Heart & Lung ■■ (2018) ■■–■■

Contents lists available at ScienceDirect

Heart & Lung

journal homepage: www.heartandlung.com

Right atrium enlargement predicts clinically significant supraventricular arrhythmia in patients with pulmonary arterial hypertension

Marcin Waligóra, MD [a], Anna Tyrka, MD, PhD [a], Tomasz Miszalski-Jamka, MD, PhD [b], Małgorzata Urbańczyk-Zawadzka, MD [b], Piotr Podolec, MD, PhD [a], Grzegorz Kopeć, MD, PhD [a,*]

[a] Department of Cardiac and Vascular Diseases, Faculty of Medicine, Jagiellonian University Medical College, John Paul II Hospital in Krakow, Pradnicka 80, Kraków, Poland
[b] Department of Radiology and Diagnostic Imaging, John Paul II Hospital in Krakow, Pradnicka 80, Kraków, Poland

ARTICLE INFO

Article history:
Received 21 May 2017
Accepted 8 January 2018
Available online

Keywords:
Pulmonary arterial hypertension
Arrhythmia
Cardiac resonance imaging
Right atrium enlargement
Atrial flutter

ABSTRACT

Background: Right atrial (RA) enlargement is a common finding in patients with pulmonary arterial hypertension (PAH) and an important predictor of mortality, however its relation to the risk of atrial arrhythmias has not been assessed.
Objectives: To assess whether RA enlargement is associated with supraventricular arrhythmias (SVA) and whether it predicts new clinically significant SVA (csSVA).
Methods: Patients with PAH were recruited between January 2010 and December 2014 and followed until January 2017. csSVA was diagnosed if it resulted in hospitalization. To assess predictors of new csSVA, only patients without a history of SVA at baseline were analyzed.
Results: Among 97 patients, any SVA was observed in 45 (46.4%) and included permanent atrial fibrillation(AF, n = 8), paroxysmal AF (n = 10), permanent atrial flutter (AFl, n = 1), paroxysmal AFl (n = 2) or other types of supraventricular tachycardia (n = 24). Patients with SVA as compared to patients without SVA were characterized by older age, lower distance in a 6-minute test, higher NT-proBNP, higher RA area index (RAai), left atrial area index, mean right atrial pressure (mRAP) and were more commonly treated with β-blocker. Eighty five patients who were in sinus rhythm at baseline assessment and had no history of significant SVA were observed for 37 ± 19.9 months. During that time csSVA occurred in 15.3%. In univariate models, the occurrence of csSVA were predicted by age, right ventricular ejection fraction, right ventricular end diastolic index, RAai and mRAP, but in multivariate model only RAai remained significant predictor for csSVA (HR of 1.23, 95%CI: 1.11–1.36, p < 0.001). The optimal threshold for RA enlargement as discriminator of csSVA was 21.7 cm2/m2.
Conclusions: In PAH patients RA enlargement is associated with increased prevalence of SVA. RAai is an independent predictor of hospitalization due to csSVA.

Abbreviations: 6MWD, six minute walk distance; AF, atrial fibrillation; AFl, atrial flutter; BSA, body surface area; csSVA, clinically significant supraventricular arrhythmias; CCB, calcium channel blockers; CI, cardiac index; cMR, cardiovascular magnetic resonance; ERA, endothelin receptor antagonists; CHD-APAH, pulmonary arterial hypertension associated with congenital heart diseases; CTD-APAH, pulmonary arterial hypertension associated with connective tissue disease; LAa, left atrial area; LAai, left atrial area index; IPAH, idiopathic pulmonary arterial hypertension; mRAP, mean right atrial pressure; mPAP, mean pulmonary artery pressure; NT-proBNP, N-terminal pro-B type natriuretic peptide level; PAH, pulmonary arterial hypertension; PVR, pulmonary vascular resistance; RA, right atrium; RAa, right atrial area; RAai, right atrial area index; RV-EDV, right ventricular end diastolic volume; RV-EDVi, right ventricular end diastolic volume index; RV-EF, right ventricle ejection fraction; RVM, right ventricle myocardial mass; RVMi, right ventricle myocardial mass index; SpO_2, oxygen saturation; SVA, supraventricular arrhythmias; WHO-FC, World Health Organization functional class.

Conflict of interests: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

* Corresponding author. Fax: +48 12 614 33 32.
E-mail address: gkopec@szpitaljp2.krakow.pl (G. Kopeć).

0147-9563/$ – see front matter © 2018 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.hrtlng.2018.01.004

Introduction

Sustained supraventricular tachyarrhythmias are important predictors of poor prognosis in patients with pulmonary arterial hypertension (PAH).[1] Their prevalence is relatively high ranging from 11.7% to 35%, and their onset is often associated with clinical worsening.[2–6]

Left atrial enlargement is an important risk factor for atrial arrhythmias as shown in several groups of patients including the elderly,[7–9] patients with hypertrophic cardiomyopathy,[10] valvular heart disease,[11] and hypertension.[12,13] Atrial dilation results in its stretch and consequently electrical remodeling.[14,15]

At present less is known about the role of right atrial (RA) remodeling in pathophysiology of supraventricular tachyarrhythmias. Recently, RA enlargement has been shown to predict the occurrence of atrial arrhythmia in patients with repaired tetralogy of Fallot[16] and in arrhythmogenic right ventricular cardiomyopathy.[17] RA enlargement is a common finding in patients with PAH and an important predictor of mortality,[18] however its relationship to the risk of atrial arrhythmias has not been assessed.

