Kardiologia Polska 2012; 70, 4: 351–358 ISSN 0022–9032

ORIGINAL ARTICLE

Benign symptomatic premature ventricular complexes: short- and long-term efficacy of antiarrhythmic drugs and radiofrequency ablation

Sebastian Stec, Agnieszka Sikorska, Beata Zaborska, Tomasz Kryński, Joanna Szymot, Piotr Kułakowski

Department of Cardiology, Postgraduate Medical School, Grochowski Hospital, Warsaw, Poland

Abstract

Background: There is little data on the long-term efficacy of antiarrhythmic drugs (AADs) and radiofrequency catheter ablation (RFCA) in patients with symptomatic premature ventricular complexes (PVCs) and no organic heart disease.

Aim: To evaluate the short- and long-term efficacy and tolerance of AAD therapy and RFCA in patients with idiopathic PVCs.

Methods: This was a prospective, crossover, open-label study performed in 84 consecutive patients (mean age 47 ± 15 years; 60% women) with symptomatic idiopathic PVCs (mean PVCs/24 h, 13,768 ± 9,424; range 1,693–42,687). Patients were treated for 2–3 weeks with metoprolol, propafenone or verapamil. Then patients were referred for RFCA, if they had drug intolerance, inefficacy or did not wish to have prolonged AAD treatment.

Results: The most efficacious agent was propafenone, followed by verapamil, and then metoprolol [35 (42%), 13 (15%) and eight (10%) responders, respectively, $p < 0.01$ *vs* propafenone]. Only responders to drug treatment had a significant reduction in symptom severity (Visual Analogue Scale score: 6.2 ± 1.4 *vs* 2.7 ± 2.0, $p < 0.001$). After AAD, 50 (60%) patients underwent RFCA. During long-term follow-up (48 ± 10 months), RFCA (mean 1.2 procedures/patient) was effective in 44/50 (88%) patients. Of the 34 remaining patients, 21 remained on effective AAD, 6 patients remained on ineffective AAD, and 7 patients were taken off AADs therapy due to spontaneous remission of PVCs or a decrease in symptom severity.

Conclusions: Short-term treatment with propafenone was more effective than verapamil or metoprolol in suppressing idiopathic PVCs. However, optimal benefit was achieved with RFCA, which was effective and safe during long-term follow-up.

Key words: premature ventricular complexes, antiarrhythmic drugs, radiofrequency ablation, ventricular arrhythmias, treatment, guidelines

Kardiol Pol 2012; 70, 4: 351–358

INTRODUCTION

The prognosis in patients with frequent premature ventricular complexes (PVCs) and no obvious organic heart disease is usually very good. However, many patients are severely symptomatic with impaired quality of life (QOL) and seek medical advice as well as effective therapy [1–10].

According to guidelines set out in 2006 by the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) for the care of patients with ventricular arrhythmias and the prevention of sudden cardiac death, the first-line therapy in patients with benign but symptomatic PVCs comprises beta-blocking agents [8]. Data in the literature supporting such an approach is, however, scarce [10, 11].

In cases of a lack of efficacy of beta blockers in patients with right ventricular outflow tract (RVOT) origin of PVCs, calcium channel-blocking agents or class IC drugs are usually the next choice. However, data in the literature documenting the efficacy of this approach is lacking, and these antiarrhythmic drugs (AADs) have been tested in few studies in patients with ventricular arrhythmias. Moreover, none of these studies specifically dealt with a large non-selected group of patients with frequent symptomatic idiopathic PVCs [12–19].

Address for correspondence:
Sebastian Stec, MD, PhD, Department of Cardiology, Grochowski Hospital, Postgraduate Medical School, ul. Grenadierow 51, 04–073 Warszawa, Poland, tel/fax: +48 22 81017 38, e-mail: smstec@wp.pl
Received: 27.07.2011 **Accepted:** 24.10.2011

The introduction of ablative techniques has changed the approach to the treatment of various types of arrhythmias, and substantially improved outcomes [20–33]. However, the role of radiofrequency catheter ablation (RFCA) in patients with benign symptomatic PVCs has not been well defined.

The present study was designed as a prospective approach for the evaluation of AADs and RFCA in a large cohort of patients with idiopathic PVCs. We evaluated consecutive patients with benign, symptomatic, frequent, idiopathic PVCs, tested three AADs, and then performed ablation in those who preferred invasive treatment after taking AADs. All patients were followed up to evaluate the long-term effects of treatment.

METHODS

All patients provided written informed consent to participate in the trial. The study protocol was approved by the Committee on Human Research at the Postgraduate Medical Centre, Warsaw, Poland.

Study design

This was a single-centre, crossover, open-label trial comparing the efficacy of three AADs (1 — metoprolol, 2 — verapamil, and 3 — propafenone) given in random order to patients with frequent, symptomatic, idiopathic PVCs. Consecutive patients were randomised to three arms of AADs treatment (1→2→3, or 2→3→1, or 3→2→1). After a period of pharmacological testing, patients were offered ablation therapy if they had drug intolerance, inefficacy or did not wish to have prolonged AAD treatment.

The pharmacological study was started in July 2004 and completed in September 2007. The last ablation procedure was carried out in December 2008. The last follow-up of the entire group of patients was undertaken in June 2009.

