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ORIGINAL ARTICLE

The Management of Supraventricular Tachyarrhythmias in Patients with Pulmonary Arterial Hypertension

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Background Atrial remodelling in pulmonary arterial hypertension (PAH) may lead to higher incidence of supraventricular arrhythmias (SVA). The purpose of this study was to evaluate the efficiency and safety of various methods for treatment of SVA in this group.

Methods This was a single centre study. Forty-eight patients (33 women and 15 men) aged 19-77 years (median 49 years) were enrolled. There were 30 patients with idiopathic PAH, 10 had PAH associated with connective tissue disease, and eight with congenital heart disease. A retrospective analysis was performed to estimate the prevalence and type of supraventricular arrhythmias, as well as efficiency and safety of treatment methods. Mean follow-up period was 28.8±17.7 months.

Results Supraventricular arrhythmias occurred in 17 patients (35%) and appeared to be atrial fibrillation, flutter or tachycardia. Supraventricular arrhythmias coexisted with elevated mean right atrial pressure in 75%. Four patients had more than one type of SVA. A flutter-like macro-reentrant form of atrial tachycardia dependent on cavo-tricuspid isthmus was found in four cases. The treatment of SVA included typical methods: antiarrhythmic drugs, direct current cardioversion (DCC), and radiofrequency (RF) ablation. All of the therapeutic methods were effective in managing acute arrhythmia. Three patients required re-ablation. Overall mortality: 14 patients (29%) in the whole study group, including six in SVA group (35%) and eight without SVA (26%).

Conclusions In patients with PAH DCC, pharmacological cardioversion and RF ablation can be applied safely and effectively. Flutter-like macro-reentrant atrial tachycardia dependent on cavo-tricuspid isthmus is observed in this group. It is more challenging, but possible, to successfully treat this arrhythmia with RF ablation.

Keywords Supraventricular arrhythmia • Pulmonary arterial hypertension • Atrial fibrillation • Atrial flutter • Atrial tachycardia • Arrhythmia substrate

Introduction

Pulmonary arterial hypertension (PAH) is a rare disease. Recent registries have shown a prevalence of PAH in the range 15-50 subjects per million in the European population [1]. Pulmonary arterial hypertension is recognised when the mean pulmonary artery pressure (mPAP) at the right heart catheterisation (RHC) is ≥ 25 mmHg with a coexisting

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pulmonary wedge pressure (PWP) $\leq$ 15 mmHg [2]. Pulmonary arterial hypertension occurs due to an impaired production of vasodilators and antiproliferative agents, such as nitric oxide and prostacyclin, along with over-expression of vasoconstrictors and proliferative substances, such as thromboxane A2 and endothelin-1 [2]. This causes thickening of pulmonary arterial walls, vasoconstriction, vascular remodelling, and increased pulmonary vascular resistance, which results in the right heart congestion. Overload of the right ventricle may lead to functional tricuspid regurgitation and increased right atrial pressure. Medi et al. [3] described atrial remodelling and alteration of electrical properties resulting from long-standing elevation of atrial pressure, which forms a potentially arrhythmogenic substrate. Some studies [4] confirm higher prevalence of supraventricular arrhythmias in patients with pulmonary hypertension and elevated right atrial pressure (RAP). This may be a marker of more serious PAH and hence the cause of a worse prognosis associated with increased mean RAP and SVA [5]. Therefore, it seems reasonable to treat the arrhythmia not only to relieve the symptoms, but also to improve the prognosis. Unfortunately, little is known about the safety and efficacy of different arrhythmia treatment methods, as well as the long-term outcome in this specific group of patients. We focussed on the evaluation of supraventricular tachyarrhythmia management and the clinical outcome.

Materials and Methods

This was a retrospective, single centre, observational study. We enrolled 48 consecutive patients diagnosed with PAH according to Dana Point classification group 1 [6,7] in a regional reference centre for the treatment of PAH. The data collection period was from August 2008 until October 2013 and the observation start date was the day of the diagnosis. Mean follow-up period was 28.8±17.7 months. The diagnosis of PAH was made by a right heart catheterisation (RHC) in all patients. Data was extracted from medical records and documents in archives. The extracted data included diagnosis, age, gender, underlying disease, BMI, WHO/NYHA functional class, laboratory data, 6 minute walking distance (6MWD), results of the echocardiography, cardiopulmonary exercise test (CPET), and cardiac catheterisation. The arrhythmia has been recognised in either standard ECG or ECG Holter monitoring or electrophysiological study. The data concerning the type of treatment and its efficacy and safety were also collected. The causes of PAH in the examined group, were: idiopathic (IPAH) in 30 patients, associated with connective tissue disease (CTD-PAH) in 10 patients, and associated with congenital heart disease (CHD-PAH) in eight patients. Other causes of pulmonary hypertension (Dana Point groups 2-5) were excluded from the study.

Baseline echocardiography, CPET, and RHC were performed in all patients. The treatment of PAH was consistent with the current guidelines (sildenafil or bosentan in first-line treatment, and treprostinil, iloprost, bosentan, or ambrisentan in second-line treatment when determinants of worse prognosis were found in the patient). Mean follow-up period was 28.8±17.7 months and it included control visits to assess the clinical state (incl. heart rhythm), WHO/NYHA functional class, and hospitalisations due to clinical state deterioration and mortality.

The primary outcome was occurrence of supraventricular arrhythmia. In the patients who were diagnosed with this, we analysed the type of arrhythmia, indication for treatment, treatment method, its safety, as well as immediate, short-, and long-term effectiveness. All-cause mortality was assessed in the whole examined group.

Statistical Analysis

The patient characteristics at baseline were reported as means ± standard deviation (SD) for continuous variables or proportions (percentages) for categorical variables. Differences between the two groups were assessed by the Mann-Whitney test or Fisher's exact test for categorical variables and the t-test or the Welch test for continuous variables. A Kaplan-Meier analysis was performed to estimate survival based on SVA occurrence; the statistical significance of differences was compared by the log-rank test. Two-tailed p values $\leq$ 0.05 were considered to be statistically significant. All statistical analyses were performed using the STATISTICA 10 software program (StatSoft Inc., Tulsa, OK, USA).

Results

Baseline Characteristics

All examined patients were divided into two groups depending on the arrhythmia occurrence. These groups did not differ significantly in age, sex, 6MWD, peak oxygen consumption ($pVO_{2\ max}$) on CPET, NT-proBNP serum level, mean pulmonary artery pressure (mPAP), or WHO/NYHA functional class. Parameters that distinguished these groups were: mRAP, which was significantly higher among patients with supraventricular arrhythmias, as well as echocardiographic parameters – tricuspid annular plane systolic excursion (TAPSE), pericardial fluid presence and right atrial area (Table 1). Comorbidities that could potentially affect the prevalence of SVA are presented in Table 2. Hypothyroidism appeared significantly more often in the group with SVA, but all of the patients had L-thyroxine supplementation and were euthyroid at that time. Pulmonary arterial hypertension specific pharmacotherapy at baseline did not differ significantly between groups (Table 3).

Arrhythmia appeared in 17 patients (35% prevalence). Most often it occurred as atrial fibrillation (n=8), either paroxysmal or permanent, then atrial tachycardia (n=6), and last as atrial flutter (n=6; paroxysmal or persistent). One patient was diagnosed with fascicular ventricular tachycardia (fVT) with atrioventricular dissociation causing severe deterioration (not included to statistical analysis). Four patients had more than one type of arrhythmia. Distribution and treatment of all