Title:

The Impact of Atrial Fibrillation and Atrial Tachycardias on the Hemodynamic Status of Patients with Pulmonary Hypertension

Short title:

Hemodynamics in arrhythmia

Authors:

Dusik Milan; Fingrova Zdenka; Marek Josef; Dytrych Vladimir; Jansa Pavel; Havranek Stepan

Affiliation:

2nd Department of Medicine - Department of Cardiovascular Medicine,
General University Hospital in Prague, 1st Faculty of Medicine, Charles University in Prague,
U Nemocnice 2, 128 08, Prague, Czech Republic

Correspondence to:

Stepan Havranek
Address: U Nemocnice 2, 12808, Prague, Czech Republic
E-mail: stepan.havranek@lf1.cuni.cz
Phone: +420723085848

Summary:

BACKGROUND: The impact of atrial fibrillation and atrial tachycardias (AF/AT), and their optimal treatment strategy in PH patients is still being discussed. The goal of this study was to evaluate the effect of AF/AT termination on the hemodynamic parameters in PH patients.

METHODS: We compared patients with pre-capillary pulmonary hypertension (PH group), left ventricular heart failure (LV-HF group), and a Control group. A repeated right heart catheterization was performed during the catheter ablation (CA) procedure. The first measurement was done in arrhythmia, the second after the sinus rhythm (SR) was restored. High frequency atrial stimulation was used to simulate AT in patients without arrhythmia presence at the time of the CA.

RESULTS: The variation of pressure parameters in PH patients did not differ significantly from the Controls. There was a significant increase in the right ventricle pressure after the SR restoration in the LV-HF group compared to the Controls and PH group (+4 vs. -2 vs. -3 mmHg, $p < 0.05$). The cardiac index (CI) variation was not significant when compared between the study groups. An increase of the CI after the SR restoration was found in those patients with AF (+0.31 l/min/m² [IQR 0.18; 0.58]) in contrast to those patients with organized AT/high frequency atrial stimulation (-0.09 l/min/m², [IQR - 0.45; 0.19]). This difference was statistically significant ($p < 0.05$).

CONCLUSION: The acute hemodynamic response to arrhythmia termination was not significantly different in the PH patients when compared to the Controls. In contrast to AT/high frequency stimulation, the restoration of SR in AF patients leads to an increased CI, irrespective of the presence or absence of PH.

Key words:

Pulmonary hypertension, Hemodynamics, Arrhythmia, Atrial fibrillation, Pulmonary artery catheterization

INTRODUCTION

Pulmonary hypertension (PH) is a hemodynamic state defined by a mean pulmonary artery pressure (mPAP) of 25mmHg or more measured at rest, according to the latest ESC guidelines. [1] The worldwide prevalence of PH is estimated to be around 1%. [2] Irrespective of the concrete cause of PH, it is generally associated with greater morbidity and mortality. Based on its aetiology, clinical manifestation, and pathophysiological mechanisms, PH can be divided into 5 groups (pulmonary arterial hypertension (PAH), PH due to left heart disease, PH due to lung disease/hypoxia, chronic thromboembolic PH (CTEPH), and PH with unclear/multifactorial mechanisms). [3] An echocardiography is a well-established screening tool for PH. [4] However, a right heart catheterization is required to confirm the diagnose of pulmonary hypertension and to distinguish between precapillary and postcapillary (i.e. connected to the left heart disease) PH. [3] To get reliable results, right heart catheterization should be performed under defined conditions, including sinus rhythm (SR). [5]

Supraventricular arrhythmias (SVTs), including atrial fibrillation (AF) and type 1 atrial flutter (AFL), are common in patients with PH. The prevalence of SVTs in all types of PH varies between 10-36%. [6-12] A recent analysis of the registry of patients from our centre showed a very high prevalence of SVTs, mainly permanent AF, in patients with post-capillary PH. [8]

According to ESC guidelines, maintenance of a stable SR in all PH patients should be considered as an important treatment goal [3], as the presence of an arrhythmia is often connected with further clinical deterioration and SR restoration can relieve patient's symptoms. [7, 9, 10, 13] Nevertheless, the optimal treatment strategy for SVTs in PH patients has not yet been established due to the lack of robust prospective data. [3] As well as the pharmacological antiarrhythmic treatment, radiofrequency catheter ablation (CA) is currently a safe and effective method for rhythm control in patients with atrial fibrillation and other atrial tachycardias (AF/AT),and is successfully performed in even PH patients. [14]

According to our knowledge, the effect of an arrhythmia presence and SR restoration on concrete hemodynamic parameters has not yet been studied in detail. It remains unclear as to whether the rhythm control strategy is hemodynamically beneficial for PH patients, and if it is connected with the cardiac output improvement. For PH patients with persistent arrhythmia, there is a lack of data on performing the hemodynamic assessment and interpreting its results when the examination is done in AF/AT. Therefore, we designed a study with the aim of identifying the differences in intracardiac pressures and cardiac output during CA in PH patients.

METHODS

In this prospective observational trial, we compared the acute haemodynamic response to rhythm change in consecutive patients with known precapillary pulmonary hypertension (PH group), patients with the left heart failure (LV-HF group), and a Control group of patients. The trial was performed according to the principles of good clinical practice and in compliance with the Declaration of Helsinki. The whole study was approved by the local Ethics committee (Ethics Committee in General University Hospital in Prague, No. 15/20). All patients gave written informed consent agreeing to data collection and analysis for scientific purposes.