Study population

The study group consisted of patients who were admitted to our department due to symptomatic PVCs. Patients were included in the study if they had: (1) symptomatic (> 4 weeks) monomorphic PVCs > 2,500/24 h; or (2) persistent (> 3 months) monomorphic PVCs < 2,500/24 h with similar PVCs (< 20% difference) on two repeated Holter monitorings, but severe symptoms clearly associated with PVCs; (3) normal standard electrocardiogram (ECG) (except PVCs); and (4) normal echocardiogram (ECHO).

The exclusion criteria were: (1) injury associated with syncope; (2) non-sustained ventricular tachycardia (nsVT) (defined as > 3 consecutive ventricular complexes) or sustained VT (defined as VT lasting > 30 s or causing haemodynamic compromise); (3) any significant cardiac disease and cardiomyopathy detected by echocardiography and, if needed, by other methods (exercise stress test and coronary angiography) and medical history; (4) channelopathies such as Brugada syndrome or long QT syndrome; (5) chronic disorders of the lung or pulmonary circulation; (6) hormonal or electrolyte disturbances; (7) pregnancy or breastfeeding; (8) use of cardiac-stimulating agents (e.g., drug abuse); (9) contraindications or previously known intolerance to metoprolol, verapamil or propafenone; and (10) lack of symptoms associated with PVCs.

Patients were classified as RVOT and non-RVOT PVCs according to the findings of 12-lead ECG with clinical PVCs and the criteria described by Ito et al. [22]. Idiopathic PVCs were defined as arrhythmia occurring in patients with normal ECHO, ischaemia excluded by past medical history, exercise stress test or, if needed, by coronary angiography.

Drug testing

Starting drug doses were 50 mg slow-release for metoprolol, 120 mg slow-release for verapamil, and 150 mg t.i.d. for propafenone. If these doses were well tolerated during short-term treatment, they were adjusted to the heart rhythm and tolerance of the patient. Patients were contacted by telephone to increase doses in outpatient care. The minimum period of treatment with a stable dose of a tested agent was two weeks, followed by ambulatory ECG monitoring. Then, after the tested agent' five half-lifes washout period, another drug was started.

Assessment of drug efficacy

Responders were classified as ≥ 90% reduction of PVC count and no proarrhythmic effects on repeated 24-h Holter monitoring [16, 19]. Complete responders were classified as patients with complete disappearance of PVCs while on the tested drug. Drug intolerance was defined as early (< 2 weeks) or late (during long-term follow-up) inability to continue drug treatment due to side effects or proarrhythmia. Proarrhythmic effects were defined as a drug-induced increase of PVCs/couplets/triplet count > 2-fold compared to baseline or the development of nsVT, torsades de pointes, or sustained VT.

Assessment of symptoms associated with arrhythmia

A detailed questionnaire concerning symptoms and their association with arrhythmia, as well as factors triggering arrhythmia, was completed by patients. The survey included symptoms frequently caused by arrhythmia (e.g. palpitations, dizziness, syncope, chest pain) and less typical symptoms (e.g. chronic cough, dysphagia, intermittent claudication, eye flashes) [30–32]. A Visual Analogue Scale (VAS) ranging from 0 (none) to 10 (extremely disabling) was used to evaluate patients' perceived overall severity of symptoms as well as each separate symptom associated with PVCs. The VAS was collected by medical staff and a graph with scale and symptoms perception was shown to the patient. Symptoms were classified as significant if the VAS score was ≥ 3.

Electrophysiology study and ablation

After initial drug testing, all patients were offered RFCA. The latter was undertaken in patients who had frequent symptomatic monomorphic PVCs that were resistant to drugs, who were intolerant to drugs, or who did not wish for long-term drug therapy. RFCA was carried out using local anaesthesia and light conscious sedation. Catheters were introduced percutaneously into the femoral vein and/or femoral artery and positioned under fluoroscopic guidance in the right (RV) or left ventricle (LV). The ablation catheter was a 7-F deflectable quadripolar catheter with a 4-mm tip electrode (Navistar, Biosense Webster, Diamond Bar, CA, USA; or Alcath Gold, Biotronik, Berlin, Germany).

First, programmed ventricular stimulation was carried out to assess propensity to sustained ventricular arrhythmia. Then, classical mapping was performed to localise the optimal site of ablation according to pace mapping and local activation mapping. The radiofrequency (RF) applications were set at 50–60 W, 50–60°C and were delivered for 60–90 s. The control selected coronary angiography and limited value of RF settings (30–50 W and 50°C) was used during application in aortic cusps. The endpoint of RFCA was complete disappearance of spontaneous PVCs for > 20 min after the last application. In patients without spontaneous ectopy at the time of the procedure, pacing and/or isoproterenol infusion were used to induce PVCs. The 3D electroanatomic system was not used in the studied group.

Follow-up

Control Holter ECG monitoring was done > 4 weeks after RFCA or prolonged pharmacological therapy as well as during the last follow-up visit. Successful RFCA was defined as > 90% reduction of target PVC count. Patients were followed up at an outpatient clinic every 6–12 months or by telephone to assess their clinical status and current therapy.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD) and range. Categorical variables are described as frequencies and percentages. A comparison of continuous variables was made by the ANOVA test. Comparison of categorical variables was made by the χ^2 test. Pearson correlation was use to evaluate correlation between the number of PVCs and symptom severity. In all tests, a p value < 0.05 was considered significant.

