently successful ablation ranges from 13 to 27%[6,9,13]. However, when the arrhythmia recurs, patients may undergo a second ablative procedure without any adjunctive risk. In our study, radiofrequency ablation was successful in all treated patients. No early complications occurred. As in the other series, the arrhythmia recurred in 22% of our patients after the first apparently successful ablation, and therefore, in this subgroup of patients, a second procedure was necessary. This anomalous pathway may be very large and this may explain the relatively high incidence of recurrences after radiofrequency ablation. Regarding the decision of when and in which cases the ablation has to be performed, we must take into consideration that, in pediatric age, complete spontaneous resolution of PJRT has been reported[3]. Our experience also seems to confirm this observation.

An unresolved issue is the invariability or otherwise of the postero-septal location of the accessory pathway in PJRT. Even if in the literature the most frequently reported localization of this pathway is the right posterior septum[4,8,11,14,17], other locations have been reported, such as the mid-septum and left lateral septum[6,7,9]. In our series, the accessory pathway was mapped in the right postero-septal region close to the coronary sinus ostium in all cases except one.

Recently, Gaita et al.[9] reported that a positive or biphasic P wave in lead I during tachycardia suggests that ablation can be performed from the right side. The sensitivity was 46% and the specificity 100%. Our results confirm this specificity because all our patients had a positive component of the retroconducted P wave in lead I.

In conclusion, the data of the study underline the efficacy of antiarrhythmic therapy in children affected by PJRT. Class I or III anthyarrhythmic drugs alone or in combination with a beta-blocker agent may be employed. This therapeutic strategy may allow one to delay the highly effective ablative treatment, thus reducing the risk of complications in small children. Taking also the data reported in the literature into consideration[15], we suggest that children < 15 kg in weight or < 4 years should be treated with amiodarone in case of ventricular dysfunction and with class I antiarrhythmic drugs in the other cases. Beta-blocking agents can be added when a single drug is not sufficient. Children > 15 kg in weight or > 4 years can be treated with RFTA, especially if they present with ventricular dysfunction.

Study limitations. Unfortunately, this retrospective study has one limitation. Eight of the 17 children studied did not undergo intracardiac electrophysiological evaluation because they were not submitted to RFTA. Nevertheless, all 8 patients underwent transesophageal atrial pacing which confirmed the reentry mechanism of the tachycardia. Considering that 7 of the 8 mentioned patients were < 1 year of age at the time of initial observation, that the atrioventricular nodal reentry mechanism is extremely rare and that the "atypical" forms have not yet been documented in this pediatric age[26], it seems very probable that at least these 7 patients were affected by PJRT.

References

1. Cruz FES, Cheriex EC, Smeets JLRM, et al. Reversibility of tachycardia-induced cardiomyopathy after cure of incessant supraventricular tachycardia. J Am Coll Cardiol 1990; 16: 739-44.
2. Dorostkar PC, Silka MJ, Morady F, et al. Clinical course of persistent junctional reciprocating tachycardia. J Am Coll Cardiol 1999; 33: 366-75.
3. Lindinger A, Heisel A, Von Bernuth G, et al. Permanent junctional re-entry tachycardia. A multicentre long-term follow-up study in infants, children and young adults. Eur Heart J 1998; 19: 936-42.
4. Critelli G. Recognizing and managing permanent junctional reciprocating tachycardia in the catheter ablation era. J Cardiovasc Electrophysiol 1997; 8: 226-36.
5. Schleich JM, Vaksmann G, Khanoyan P, et al. Les tachycardies jonctionelles permanentes par rythme reciproque chez l'enfant et l'adolescent. Arch Mal Coeur Vaiss 1992; 85: 553-9.
6. Ticho BS, Saul JP, Hulse JE, et al. Variable location of accessory pathways associated with the permanent form of junctional reciprocating tachycardia and confirmation with radiofrequency ablation. Am J Cardiol 1992; 70: 1559-64.
7. Shih HT, Miles WM, Klein LS, et al. Multiple accessory pathways in the permanent form of junctional reciprocating tachycardia. Am J Cardiol 1994; 73: 361-7.
8. Smith RT, Gillette PC, Massumi A, et al. Transcatheter ablative techniques for treatment of the permanent form of junctional reciprocating tachycardia in young patients. J Am Coll Cardiol 1986; 8: 385-90.
9. Gaita F, Haissaguerre M, Giustetto C, et al. Catheter ablation