Subjects

The main inclusion criterion for all subjects was a diagnosis of paroxysmal, persistent or long-standing persistent atrial fibrillation (AF), or atrial tachycardia (AT) including AFL indicated to the treatment by CA based on the current guidelines. We set up the exclusion criteria as follows: an age of less than 18 or over 85 years, the presence of another arrhythmia that makes valid hemodynamical measurement impossible (frequent atrial or ventricular extrabeats, other clinically relevant arrhythmia than AF / AT indicated to CA, stimulated rhythm), significant valvular disease, NYHA IV, cardiogenic shock or severe peripheral oedema, or the non-cooperation of the patient.

For the purpose of our study, precapillary pulmonary hypertension was defined as mPAP ≥ 25 mmHg, pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg, and pulmonary vascular resistance (PVR) ≥ 3 W.U. measured by right heart catheterization. For the diagnosis of the left heart failure, the presence of both signs (clinical and echo findings, NTpro-BNP elevation) and symptoms (dyspnoea, fatigue, etc.) was required. We did not set any cut-off in left ventricular ejection fraction values, i.e. patients with heart failure with reduced as well as preserved ejection fraction were included. The control group consisted of patients without known pulmonary hypertension, heart failure, or another structural heart disease.

Study procedures

All study procedures were performed during standard hospitalization for CA. At the time of admission, all patients had underwent a complex assessment including personal data and medical history collection, evaluation of symptoms, physical examination by a doctor, and laboratory tests (routine biochemistry, blood count, NT-proBNP). A 12-lead ECG was obtained in every patient.

1. Hemodynamic measurement:

The main study procedure was a repeated right heart catheterization using the Swan-Ganz catheter (Corodyn TD TouchFree 7F. 110cm, B.Braun, Melsungen AG, Germany) done at the beginning and at the end of the CA. The catheter ablation was performed in a fasting state under mild analgosedation with fentanyl and midazolam. Briefly, in patients with AF, the CA was guided by electroanatomic mapping using a CARTO™ system (Biosense-Webster, Diamond Bar, CA, USA) and intracardiac echocardiography (AcuNav™ catheter, Siemens, Germany) according to local standards. The double transseptal puncture was used to enter the left atrium (LA). A single 20-polar circular catheter (Lasso™, Biosense-Webster, Diamond Bar, CA, USA) was placed at the ostia of the pulmonary veins (PV) to record PV potentials. An open irrigation 3.5-mm-tip ablation catheter (NaviStar Thermocool, Biosense-Webster) was used both for electroanatomic mapping of the LA and radiofrequency (RF) ablation. The standard procedure consisted of an isolation of the pulmonary veins. A single circumferential set of RF lesions was created point-by-point to isolate ipsilateral pulmonary veins. The extension of ablation of extrapulmonary substrate was left to the operator's discretion. In patients with ATs, the concrete consecution of CA differed according to the exact type and mechanism of arrhythmia. Cavo-tricuspid ablation was done in all patients with typical AFL.

Direct current electrical cardioversion under sedation with propofol using a synchronized biphasic shock with energy 120-200J (according to the discretion of physician) was standardly performed at the end of the CA procedure if the SR was not previously restored. The administration of the antiarrhythmic drugs during the CA was not standardized and depended on the operator's decision.

The first hemodynamic assessment was done in arrhythmia and the second assessment was done after the SR was restored. In patients without the presence of actual arrhythmia during the catheter ablation (mainly patients with paroxysmal arrhythmia), the anterograde Wenckebach point (e. g. the lowest atrial pacing rate at which atrioventricular block is observed) was determined. High frequency

atrial stimulation (stimulation rate = Wenckebach point + 10 bpm) was used to simulate the AT with irregular ventricular response.

In each of the measurements we acquired a complete dataset of pressure curves taken from the right atrium (RA), right ventricle (RV), pulmonary artery, and the PAWP curve. The pressure curves were optimally recorded at the end of exhalation during calm breathing. The systolic and diastolic values as well as the mean pressures were deducted. Cardiac output was measured by the thermodilution technique. Standardly, three measurements of the cardiac output were made and the mean value was used for further calculations. In case the variation between the measurements was bigger than 10%, another measurement was performed and the most distinct value was omitted to reduce possible mistakes. The calculated cardiac index, i.e. cardiac output indexed on the patient's body surface area, was used for statistical analysis instead. Later, the pressure and cardiac index values obtained in the arrhythmia were subtracted from the SR values in order to evaluate the size and significance of the SR restoration on each of the hemodynamical parameters.