RESULTS

Patient characteristics

Eighty-four consecutive patients (mean age ± SD: 47 ± 15 years, range: 18–79) with symptomatic PVCs were prospectively evaluated. The study group consisted of 60 women and 24 men. Details concerning symptoms, baseline Holter ECG and ECHO, concomitant diseases and previous usage of antiarrhythmic drugs are presented in Table 1.

The mean number of PVCs during baseline 24-h Holter monitoring was 13,768 ± 9,424 (range 1,693–42,687). Couplets or triplets of PVCs were present in 48 (57%) and 12 (14%) patients, respectively. Previous attempts at antiarrhythmic treatment were reported by 36 (43%) patients; no patient had a previous RF ablation procedure for PVCs. The morphology of PVCs typical for RVOT was present in 43/84 (51%) patients. All patients had normal, or only slightly reduced, left ventricular ejection fraction (mean LVEF [%], 61 ± 7; range 46–80) without signs of significant valvular or organic heart disease.

Symptoms

According to evaluation of the medical history, the single factor associated with symptom onset was infection (17%), prolonged period of extreme stress (18%), any stress (6%), hormonal changes in females (8%) or extreme physical strain (6%). In 46% of patients, no detectable factor associated with the beginning of symptoms and arrhythmia was detected.

The mean interval between symptom onset and electrophysiological (EP) evaluation was > 4 years. The most frequently encountered symptoms associated with arrhythmia were palpitations, followed by fatigue, reduced physical capacity, dizziness and chest pain (Table 1). The mean severity of symptoms according to the VAS was 6.2 ± 1.2. The severity of individual symptoms did not differ significantly and ranged from 4.8 ± 1.7 to 5.9 ± 1.1 according to the VAS.

There was no significant correlation between the baseline number of PVCs and symptom severity (r = –0.07, NS, VAS score = 6.2 ± 1.4) in the entire group as well as in a subgroup with frequent (< 20,000 PVCs/24 h, r = –0.06, NS, VAS score = 6.3 ± 1.4) and very frequent PVCs (> 20,000 PVCs/24 h, r = 0.17, NS, VAS score = 5.8 ± 1.3).

Short-term efficacy of AAD treatment

The efficacy of tested AADs assessed by serial Holter ECG recordings is presented in Figure 1 and Table 2. The mean daily doses of metoprolol, verapamil and propafenone were 67 ± 24 mg, 171 ± 73 mg, and 704 ± 113 mg, respectively. The most effective agent was propafenone (35 [42%] responders), followed by verapamil (13 [15%] responders), and metoprolol (eight [10%] responders) (p < 0.01 when comparing propafenone *vs* verapamil or metoprolol). Verapamil/propafenone or metoprolol/propafenone were effective in eight patients and one patient, respectively. All three tested drugs were effective in two patients. Proarrhythmia was documented in two patients treated with metoprolol, one with propafenone, and none with verapamil. There were no acute (after first dose) life-threatening side effects except for one case of severe hypotension after initiation of propafenone treatment.

Other side effects occurring during a two-week period of treatment necessitating withdrawal of a tested agent occurred

Table 1. Patient characteristics

Age [years] (range)	47 ± 15 (18–79)
Males	24 (29%)
Duration of symptoms [years] (range)	4.3 ± 6.9 (0.1–29)
Symptom severity associated with arrhythmia (VAS score) (range)	6.2 ± 1.4 (3–9)
Symptoms:	
Palpitations	54 (64%)
Unpleasant feeling of extra heartbeats	45 (53%)
Dyspnoea	39 (47%)
Reduced physical capacity	37 (44%)
Chronic fatigue	36 (43%)
Dizziness	35 (42%)
Chest pain	34 (40%)
Blurred vision or eye flashes	16 (19%)
Presyncope	15 (18%)
Syncope	10 (12%)
Arrhythmia-associated cough	5 (6%)
Arrhythmia-associated dysphagia	5 (6%)
Concomitant diseases:	
Hypertension	17 (20%)
Gastro-oesophageal reflux disease	4 (5%)
Diabetes	3 (4%)
Previous usage of antiarrhythmic drugs:	
Any drug	36 (43%)
Beta-blockers	29 (34%)
Sotalol	11 (13%)
Amiodarone	7 (8%)
Propafenone	7 (8%)
Other drugs	19 (23%)
Echocardiographic data (range):	
LVEF [%]	61 ± 7 (46–80)
LA diameter [mm]	34 ± 5 (23–50)
LVESD [mm]	32 ± 5 (20–48)
LVEDD [mm]	48 ± 4 (39–60)
IVS diameter [mm]	10 ± 1 (10–13)
Baseline Holter data (range):	
PVC count per 24 h (84 pts)	13,768 ± 9,424 (1,693–42,687)
Couplets of PVC per 24 h (48 pts)	365 ± 1,077 (1–6,377)
Triplets of PVC per 24 h (12 pts)	65 ± 129 (1–409)
Mean heart rate	75 ± 9 (55–95)
Minimal heart rate	48 ± 7 (33–64)
Maximal heart rate	128 ± 26 (73–210)

LA — left atrial; LVEF — left ventricular ejection fraction; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; IVS — interventricular septum; PVC — premature ventricular complexes