of permanent junctional reciprocating tachycardia with radiofrequency current. J Am Coll Cardiol 1995; 25: 648-54.
10. Balaji S, Gillette PC, Case CL. Successful radiofrequency ablation of permanent junctional reciprocating tachycardia in an 18-month-old child. Am Heart J 1994; 127: 1420-1.
11. Yang Y, Greco C, Ciccaglioni A, et al. Curative radiofrequency catheter ablation for permanent junctional reciprocating tachycardia. Pacing Clin Electrophysiol 1993; 16: 1373-9.
12. Saoudi N, Kirkorian G, Atallah G, et al. Catheter ablation induced reversal of chronic left ventricular dysfunction in permanent junctional tachycardia. Pacing Clin Electrophysiol 1993; 16: 954-8.
13. Aguinaga L, Primo J, Anguera I, et al. Long-term follow-up in patients with the permanent form of junctional reciprocating tachycardia treated with radiofrequency ablation. Pacing Clin Electrophysiol 1998; 21 (Part 1): 2073-8.
14. Chien WW, Cohen TJ, Lee MA, et al. Electrophysiological findings and long-term follow-up of patients with the permanent form of junctional reciprocating tachycardia treated by catheter ablation. Circulation 1992; 85: 1329-36.
15. Kugler JD, Danford DA, Deal BJ, et al. Radiofrequency catheter ablation for tachyarrhythmias in children and adolescents. The Pediatric Electrophysiology Society. N Engl J Med 1994; 21: 1481-7.
16. Drago F, Turchetta A, Guccione P, et al. Usefulness of transesophageal atrial pacing in the chronic treatment of supraventricular reciprocating tachycardia in infants. G Ital Cardiol 1995; 25: 11-6.
17. Drago F, Turchetta A, Calzolari A, et al. Detection of atrial tachyarrhythmias by transesophageal pacing and recording at rest and during exercise in children with ventricular preexcitation. Am J Cardiol 1992; 69: 1098-9.
18. Perry JC, McQuinn RL, Smith RT, et al. Flecainide acetate for resistant arrhythmias in the young: efficacy and pharmacokinetics. J Am Coll Cardiol 1989; 14: 185-91.
19. Manolis AS, Ester NA. Reversal of electrophysiologic effects of flecainide on the accessory pathways by isoproterenol in the Wolff-Parkinson-White syndrome. Am J Cardiol 1989; 64: 194-8.
20. Stern H, Scheininger M, Theisen F, et al. Antiarrhythmic therapy with flecainide in combination and in comparison with propranolol. Drugs 1985; 29 (Suppl 4): 77-85.
21. Myeburg RJ, Kesslre KM, Cox MM, et al. Reversal of proarrhythmic effects of flecainide acetate and encainide hydrochloride by propranolol. Circulation 1989; 80: 157-9.
22. Bashir Y, Paul VE, Griffith MJ, et al. A prospective study of the efficacy and safety of adjuvant metoprolol and xamoterol in combination with amiodarone for resistant ventricular tachycardia associated with impaired left ventricular function. Am Heart J 1992; 124: 1233-40.
23. Sanguinetti MC, Iurkiewicz NK, Scott A, Siegl PK. Isoproterenol antagonizes prolongation of refractory period by the class III antiarrhythmic agent E-4031 in guinea pig myocytes. Mechanism of action. Circ Res 1991; 68: 77-84.
24. Fish FA, Gillette PC, Benson DW. Proarrhythmia, cardiac arrest and death in young patients receiving encainide and flecainide. J Am Coll Cardiol 1991; 18: 356-65.
25. Guccione P, Paul T, Garson A Jr. Long-term follow-up of amiodarone therapy in the young: continued efficacy, unimpaired growth, moderate side effects. J Am Coll Cardiol 1990; 15: 1118-24.
26. Kon Ko J, Deal BJ, Strasburger JF, et al. Supraventricular tachycardia mechanisms and their age of distribution in pediatric patients. Am J Cardiol 1992; 69: 1028-32.