Transthoracic echocardiogram:

A transthoracic echocardiogram was performed on the day after the CA. All echocardiograms were performed on Vivid 9 or Vivid E95 ultrasound machines (GE Healthcare, Chicago, IL, USA). Interventricular septal thickness, LV end-diastolic diameter, LV posterior wall thickness, and the left atrial diameter were assessed by 2D measurements in the parasternal long axis view. Left ventricular volumes, the ejection fraction, and the left atrial volume were measured in the apical four chamber view using biplane Simpson's method. Trans-mitral flow and tissue velocities on the mitral and tricuspidal annulus were recorded using a pulsed-wave Doppler. The function of the right ventricle was evaluated using a tricuspid annular plane systolic excursion (TAPSE), right ventricular fractional area change (FAC), and right ventricular free wall strain. The right atrial area was measured in the apical four chamber view, and dimensions of the inferior vena cava were measured using the subxiphoid view. All measurements were performed in accordance with current recommendations. [15]

Statistical analysis

The data acquired was statistically analysed using the software Statistica, ver. 12 (StatSoft, Inc., Tulsa, USA). The Shapiro-Wilk test was used to evaluate the normal distribution of continuous variables. The continuous variables were expressed as medians with interquartile range (IQR). The categorical variables were expressed as a quantity and percentages. Non-parametrical statistical methods were used to evaluate the differences between the groups (U test, F test, Kruskal-Wallis test, Spearman's correlation coefficient). A P-value of < 0.05 was considered as statistically significant.

RESULTS

Subjects' characteristics

The baseline clinical and demographical characteristics of the study groups are summarised in Table 1. Overall, 27 patients (13 males; age range 41 – 85 years) completed the study. Both the PH group and the LV-HF group finally consisted of 10 subjects, and there were 7 patients in the Control group. Four more patients had to be excluded from the study. One patient did not meet the hemodynamic inclusion criteria, despite the previously known diagnosis of precapillary PH. In one patient the SR restoration during the CA was not successful. In two patients, various technical problems occurred during the hemodynamic assessment leading to the failure of relevant measurements.

In the PH group, there were 6 patients with idiopathic PAH, one patient with PAH associated with connective tissue disease, 2 patients with inoperable CTEPH, and one patient had residual PH after the pulmonary endarterectomy. The LV-HF group contained 1 patient with heart failure with reduced ejection fraction, 3 patients with heart failure with mildly reduced ejection fraction, and 6 patients with preserved ejection fraction. As we can see in Table 1, patients in the Control group were significantly younger and their NT-proBNP levels were lower.

The echo parameters used for the evaluation of the right ventricle systolic function were significantly decreased in the PH group (RV fractional area change ($p = 0.004$), RV free wall strain ($p = 0.01$)). There was no significant difference in other echocardiographic characteristics across the groups.

Hemodynamic measurement

Overall, in 15 patients the CA was started in the SR. 6 patients presented with the AF, and AT was the first recorded rhythm during the CA procedure in 6 patients.

The pulmonary artery and right ventricle pressures were significantly higher in the PH and LV-HF groups compared to the control group. The PH patients differed from the rest of the study population with a significantly higher transpulmonary gradient. Other resulting hemodynamical parameters were comparable, as listed in Table 1.

The magnitudes of the changes in particular hemodynamic parameters after restoration of SR are described in Table 2. Overall, the studied parameters did not vary significantly between our study groups, except the different dynamics of the RV mean pressure. In the controls and PH patients, the RV mean pressure slightly decreased in SR after arrhythmia termination. In the LV-HF group, an increase of the mean and maximal RV pressure was detected in SR. This difference reached statistical significance ($p < 0.05$), Table 2 and Figure 1

In patients with organized AT (or high frequency atrial stimulation), the CI remained the same in the arrhythmia (pacing) and in SR (CI difference -0.09 (-0.45; +0.19) $l/min/m^2$). This data contrasted with the significant rise of CI after the SR restoration in AF patients (CI difference +0.31 (+0.18; +0.58) $l/min/m^2$). The disparity between CI change in AF and AT (pacing) patients was significant ($p < 0.05$), and this reaction was uniform in each of our three groups, Figure 2.

DISCUSSION

The presence of an AF/AT affects the hemodynamical state through numerous mechanisms. SVTs generally lead to a faster heart rate, irregular ventricular contractions, and diminished contractile function of the atria resulting especially in an impaired ventricular filling. [16]

Right heart catheterization is required to confirm the diagnosis of pulmonary hypertension [3] and it should be performed under defined conditions to obtain reliable results. [5] In our clinical practice, we attempt to restore the SR before the planned right heart catheterization. However, this is not always feasible and mainly in patients with longstanding persistent or permanent AF/AT we are forced to perform the assessment during arrhythmia, which can lead to distorted results. For example, it has already been proven that the relationship between the PAWP and the left ventricular end-diastolic pressure (LVEDP) depends on the heart rhythm. In AF patients, the PAWP is higher than LVEDP. This can produce significant mistakes when distinguishing between pre-capillary and post-capillary PH. [17] Although an acute effect of cardioversion or CA is not known, hemodynamics is frequently evaluated immediately after the restoration of SR in routine clinical practice.