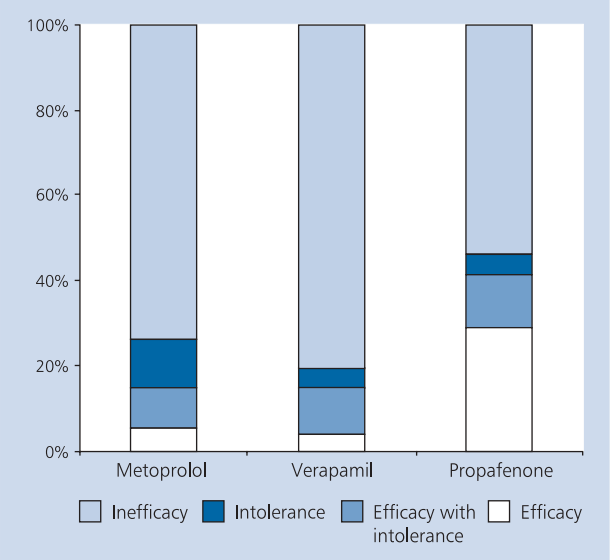

Figure 1. Short-term efficacy, intolerance and inefficacy of drug treatment. Some patients in whom the drug was efficacious had intolerance that led to discontinuation of treatment after a short period of evaluation

in 21% of patients treated with metoprolol, in 17% receiving propafenone, and in 15% treated with verapamil (NS). The most frequent single effective and well-tolerated agent chosen for long-term treatment was propafenone (24 patients, 29%), followed by metoprolol (four patients, 5%) and verapamil (three patients, 4%). Therefore, at least one of three tested drugs was effective and well-tolerated in 31/84 (37%) patients.

In patients classified as non-RVOT PVCs (41/84, 49%), the most effective drug was propafenone (10/41, 32%), followed by verapamil (3/41, 10%), and then metoprolol (2/41, 6%). In patients with morphology of PVCs classified as of RVOT origin, the efficacy of AADs was similar to the patients with non-RVOT PVCs (16/43, 37% *vs* 15/41, 36%, NS).

A positive response to drug treatment (90% reduction of PVCs, from mean 13,767 ± 9,423 to 251 ± 390, $p < 0.0001$) was associated with a significant reduction in the severity of symptoms (6.2 ± 1.4 *vs* 2.7 ± 2.0, $p < 0.001$). In non-responders, there was only a mild (albeit significant) reduction of PVCs (13,767 ± 9,423 *vs* 7,850 ± 6,328, $p < 0.003$) which had no effect on symptom severity (6.2 ± 1.4 *vs* 5.9 ± 1.9, NS).

Detailed results of the mean number of PVCs during each drug treatment and corresponding mean VAS scores are presented in Table 2.

Short-term efficacy of RF ablation

Fifty (60%) patients were referred for RFCA. In eight patients, an additional redo procedure was undertaken, which gave a mean of 1.2 procedures per patient. The RVOT area was the site of origin of PVCs in 36/50 (72%) patients. In the re-

Table 2. Short-term efficacy of antiarrhythmic drugs

Parameter	Baseline	Metoprolol	Verapamil	Propafenone
Number of PVCs	13,767 ± 9,423	12,482 ± 13,417†	9,241 ± 9,676*,†	4,110 ± 6,002‡
VAS score	6.2 ± 1.4	5.7 ± 1.7†	5.7 ± 1.8†	4.4 ± 2.6‡
90% reduction of PVC	NA	9/84†	14/84†	36/84
80% reduction of PVC	NA	12/84†	20/84†	43/84
Complete responders	NA	0/84†	1/84†	15/84

PVC — premature ventricular complexes; VAS — visual analogue scale; complete responders = total elimination of PVC by tested agent; *$p < 0.003$ *vs* baseline; †$p < 0.001$ *vs* propafenone; ‡$p < 0.0001$ *vs* baseline; NA — not available

maining patients, a non-RVOT origin of PVCs was found (RV/tricuspid annulus [n = 2], aortic cusps [n = 4], LV outflow tract/aorto-mitral continuity/superior mitral annulus [n = 4], LV inflow tract [n = 2], posterior [n = 1] and anterior fascicle [n = 1] of left bundle branch).

None of the patients had inducible sustained VT during baseline EP study. There were no severe acute or late complications related to RFCA (death, stroke, myocardial infarction, tamponade, atrioventricular block) and all patients were discharged home within two days after RFCA. Based on Holter ECG recordings performed one month after successful RFCA or second RFCA, the procedure was successful in 44/50 (88%) patients.

The site of origin of PVCs did not affect the long-term efficacy of therapy. Out of 54 patients (50 with RFCA and four who underwent EP and mapping only, due to arrhythmia disappearance before RFCA and non-inducibility [n = 1], suspected left epicardial origin [n = 2] or ablation refusal after completing EP and mapping [n = 1]) in whom the arrhythmia focus was precisely localised, the efficacy of therapy in RVOT PVCs was 90% *vs* 86% in non-RVOT localisation of PVCs (NS).