Therefore, we assessed whether PAH patients with supraventricular arrhythmias (SVA) have larger RA than patients without SVA and whether RA enlargement predicts the occurrence of new clinically significant SVA (csSVA) in the long-term follow-up.

Methods

Patients

All study participants were recruited consecutively at the Pulmonary Hypertension reference center between January 2010 and December 2014 as a part of observational cohort study described in our previous paper.[19] Briefly, the study sample included all PAH patients who were over 18 years old and did not have contraindications to cardiovascular magnetic resonance (cMR). Pulmonary hypertension and PAH were diagnosed according to the current guidelines.[20] Both patients who were treatment naive (not treated with therapies specific for PAH) and who were already treated with PAH targeted medications were included. From the study sample we distinguished the follow-up group to assess whether RA enlargement predicted the incidence of clinically significant SVA. The follow-up group consisted of patients who were in sinus rhythm at presentation and who did not have any history of SVA (the follow-up group). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the institutional ethics committee. Informed consent was obtained from each patient before starting the study.

Baseline assessment

At the time of enrollment we assessed medical history, level of N-terminal pro-B type natriuretic peptide (NT-proBNP), distance in the six minute walk test (6MWD), and functional class according to the World Health Organization (WHO-FC). In every patient we also performed a 12-lead surface ECG, a three lead 24h-Holter electrocardiogram (Holter ECG), cardiovascular magnetic resonance (cMR), and right heart catheterization. We used the Mosteller formula[21] to estimate the body surface area (BSA). All of the above measurements were made during one hospitalization. The WHO-FC was assessed as recommended by the guidelines[20] (*supplementary materials*). The 6MWD was performed with a standard protocol as previously recommended on a corridor with the walking distance of 30 m.[22] Hemodynamic evaluation was performed during right heart catheterization using a pulmonary artery catheter. Cardiac output was measured using the Fick oxygen consumption method with a direct measurement of oxygen consumption. Patients were treated with PAH targeted drugs according to the guidelines of the European Society of Cardiology (ESC)[20,23] and local standards.

Follow-up assessment

The observation period started at the time of baseline assessment of the patient in our center and extended until January 2017. Each patient was assessed in an out-patient department or in the hospital ward every 3 months and an ECG was performed at each visit. Holter ECG was performed at least once a year or in case of symptoms of arrhythmia reported to the leading physician. The following symptoms were considered as suggestive of SVA: palpitations, lightheadedness, presyncope, syncope.[24]

Cardiovascular magnetic resonance imaging

As previously described,[25] breath-hold, ECG-gated imaging was performed using cardiac-phased array coil on 1.5T whole-body scanner (Magnetom Sonata Maestro Class, Siemens, Erlangen, Germany), the details are shown in the *supplementary material*. The following measurements were made for the purpose of the study: RA area (RAa), left atrial area (LAa), right ventricular (RV) end diastolic volume (RV-EDV), RV myocardial mass (RVM), and RV ejection fraction (RV-EF). All parameters were divided by body surface are and expressed as RAa index (RAai), LAa index (LAai), RV-EDV index (RV-EDVi), RVM index (RVMi).[26,27]

12-lead ECG

A 12-lead standard ECG (10 mm = 1 mV, 25 mm/s) was acquired in a supine position during quiet respiration at baseline and follow-up visits. All ECG records were assessed by an experienced cardiologist.

Holter ECG monitoring

Holter ECG was performed with the use of a three lead DelMar 563 recorder and analyzed on the DelMar Avionix software. We defined SVA as any supraventricular tachycardia (SVT), atrial flutter (AFl) or atrial fibrillation (AF) that was diagnosed at initial assessment or at follow-up. SVT was defined as at least three consecutive beats at the rate of >100 beats/min excluding sinus tachycardia. AF was defined as an irregular rhythm without visible p waves, while AFl as a regular or irregular rhythm with flutter waves. Both AF and AFl must have been lasting for at least 30 seconds to be diagnosed. Recurrent SVA was diagnosed when it was present in at least two different ECG records performed on different visit. csSVA was defined as any SVA which lasted over 30 seconds and required hospitalization.[28] The type of csSVA was analyzed in a 12-lead standard ECG (10 mm = 1 mV, 25 mm/s) and defined according to standards.[29,30] All arrhythmias were confirmed visually before they were included in the Holter ECG report.[31]

Statistics

Statistical analysis was performed with Statistica PL software [Dell Inc. (2016). Dell Statistica (data analysis software system), version 13, software.dell.com] and MedCalc Statistical Software version 16.8 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). The significance level was set at alpha level of 0.05. Continuous variables are reported using means and standard deviations. Categorical variables are described as counts and percentages. Continuous variables were compared using the Mann Whitney U-test. The χ^2-test was used to compare categorical variables. McNemar