To be thorough, we decided to compare the data obtained for the population of interest, i.e. patients with a pre-capillary PH, not only with a Control group, but also with an added LV-HF group representing patients with a post-capillary PH, typically evaluated in cath labs. As expected, the Control group consists of younger patients with low NT-proBNP values, which documents the absence of any other heart disease except AF/AT. In each of our three groups, the median PAWP was higher than 15mmHg, which is arbitrarily set as a cut-off value for distinguishing between pre-capillary and post-capillary PH. We assume that this can be caused by the applied study protocol, when the right heart catheterization in the SR was performed at the very end of the CA procedure, which is always connected with significant intravenous fluid intake. Extensive RF lesion creation and atrial stunning after periprocedurally performed DC version, could also lead to increased PAWP. On the other hand, there is some evidence that the tendency to higher PAWP values could be typical for pre-capillary PH patients who suffer from recurrent arrhythmias. In previous works from our centre we have documented the important role of the LA substrate in arrhythmogenesis in PH patients and an increased incidence of SVTs in pre-capillary PH patients with near to elevated PAWP. [18, 19]

Both the PH and LV-HF groups fulfil the PH criteria with mPAP of 25mmHg and more. However, the high PAWP with low transpulmonary gradient value (TPG) in the LV-HF group emphasises the impact of the post-capillary component. In the Control group, the mPAP values were higher than expected, although not reaching the criteria for PH presence. With a TPG being low, this is mainly caused by an observed higher PAWP, as already discussed above.

According to our measurement, there were generally only slight differences between the hemodynamical parameters measured in the SR and arrhythmia. It is questionable how much this is caused by the short-term design of our study. It has already been proven that the real mechanical function of the atrium lags behind the actual electrical activity, and atrial stunning after the DC cardioversion is a generally known phenomena. There is data proving that the full recovery of mechanical atrial function can take up to even one month in patients with prolonged AF. [20] In other words, we assume that the hemodynamic characteristics could become more distinct if those two hemodynamical assessments were performed with a greater time interval. However, further studies are needed to prove this theory.

The hemodynamic reaction of the PH patients to the SR rhythm restoration did not differ significantly from the Control group. In the LV-HF group, the RV pressure after the SR restoration increased significantly compared to the Control and PH group. We believe that the presence of AF/AT in patients with a chronic heart failure leads to decreased pressures in the pulmonary circulation, being parallel to a decrease of the systemic arterial pressure, which is attributed mainly to the lack of atrial contraction and impaired diastolic filling of the ventricle because of the tachycardia and irregular heart rate. [21, 22] It is probable that patients in the Control group, who do not suffer from any other cardiac disease than arrhythmia, can handle the presence of arrhythmia better and maintain the values of both systemic and pulmonary pressures. The reason for the absence of a significant variation of the chronically elevated RV pressure in the PH patients is probably different. In those patients, pulmonary pressures are mainly determined by a pathological remodelling of pulmonary vessels and the presence or absence of arrhythmia is not significant enough to affect it.

The CI did not change significantly in any of our groups after the SR restoration. However, we observed a significant increase of the CI when we analysed the data of patients with AF regardless of the concrete study group. This is well in line with the currently available literature data proving the significant reduction in CI in patients with chronic AF and a heart failure. [23, 24] On the other hand, we did not observe the improvement of CI after the arrhythmia termination in patients with other AT except AF. We assume that the organized ATs do not have such a negative impact on CI, because of

the absence of several features which are usually put into context with impaired diastolic filling of the ventricle and therefore decreased CI in AF. ATs differs from AF by the more organized mechanical activity of atria leading to much more regular ventricular response. This means avoidance of excessive tachycardia with very short cycles, and probably the preservation of some atrial contribution even in running AT, at least in some patients. [16, 25] The dependence of cardiac output on heart rate can be described as an inverted U-shape. By other words, cardiac output increases to a maximum with increasing HR and then declines with further HR increase. [26] Therefore, certain "reasonable" tachycardia can play an important role in preserving cardiac output when the function of the ventricle is reduced. This is a possible explanation of the decrease in the cardiac output after the SR restoration that was observed in some patients with AT. Those findings corroborate the importance of rhythm control strategy in patients with atrial fibrillation.

An echo was performed standardly on the day after CA in order to avoid the distortion possibly caused by intravenous fluid intake during the CA and to maximize the portion of patients examined in the SR. TAPSE as a standardly used parameter for assessment of the right ventricle systolic function did not differ between our groups. However, other parameters characterising the systolic function of the RV – the FAC and the free wall strain - were significantly decreased in the PH group. Those findings corroborate the use of the RV FAC and the RV free wall strain, instead of TAPSE for monitoring PH patients. [27, 28]

The main limitations of our study are its single-centre and short-term design. The hemodynamic response to the arrhythmia termination would have become more pronounced if the second assessment had been performed in a greater time interval. Nevertheless, this would mean the necessity of performing a second invasive procedure only for the purpose of this study, which we found ethically unacceptable. Also, the continuous invasive arterial pressure monitoring during the procedure could have provided important data but was not performed in order to not further increase the risk for the patient connected with the participation in this study.

CONCLUSION

The presence of AF/AT affects the hemodynamic state of the patient. The hemodynamic response to the arrhythmia termination was not significantly different in the PH patients compared to the Control group. There was a significant increase in the RV pressure after the SR restoration in the LV-HF group. The SR restoration improved the CI in AF patients emphasizing the rhythm control strategy. In patients with organized AT, the CI did not change significantly.

ACKNOWLEDGEMENTS

Supported by Ministry of Health, Czech Republic – conceptual development of research organization *(General University Hospital in Prague – VFN, 00064165).* We would like to thank Mgr. Zachary H. K. Kendall, B.A. for the language editing.

TABLES AND FIGURES:

Table 1: Baseline study groups characteristics.