Long-term follow-up

All patients completed long-term follow-up of a mean duration of 48 ± 10 months. Significant events such as sudden cardiac death, implantation of a cardioverter-defibrillator, cardiac surgery or myocardial infarction were not documented. Out of 84 patients, all 44 patients who underwent successful RFCA remained free of symptoms, 21 remained on effective drug treatment, six remained on ineffective drug therapy after failed RFCA, seven had spontaneous remission and four remained without antiarrhythmic therapy (all three tested agents were ineffective, refusal to undergo RFCA and mild symptoms) (Fig. 2).

In two patients with normal baseline ECHO, arrhythmia-induced cardiomyopathy developed within 12 months of ineffective drug treatment and preliminary refusal of RFCA. The PVC burden of these patients was 16% and 25%. Patients were successfully ablated with complete elimination of PVCs and resolution of LVEF (from 40% and 35% to 65%) within three months.

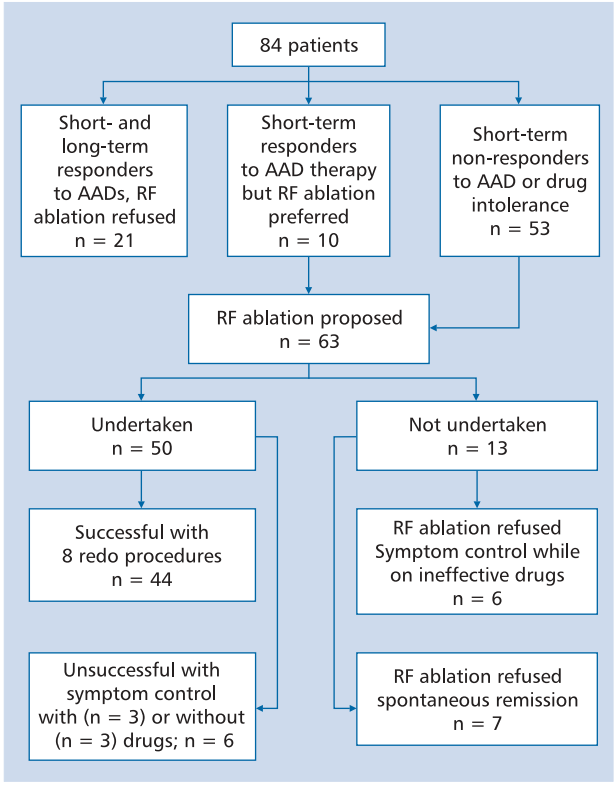

Figure 2. Short- and long-term treatment of the study group

DISCUSSION

The main findings of the present study were that, in patients with symptomatic idiopathic PVCs, propafenone was significantly more effective than metoprolol or verapamil. Secondly, optimal long-term benefit of therapy was achieved in patients who were referred for RFCA; this was highly effective and safe in this group of patients.

Symptoms

In patients with frequent PVCs and no organic heart disease, who are at low risk of sudden cardiac death, a decrease in QOL and severity of symptoms are the main indications for treatment with antiarrhythmic agents [8, 9]. Besides typical symptoms of PVCs (palpitation, chest discomfort, fati-

gue, dyspnoea, dizziness, syncope), we have previously reported various atypical symptoms (dysphagia, cough reflex, intermittent claudication, eye flashes) associated with frequent PVCs [28–31]. Many symptoms can be associated with haemodynamic consequences of PVCs, but others are triggered by cardiac reflexes and neural network interaction [8, 30–32]. Therefore, the finding that symptoms are associated with PVCs is of great importance because in this population, symptoms are the main reason for implementation of therapy.

We showed that suppression of PVCs was associated with improved VAS score. This confirmed that our patients were symptomatic due to the presence of arrhythmia and no other factors. However, to some extent, a placebo effect may occur in these patients, as shown by Krittayaphong et al. [10]. Nevertheless, in our study population, improvement in VAS score was significantly higher in responders than in non-responders. This is important because this is usually benign arrhythmia, and a reduction in symptoms is the main aim of treatment.

Moreover, symptom severity did not correlate with PVC count. This emphasises the need to use arrhythmia-specific questionnaires to assess arrhythmia-related symptoms and QOL.

Niwano et al. [7] reported that, in a large group of asymptomatic or mildly symptomatic patients with frequent PVCs, RFCA was not indicated in a mean follow-up of four years. Although those patients were asymptomatic, some had arrhythmia-induced LV dysfunction.

Efficacy of antiarrhythmic drugs

The present study showed that propafenone was significantly more effective than metoprolol or verapamil in suppressing PVCs and arrhythmia-associated symptoms. It is difficult to compare our study with those in the literature. No large, randomised study comparing these three agents in patients with PVCs and no organic heart disease has been published. Also, different definitions of drug efficacy have been used (75–80% reduction of PVCs) [8, 11, 19]. Propafenone has been tested mostly in patients with ventricular arrhythmias and organic heart disease — a population different to those evaluated in the present study [11–16].

Beta-blockers have been tested in patients with idiopathic PVCs. Their efficacy was modest (25% for metoprolol) or not superior to a placebo (atenolol) [11, 12]. Our results are similar: the efficacy of metoprolol was only 10% [12].

Verapamil has been reported to be effective in patients with idiopathic VT [3, 7, 8]. A low efficacy of verapamil in idiopathic PVCs, as shown in the present study, may suggest that these arrhythmias may have different mechanisms than idiopathic VT.