	Controls	**PH**	**LV-HF**
No. of subjects	7	10	10
Man / women	5/2	5/5	3/7
Age (years)	55 (47; 60)	72 (67; 76)	66 (60; 69)
Atrial fibrillation (total)	5 (71%)	6 (60%)	9 (90%)
- **Paroxysmal**	4 (57%)	3 (30%)	5 (50%)
- **Non-paroxysmal**	1 (14%)	3 (30%)	4 (40%)
Atrial tachycardia	3 (43%)	7 (70%)	3 (30%)
Arterial hypertension	5 (71%)	10 (100%)	8 (80%)
Diabetes mellitus	0 (0%)	4 (40%)	0 (0%)
Coronary artery disease	1 (14%)	2 (20%)	2 (20%)
CHA_2DS_2VASc	1 (1; 2)	4 (3; 5)	4 (3; 4)
NT-proBNP (pg/ml)	185 (152; 247)	883 (747; 1625) *	706 (540; 1859) *
Beta-blocker	5 (71%)	6 (60%)	9 (90%)
Amiodarone / propafenone	3 (43%)	1 (10%)	6 (60%)
CA in sinus rhythm	4 (57%)	6 (60%)	5 (50%)
DC cardioversion during CA	3 (43%)	8 (80%)	4 (40%)
Hemodynamic parameters (sinus rhythm)			
Systolic blood pres. (mmHg)	110 (96; 133)	130 (127; 147)	134 (105; 141)
Diastolic blood pres. (mmHg)	68 (60; 82)	67 (60; 76)	72 (61; 78)
Right atrium mean pres. (mmHg)	12 (7; 18)	20 (17; 23)	21 (15; 24)
Right ventricle mean pres. (mmHg)	20 (17; 24)	31 (26; 32) *	27 (25; 32) *
Pulmonary artery mean pres. (mmHg)	23 (18; 28)	39 (37; 46) *	33 (30; 38) *
Pulm. capillary wedge pres. (mmHg)	17 (12; 21)	21 (20; 23)	25 (20; 29)
Transpulmonary gradient (mmHg)	5 (3; 8)	20 (15; 24) *	8 (3; 12)
Cardiac index ($l/min/m^2$)	2,7 (2,2; 2,9)	2,3 (1,9; 2,5)	2,2 (2,1; 2,7)
Echocardiographic parameters			
Left ventricle EF (%)	61 (57; 62)	70 (64; 72)	56 (47; 62)
Left ventricle EDD (mm)	48 (46; 52)	53 (48; 55)	52 (47; 55)
Left atrium diameter (PLAX)	42 (38; 45)	46 (43; 48)	45 (44; 55)
LAVi (ml/m^2)	47 (45; 53)	43 (32; 54)	47 (42; 70)
TAPSE (mm)	25 (20; 27)	23 (21; 25)	23 (22; 26)
Right ventricle free wall strain (%)	28 (26; 28)	15 (13; 18) *	28 (24; 33)
Right ventricle FAC (%)	53 (51; 56)	32 (28; 36) *	42 (41; 46)
Right ventricle diameter	38 (35; 40)	43 (39; 47)	38 (35; 44)
Right atrium area (cm^2)	20 (18; 23)	24 (22; 26)	21 (19; 26)

Data are expressed as N (%) or median (IQR). *$p < 0.05$.

Abbreviations: CA – catheter ablation, DC – direct current, EF – ejection fraction, EDD – end-diastolic diameter, FAC – fractional area change, LAVi - indexed left atrial volume by body surface area, pres. – pressure, TAPSE – Tricuspid annular plane systolic excursion

Table 2: Differences between arrhythmia and SR in measured pressure and cardiac index in study groups.

	Controls	PH	LV-HF
RA mean pressure (mmHg)	+2 (-1; +2)	0 (-3; +3)	+2 (0; +4)
RA max pressure (mmHg)	0 (-3; +6)	+4 (-4; +5)	+2 (-1; +6)
RA min pressure (mmHg)	-2 (-6; +2)	+1 (-4; +4)	-1 (-2; +2)
RV mean pressure (mmHg)	-2 (-3; -2)	-3 (-4; -1)	+4 (+1; +6) *
RV max pressure (mmHg)	0 (-6; +2)	+5 (+1; +9)	+4 (+3; +7) *
RV min pressure (mmHg)	+3 (-1; +3)	0 (-2; +2)	+4 (+1; +6)
PA mean pressure (mmHg)	0 (-1; +1)	0 (-2; +3)	+2 (-4; +7)
PA max pressure (mmHg)	-1 (-4; +3)	+2 (-1; +6)	+6 (0; +11)
PA min pressure (mmHg)	0 (-4; +1)	0 (-2; +3)	0 (-7; +5)
PAW mean pressure (mmHg)	-2 (-6; 0)	-1 (-2; 0)	-1 (-2; +2)
PAW max pressure (mmHg)	-2 (-11; -1)	-2 (-5; +2)	+1 (-1; +5) *
PAW min pressure (mmHg)	+2 (0; +4)	+1 (0; +2)	+3 (-2; +4)
Cardiac index (l/min/m^2)	0.14 (-0.48; +0.33)	-0.02 (-0.11; +0.19)	-0.07 (-0.41; +0.29)

Data are expressed as median (IQR). Difference means parameter in SR minus parameter in arrhythmia (i. e. positive value means increase after the sinus rhythm restoration). *$p < 0.05$.

Abbreviations: PA – pulmonary artery, PAW – pulmonary arterial wedge**,** RA – right atrium, RV – right ventricle

Figure 1: Difference in mean right ventricular pressure in arrhythmia and in sinus rhythm.

Box and whiskers show median and IQR.
Abbreviations: LV-HF – left heart failure; PH – pulmonary hypertension; RV – right ventricle; SR – sinus rhythm.

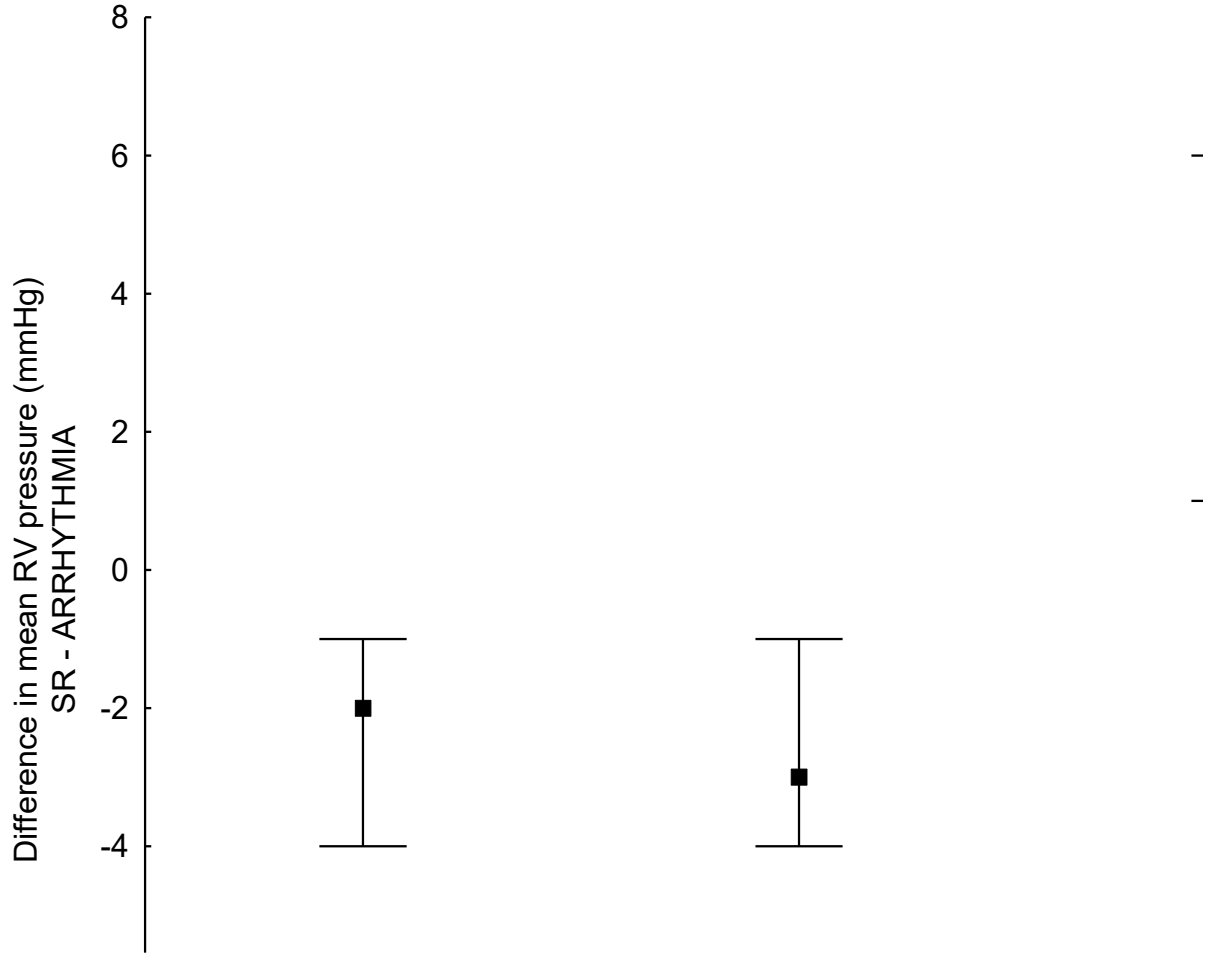
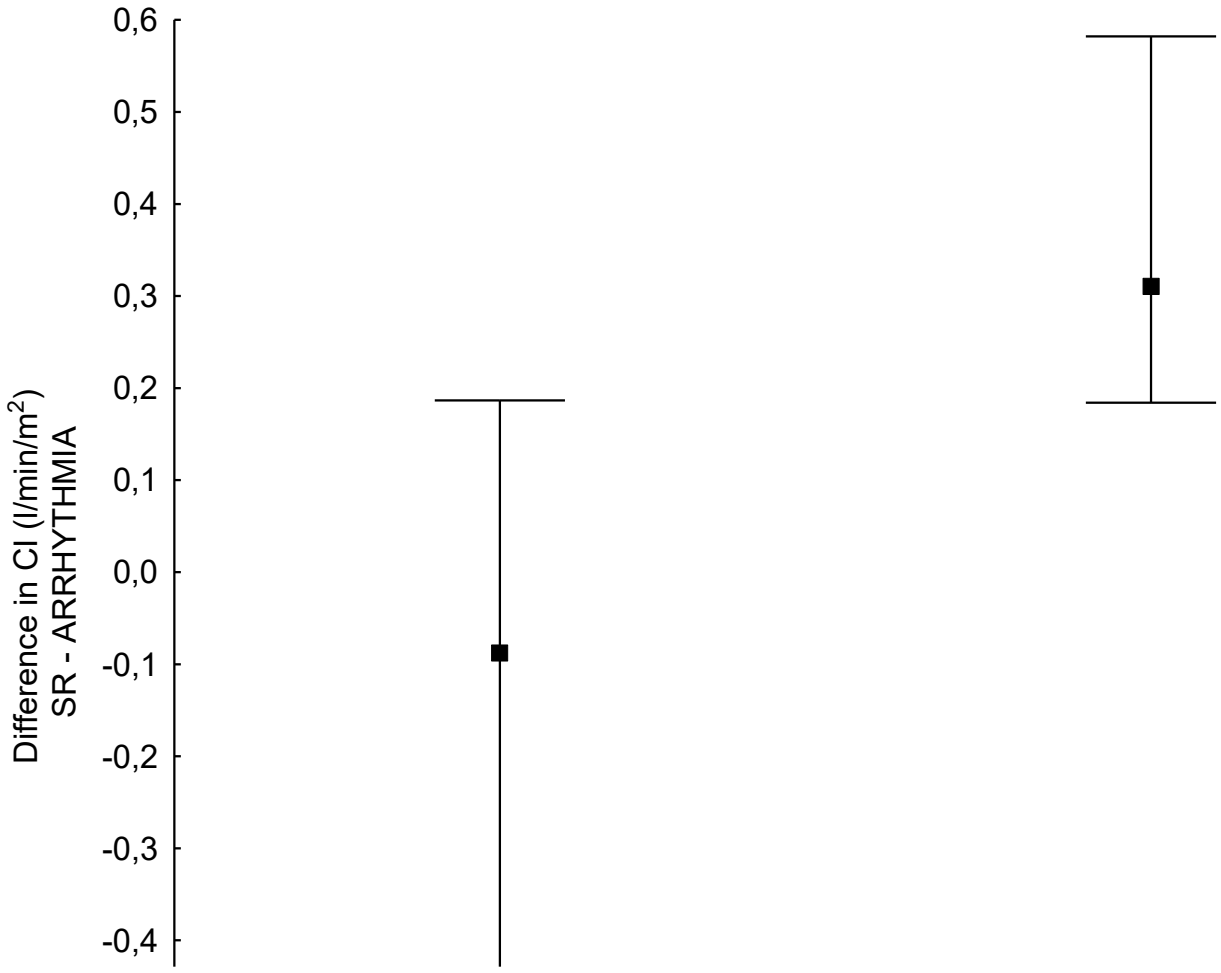