Currently, the use of metoprolol, propafenone and verapamil is recommended in patients with PVCs of RVOT origin [8]. Studies have reported drug-treatment results only for patients with RVOT or an unclassified origin of PVCs [5–7, 10–15]. The present study suggested that, in various sites of origin of non-RVOT PVCs, the efficacy of drugs or RF ablation is similar to that for RVOT PVCs.

Multiple comparisons of AADs in the same patient allow a rational approach to therapy tailored in the outpatient clinic for individual patients. However, the present study showed that, despite testing three drugs, most patients were referred for RFCA according to a current IIa (level of evidence: C) recommendation [8].

RFCA ablation

In the group of patients who underwent RFCA, long-term efficacy of 88% was achieved during long-term follow-up. This was a higher prevalence of success than that reported by Tada et al. [21] or Sacher et al. [26]. However, localisation of the origin of arrhythmia and presence of history of sustained VT differed in our group compared to those in other studies.

Interestingly, the long-term effect was better than that reported by Ventura et al., who documented a prevalence of recurrence of ≤ 50% during very long-term follow-up [6]. However, the patients in that study had also documented sustained VT from RVOT and PVCs of various sites of origin. Also, the duration of follow-up in that study was longer than in the present study.

We had two patients with arrhythmia-induced cardiomyopathy that developed after 12 months of ineffective drug treatment. Therefore, we documented that frequent PVCs with normal baseline ECHO and ineffective drug treatment may rarely lead to the development of reversible cardiomyopathy. Studies have documented that highly frequent PVCs (> 20,000 beats/day) or baseline decreased LVEF exhibit a significant decrease in LVEF during long-term follow-up [7, 33]. Bogun et al. [33] reported that effective RFCA can improve LV dysfunction associated with frequent PVCs. On the other hand, ineffective or unattempted RFCA was associated with persistence of cardiomyopathy.

RFCA of frequent symptomatic PVCs may have a significant effect on various parameters of myocardial performance, exercise capacity, haemodynamic parameters, symptoms and QOL [7, 25, 28–35]. Therefore, despite a benign prognosis, several studies support definitive cure and an invasive approach for frequent, symptomatic, idiopathic PVCs with and without systolic dysfunction [8, 9, 28–35]. Sheldon et al. [36] suggested that RFCA should even be the preferred, definitive treatment in those patients that improve with AADs therapy and do not accept long-term AADs treatment.

Limitations of the study

Firstly, this was an open-label study of a relatively limited number of patients. Secondly, more than 40% of patients had previous unsuccessful attempts at treatment. Thirdly, there was no randomisation to drugs *vs* RFCA, so we could not ascertain which treatment was superior. Fourthly, the definition of responder may not be applicable to all patients. Moreover, we

did not use an arrhythmia-specific questionnaire to evaluate treatment efficacy and physicians were not blinded to the patients' therapy. No large, prospective, multicentre studies or QOL and cost–effectiveness studies on the comparison of invasive *vs* non-invasive strategies in symptomatic patients with idiopathic PVCs have been undertaken, so various approaches cannot be compared. Lastly, the placebo effect, late spontaneous remission or recurrences, efficacy of treatment for a multifocal origin of PVCs, and lack of a standardised arrhythmia-specific questionnaire should be taken into consideration in evaluating the results of the present study and future trials.

CONCLUSIONS

Propafenone was more effective than verapamil or metoprolol in suppressing idiopathic PVCs. Most patients with frequent symptomatic idiopathic PVCs had indications for RFCA. RFCA with classical mapping and navigation was a safe and highly effective therapeutic option.

This study was supported by research grant number 501-2-1--10-72/04 from the Postgraduate Medical School, Warsaw, Poland.