Figure 2: Difference in cardiac index between arrhythmia and sinus rhythm.

Box and whiskers show median and IQR.
Abbreviations: AF – atrial fibrillation; AT – atrial tachycardia; CI – cardiac index; SR – sinus rhythm.



References:

1. Hoeper MM, Bogaard HJ, Condliffe R, Frantz R, Khanna D, Kurzyna M, Langleben D, Manes A, Satoh T, Torres F, Wilkins MR, Badesch DB. Definitions and diagnosis of pulmonary hypertension. J Am Coll Cardiol. 2013;62:D42-50.
2. Hoeper MM, Humbert M, Souza R, Idrees M, Kawut SM, Sliwa-Hahnle K, Jing ZC, Gibbs JS. A global view of pulmonary hypertension. Lancet Respir Med. 2016;4:306-322.
3. Galie N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, Simonneau G, Peacock A, Vonk Noordegraaf A, Beghetti M, Ghofrani A, Gomez Sanchez MA, Hansmann G, Klepetko W, Lancellotti P, Matucci M, McDonagh T, Pierard LA, Trindade PT, Zompatori M, Hoeper M, Group ESCSD. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016;37:67-119.
4. Hoeper MM, Ghofrani HA, Grunig E, Klose H, Olschewski H, Rosenkranz S. Pulmonary Hypertension. Dtsch Arztebl Int. 2017;114:73-84.
5. Rosenkranz S, Preston IR. Right heart catheterisation: best practice and pitfalls in pulmonary hypertension. Eur Respir Rev. 2015;24:642-652.
6. Middleton JT, Maulik A, Lewis R, Kiely DG, Toshner M, Charalampopoulos A, Kyriacou A, Rothman A. Arrhythmic Burden and Outcomes in Pulmonary Arterial Hypertension. Front Med (Lausanne). 2019;6:169.
7. Tongers J, Schwerdtfeger B, Klein G, Kempf T, Schaefer A, Knapp JM, Niehaus M, Korte T, Hoeper MM. Incidence and clinical relevance of supraventricular tachyarrhythmias in pulmonary hypertension. Am Heart J. 2007;153:127-132.
8. Fingrova Z, Ambroz D, Jansa P, Kuchar J, Lindner J, Kunstyr J, Aschermann M, Linhart A, Havranek S. The prevalence and clinical outcome of supraventricular tachycardia in different etiologies of pulmonary hypertension. PLoS One. 2021;16:e0245752.
9. Wen L, Sun ML, An P, Jiang X, Sun K, Zheng L, Liu QQ, Wang L, Zhao QH, He J, Jing ZC. Frequency of Supraventricular Arrhythmias in Patients With Idiopathic Pulmonary Arterial Hypertension. American Journal of Cardiology. 2014;114:1420-1425.
10. Ruiz-Cano MJ, Gonzalez-Mansilla A, Escribano P, Delgado J, Arribas F, Torres J, Flox A, Riva M, Gomez MA, Saenz C. Clinical implications of supraventricular arrhythmias in patients with severe pulmonary arterial hypertension. Int J Cardiol. 2011;146:105-106.
11. Olsson KM, Nickel NP, Tongers J, Hoeper MM. Atrial flutter and fibrillation in patients with pulmonary hypertension. Int J Cardiol. 2013;167:2300-2305.
12. Rottlaender D, Motloch LJ, Schmidt D, Reda S, Larbig R, Wolny M, Dumitrescu D, Rosenkranz S, Erdmann E, Hoppe UC. Clinical impact of atrial fibrillation in patients with pulmonary hypertension. PLoS One. 2012;7:e33902.
13. Daliento L, Somerville J, Presbitero P, Menti L, Brach-Prever S, Rizzoli G, Stone S. Eisenmenger syndrome. Factors relating to deterioration and death. Eur Heart J. 1998;19:1845-1855.
14. Zhou B, Zhu YJ, Zhai ZQ, Weng SX, Ma YZ, Yu FY, Qi YJ, Jiang YZ, Gao X, Xu XQ, Jiang X, Jing ZC, Tang M. Radiofrequency Catheter Ablation of Supraventricular Tachycardia in Patients With Pulmonary Hypertension: Feasibility and Long-Term Outcome. Front Physiol. 2021;12:674909.
15. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2015;16:233-270.
16. Viswanathan K, Daniak SM, Salomone K, Kiely T, Patel U, Converso K, Manning WJ, Silverman DI. Effect of cardioversion of atrial fibrillation on improvement in left ventricular performance. Am J Cardiol. 2001;88:439-441.

17. Dickinson MG, Lam CS, Rienstra M, Vonck TE, Hummel YM, Voors AA, Hoendermis ES. Atrial fibrillation modifies the association between pulmonary artery wedge pressure and left ventricular end-diastolic pressure. Eur J Heart Fail. 2017;19:1483-1490.
18. Fingrova Z, Havranek S, Ambroz D, Jansa P, Linhart A. The left atrial substrate plays a significant role in the development of complex atrial tachycardia in patients with precapillary pulmonary hypertension. BMC Cardiovasc Disord. 2019;19:157.
19. Dusik M, Fingrova Z, Ambroz D, Jansa P, Linhart A, Havranek S. The Role of Pulmonary Artery Wedge Pressure on the Incidence of Atrial Fibrillation and Atrial Tachycardias in Patients With Isolated Pre-capillary Pulmonary Hypertension. Physiol Res. 2021;70:841-849.
20. Manning WJ, Silverman DI, Katz SE, Riley MF, Come PC, Doherty RM, Munson JT, Douglas PS. Impaired left atrial mechanical function after cardioversion: relation to the duration of atrial fibrillation. J Am Coll Cardiol. 1994;23:1535-1540.
21. Samet P, Bernstein W, Levine S. Significance of the Atrial Contribution to Ventricular Filling. Am J Cardiol. 1965;15:195-202.
22. Carlisle MA, Fudim M, DeVore AD, Piccini JP. Heart Failure and Atrial Fibrillation, Like Fire and Fury. JACC Heart Fail. 2019;7:447-456.
23. Pozzoli M, Cioffi G, Traversi E, Pinna GD, Cobelli F, Tavazzi L. Predictors of primary atrial fibrillation and concomitant clinical and hemodynamic changes in patients with chronic heart failure: a prospective study in 344 patients with baseline sinus rhythm. J Am Coll Cardiol. 1998;32:197-204.
24. Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. Am J Cardiol. 2003;91:2D-8D.
25. Raymond RJ, Lee AJ, Messineo FC, Manning WJ, Silverman DI. Cardiac performance early after cardioversion from atrial fibrillation. Am Heart J. 1998;136:435-442.
26. Sugimoto T, Sagawa K, Guyton AC. Effect of tachycardia on cardiac output during normal and increased venous return. Am J Physiol. 1966;211:288-292.
27. Puwanant S, Park M, Popovic ZB, Tang WH, Farha S, George D, Sharp J, Puntawangkoon J, Loyd JE, Erzurum SC, Thomas JD. Ventricular geometry, strain, and rotational mechanics in pulmonary hypertension. Circulation. 2010;121:259-266.
28. van Kessel M, Seaton D, Chan J, Yamada A, Kermeen F, Hamilton-Craig C, Butler T, Sabapathy S, Morris N. Prognostic value of right ventricular free wall strain in pulmonary hypertension patients with pseudo-normalized tricuspid annular plane systolic excursion values. Int J Cardiovasc Imaging. 2016;32:905-912.