Conflict of interest: *none declared*

References

1. Barrett PA, Peter CT, Swan HJ et al. The frequency and prognostic significance of electrocardiographic abnormalities in clinically normal individuals. Prog Cardiovasc Dis, 1981; 23: 299–319.
2. Buxton AE, Waxman HL, Marchlinski FE et al. Right ventricular tachycardia: clinical and electrophysiologic characteristics. Circulation, 1983; 68: 917–927.
3. Lerman BB, Stein KM, Markowitz SM. Idiopathic right ventricular outflow tract tachycardia: a clinical approach. Pacing Clin Electrophysiol, 1996; 19: 2120–137.
4. Busby MJ, Shefrin EA, Fleg JL. Prevalence and long-term significance of exercise-induced frequent or repetitive ventricular ectopic beats in apparently healthy volunteers. J Am Coll Cardiol, 1989; 14: 1659–1665.
5. Gaita F, Giustetto C, Di Donna P et al. Long-term follow-up of right ventricular monomorphic extrasystoles. J Am Coll Cardiol, 2001; 38: 364–370.
6. Ventura R, Steven D, Klemm HU et al. Decennial follow-up in patients with recurrent tachycardia originating from the right ventricular outflow tract: electrophysiologic characteristics and response to treatment. Eur Heart J, 2007; 28: 2338–2345.
7. Niwano S, Wakisaka Y, Niwano H et al. Prognostic significance of frequent premature ventricular contractions originating from the ventricular outflow tract in patients with normal left ventricular function. Heart, 2009; 95: 1230–1237.
8. Zipes DP, Camm AJ, Borggrefe M et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death. J Am Coll Cardiol, 2006; 48: e247–e484.
9. Aliot EM, Stevenson WG, Almendral-Garrote JM et al. European Heart Rhythm Association (EHRA); Registered Branch of the European Society of Cardiology (ESC); Heart Rhythm Society (HRS); American College of Cardiology (ACC); American Heart Association (AHA). EHRA/HRS Expert Consensus on Catheter Ablation of Ventricular Arrhythmias: developed in a partnership with the EHRA, a Registered Branch of the ESC, and the HRS; in collaboration with the ACC and the AHA. Heart Rhythm, 2009; 6: 886–933.
10. Krittayaphong R, Bhuripanyo K, Punlee K, Kangkagate C, Chaithiraphan S. Effect of atenolol on symptomatic ventricular arrhythmia without structural heart disease: a randomized placebo-controlled study. Am Heart J, 2002; 144: e10.
11. Capucci A, Frabetti L, Gubelli S et al. Tocainide and metoprolol: an efficacious therapeutic combination in the treatment of premature ventricular beats. Clin Cardiol, 1989; 12: 322–331.
12. Saikawa T, Niwa H, Ito M et al. The effect of propafenone on premature ventricular contractions (PVCS): an analysis based on heart rate dependency of PVCSs. Jpn Heart J, 2001; 42: 701–711.
13. Paperini L, Davini A, Lattanzi F et al. Propafenone and flecainide in the therapy of ventricular arrhythmias. Minerva Cardioangiol, 1995; 43: 449–457.
14. Babuty D, Cosnay P, Rouesnel P, Bine-Scheck F, Arnaud R, Fauchier JP. Comparison of the efficacy/tolerability ratio of cibenzoline and propafenone in the treatment of ventricular arrhythmia. Ann Cardiol Angeiol, 1992; 41: 225–234
15. Klein RC, Huang SK, Marcus FI et al. Enhanced antiarrhythmic efficacy of propafenone when used in combination with procainamide or quinidine. Am Heart J, 1987; 114: 551–558.
16. Facchini M, Bonazzi P, Priori SG, Varisco T, Zuanetti G, Schwarz PJ. Multiple comparison of several antiarrhythmic agents by acute oral testing in patients with chronic ventricular arrhythmias. Eur Heart J, 1988; 9: 462–470.
17. Gill JS, Blaszyk K, Ward DE, Camm AJ. Verapamil for the suppression of idiopathic ventricular tachycardia of the left bundle branch block-like morphology. Am Heart J, 1993; 126: 1126–1133.
18. Giani P, Landolina M, Giudici V et al. Pharmacokinetics and pharmacodynamics of propafenone during acute and chronic administration. Eur J Clin Pharmacol, 1988; 34: 187–194.
19. Winkle RA. Antiarrhythmic drug effect mimicked by spontaneous variability of ventricular ectopy. Circulation, 1978; 57: 1116–1121.
20. Tada H, Tadokoro K, Miyaji K et al. Idiopathic ventricular arrhythmias arising from the pulmonary artery: prevalence, characteristics, and topography of the arrhythmia origin. Heart Rhythm, 2008; 5: 419–426.
21. Tada H, Tadokoro K, Ito S et al. Idiopathic ventricular arrhythmias originating from the tricuspid annulus: Prevalence, electrocardiographic characteristics, and results of radiofrequency catheter ablation. Heart Rhythm, 2007; 4: 7–16.
22. Ito S, Tada H, Naito S et al. Development and validation of an ECG algorithm for identifying the optimal ablation site for idiopathic ventricular outflow tract tachycardia. J Cardiovasc Electrophysiol, 2003; 14: 1280–1286.
23. Tada H, Ito S, Shinbo G et al. Significance and utility of plasma brain natriuretic peptide concentrations in patients with idiopathic ventricular arrhythmias. Pacing Clin Electrophysiol, 2006; 29: 1395–1403.
24. Sekiguchi Y, Aonuma K, Yamauchi Y et al. Chronic hemodynamic effects after radiofrequency catheter ablation of frequent monomorphic ventricular premature beats. J Cardiovasc Electrophysiol, 2005; 16: 1057–1063.
25. Takemoto M, Yoshimura H, Ohba Y et al. Radiofrequency catheter ablation of premature ventricular complexes from right ventricular outflow tract improves left ventricular dilation and clinical status in patients without structural heart disease. J Am Coll Cardiol, 2005; 45: 1259–1265.
26. Sacher F, Tedrow UB, Field ME et al. Ventricular tachycardia ablation: evolution of patients and procedures over 8 years. Circ Arrhythmia Electrophysiol, 2008; 1: 153–161.
27. Yamada T, Yoshida N, Murakami Y et al. Electrocardiographic characteristics of ventricular arrhythmias originating from the junction of the left and right coronary sinuses of valsalva in the aorta: the activation pattern as a rationale for the electrocardiographic characteristics. Heart Rhythm, 2008; 5: 184–192.
28. Stec SM, Grabczak EM, Bielicki P et al. Diagnosis and management of premature ventricular complexes-associated chronic cough. Chest, 2009; 135: 1535–1541.
29. Stec S, Tarnowski W, Binda A, Kulakowski P. Videofluoroscopic modified barium swallow study for premature ventricular complexes-associated dysphagia. Circ Arrhythmia Electrophysiol, 2008; 1: e1.
30. Stec S, Tarnowski W, Kalin K, Sikora K, Kulakowski P. High-resolution esophageal manometry with ECG monitoring for management of premature. ventricular complexes-associated dysphagia. Dysphagia, 2010; 25: 66–69.
31. Stec S, Zaborska B, Pilus A, Lewandowski P, Kulakowski P. Intermittent claudication caused by frequent premature ventricular complexes: resolution after radiofrequency ablation. Angiology, 2009; 60: 378–381.
32. Lelakowski J, Dreher A, Majewski J, Bednarek J. Effects of catheter ablation of idiopathic ventricular ectopic beats on left ventricular function and exercise capacity. Kardiol Pol, 2009; 67: 847–855.
33. Bogun F, Crawford T, Reich S et al. Radiofrequency ablation of frequent, idiopathic premature ventricular complexes: comparison with a control group without intervention. Heart Rhythm, 2007; 4: 863–867.
34. Wijnmaalen AP, Delgado V, Schalij MJ et al. Beneficial effects of catheter ablation on left ventricular and right ventricular function in patients with frequent premature ventricular contractions and preserved ejection fraction. Heart, 2010; 96: 1275–1280.
35. Baman TS, Lange DC, Ilg KJ et al. Relationship between burden of premature ventricular complexes and left ventricular function. Heart Rhythm, 2010; 7: 865–869.
36. Sheldon SH, Gard JJ, Asirvatham SJ. Premature ventricular contractions and non-sustained ventricular tachycardia: association with sudden cardiac death, risk stratification, and management strategies. Indian Pacing Electrophysiol J, 2010; 10: 357–371.

Idiopatyczne objawowe przedwczesne skurcze dodatkowe komorowe: krótko- i długoterminowa ocena skuteczności leczenia antyarytmicznego i ablacji

Sebastian Stec, Agnieszka Sikorska, Beata Zaborska, Tomasz Kryński, Joanna Szymot, Piotr Kułakowski

Oddział Kliniczny Kardiologii, Centrum Medycznego Kształcenia Podyplomowego, Szpital Grochowski, Warszawa

Streszczenie

Wstęp: Wiedza na temat długoterminowej skuteczności leków antyarytmicznych (AADs) i przezskórnej ablacji prądem o wysokiej częstotliwości (RFCA) u pacjentów z objawowymi przedwczesnymi skurczami dodatkowymi (PVCs) bez organicznej choroby serca jest ograniczona.

Cel: Celem pracy była ocena krótko- i długoterminowej skuteczności oraz tolerancji leczenia AADs i RFCA u chorych z idiopatycznymi PVCs.

Metody: Do prospektywnego, otwartego badania typu krzyżowego włączono 84 kolejnych chorych (średni wiek 47 ± 15 lat; 60% kobiet) z objawowymi idiopatycznymi PVCs (średnia liczba PVCs/24 h 13 768 ± 9424; zakres: 1693–42 687). Chorzy byli leczeni w sposób losowy przez 2–3 tygodnie metoprololem, propafenonem i werapamilem. Następnie pacjentów kierowano na zabieg RFCA, jeśli stwierdzono u nich nieskuteczność, nietolerancję lub niechęć do długoterminowego leczenia AADs.

Wyniki: W obserwacji krótkotermnowej najskuteczniejszym lekiem był propafenon, a w dalszej kolejności werapamil i metoprolol [35 (42%), 13 (15%) i 8 (10%) chorych uznanych za *responders*, kolejno, $p < 0,01$ *v.* propafenon]. Tylko u pacjentów zakwalifikowanych jako *AADs responders* osiągnięto istotną redukcję nasilenia objawów arytmii (*Visual Analog Scale*: 6,2 ± ± 1,4 *v.* 2,7 ± 2,0; $p < 0,001$). Po próbie doboru farmakoterapii 50 (60%) osób poddano RFCA. Podczas obserwacji długoterminowej (48 ± 10 miesięcy) RFCA (średnio 1,2 procedury/chorego) była skuteczna u 44/50 (88%) chorych. Spośród pozostałych 34 pacjentów 21 chorych było skutecznie leczonych AADs, 6 było leczonych AADs nieskutecznie, a u 7 chorych zrezygnowano z terapii AADs z powodu spontanicznej remisji PVCs lub istotnego zmniejszenia nasilenia objawów PVCs.

Wnioski: Krótkoterminowe leczenie propafenonem jest skuteczniejsze niż werapamilem i metoprololem w redukcji liczby oraz objawów idiopatycznych PVCs, jednak optymalny efekt długoterminowy odnoszą chorzy poddani zabiegowi ablacji.

Słowa kluczowe: przedwczesne skurcze dodatkowe, leki antyarytmiczne, ablacja prądem o wysokiej częstotliwości, arytmie komorowe, leczenie, standardy

Kardiol Pol 2012; 70, 4: 351–358

Adres do korespondencji:
dr n. med. Sebastian Stec, Oddział Kliniczny Kardiologii, Centrum Medycznego Kształcenia Podyplomowego, Szpital Grochowski, ul. Grenadierów 51, 04–073 Warszawa, email:smstec@wp.pl
Praca wpłynęła: 27.07.2011 r. **Zaakceptowana do druku:** 24.10.2011 r.