

Clinical significance of dynamic pulmonary vascular resistance in two populations at risk of pulmonary arterial hypertension

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Aims

Patients at risk of pulmonary arterial hypertension (PAH) may present with abnormal dynamic pulmonary vascular resistance (PVR) during exercise. However, its clinical significance remains unclear. The present study aimed at analysing the meaning of dynamic PVR in two populations at risk of PAH: secundum atrial septal defect (ASD) and systemic sclerosis (SSc).

Methods and results

Adult patients with corrected ASD were consecutively selected from the database of Pediatric and Congenital Heart Disease of the University Hospitals Leuven. Patients with SSc were consecutively selected from the rheumatology database of the University Hospital Liège. At inclusion, all underwent a rest and bicycle stress echocardiography to obtain baseline right heart characteristics and dynamic PVR. Routine follow-up echocardiography was performed. Twenty-eight patients with corrected ASD (mean age 41 ± 17 years, 79% female) were followed for a median time of 3.7 [inter-quartile range (IQR) 2.9–4.1] years. No patient developed PAH. Dynamic PVR was significantly associated with right atrial dilatation at latest follow-up (Spearman's ρ 0.51, $P = 0.013$). Forty-five SSc patients (mean age 54 ± 13 years, 76% female) were followed for a median time of 2.4 (IQR 0.8–2.9) years. Thirteen patients (30%) developed PAH. Dynamic PVR was the only independent predictor of PAH (hazards ratio 1.22, 95% confidence interval 1.01–1.47). No significant right heart morphometric changes occurred.

Conclusion

Dynamic PVR predicted PAH development in patients with SSc, whereas dynamic PVR was associated with right heart morphometric changes after ASD closure. The predictive role of dynamic PVR might depend on the underlying disease type. Larger studies are needed to confirm this hypothesis.

Keywords

atrial septal defect • systemic sclerosis • pulmonary vascular disease • stress echocardiography

Introduction

Pulmonary arterial hypertension (PAH), characterized by a progressive increase in pulmonary vascular resistance (PVR), is associated with considerable morbidity and mortality.¹ Unfortunately, PAH is usually detected when patients develop symptoms and pulmonary vascular disease (PVD) has already evolved to an advanced (irreversible) stage.^{2,3} Hence, treatment is often initiated too late, and results

are unsatisfactory. Therefore, developing an early detection method for mild PVD is crucially important.

In the last years, many studies have demonstrated an abnormal increase in pulmonary artery pressure (PAP) and/or PVR during exercise testing in different populations at risk of PAH development.^{4–12} This so-called exercise-induced PAH has been associated with decreased oxygen uptake during exercise and impaired exercise capacity.^{13–15} It has been suggested that the slope of a PAP-flow

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plot, defining dynamic PVR, provides a better representation of PVR.¹⁶ However, the clinical significance of dynamic PVR remains unclear. Does a high-dynamic PVR represent a stable self-contained entity or could it equal an early stage in the 'disease spectrum of PAH'?^{14,15,17}

The aetiology of PVD is very diverse and explains why the pace of disease progression might differ substantially between several types of PVD. Idiopathic PVD and PVD associated with connective tissue disease usually evolve fast, whereas PVD secondary to shunt-related congenital heart disease (CHD) is mostly avoided in case of early closure of septal defects in childhood.^{1,18,19} However, after paediatric age, there is no evidence that closure of septal defects can prevent PVD progression, and prognosis may even be worsened by late closure.²⁰ This different pace of PVD progression might lead to a different predictive role of dynamic PVR.

This study aimed at determining the significance of dynamic PVR in two populations at risk of developing PAH: patients with secundum atrial septal defect (ASD), mostly closed later in life, and patients with systemic sclerosis (SSc).

Methods

Patient selection

Patients with secundum ASD closure were consecutively selected from the database of Pediatric and Congenital Heart Disease of the University Hospitals Leuven from March to November 2009. Minimum age at inclusion was 18 years, and patients had to be able to perform a bicycle stress test. Patients with associated complex diseases (coronary artery disease, significant valvular diseases other than mild tricuspid or mitral regurgitation, pulmonary disease, history of pulmonary embolism, concomitant CHD) were excluded. Patients with a history of arrhythmias or current arrhythmias were also excluded because of practical and safety reasons. Similarly, patients with SSc were consecutively selected from the rheumatology database of the University Hospital of Liège from January 2008 to November 2012.²¹ All patients signed informed consent, after the University Hospitals Institutional Review Boards approved the study protocol.

Rest and bicycle stress echocardiography

At inclusion, all patients underwent complete transthoracic echocardiographic exam at rest in the supine position, followed by bicycle stress echocardiography in semi-supine position. For the ASD group, a Vivid 7 or 9 ultrasound system (General Electric Vingmed Ultrasound, Horten, Norway), for the SSc group a Vivid 9 ultrasound system (General Electric Healthcare, Little Chalfont, UK), was used. Methodological details and baseline characteristics have already been published.^{6,21} Bicycle stress echocardiography was performed in a semi-supine position, with the exercise table tilted 20–30° to the left. Patients started at an initial workload of 25 W, which was increased by 25 W every 2 min, until the maximal tolerated workload. A 12-lead ECG and blood pressure were recorded at rest and at every 2 min during exercise. Analyses were performed by a single observer using customized software (Echopac). All measurements were calculated in triplicate and presented as means. Measurements were performed and analysed according to the 2006 guidelines on chamber quantification.²²

Basic echocardiogram mainly focused on right heart geometry [right atrial (RA) diameter, right ventricular (RV) diameter, grade of tricuspid valve regurgitation (TR)] and tricuspid regurgitation velocity (TRV), from which the pressure difference between RV and RA was calculated using the simplified Bernoulli equation. Adding RA pressure (RAP)

resulted in the estimate of systolic PAP (sPAP). RAP was calculated from diameter and breath-induced variability of inferior vena cava (IVC). For all patients, due to normal IVC diameter and decrease in IVC diameter >50% after deep inspiration, RAP was estimated at 5 mmHg at rest and at 10 mmHg at peak exercise, similar to the methodology of other studies.^{13,17,23–25}

Total PVR was calculated as the ratio of sPAP and left ventricular cardiac output (flow, calculated from the velocity time integral in the left ventricular outflow tract), at rest and at peak exercise. The slope of the sPAP-flow plot was obtained and determined as dynamic PVR, using linear regression analysis with two measurement points (rest and peak exercise). Dynamic PVR thus represents change in sPAP per unit change in cardiac output from rest to peak exercise.

RA and RV dilatation was graded normal (0/3), mild (1/3), moderate (2/3) or severe (3/3), based on measurements in apical four-chamber view (RA: long-axis diameter and area at end-systole; RV: short-axis diameter at the mid-ventricular level and area at end-diastole).²² TR was graded semi-quantitatively using colour Doppler echocardiography (x/4).²⁶

Follow-up

All patients were followed systematically. Rest transthoracic echocardiogram at latest follow-up was considered the study endpoint, with focus on right heart geometry and the presence of PAH. RA and RV change were graded (0 = no increase in dilatation grade, 1 = increase in dilatation of 1 grade, 2 = increase in dilatation of 2 grades). TR change was defined similarly based on the increase in regurgitation grade. PAH at rest was diagnosed when estimated sPAP ≥ 37 mmHg (TRV ≥ 2.9 m/s + RAP 5 mmHg), following ESC/ERS guidelines on pulmonary hypertension.¹

Statistical analysis

Statistical analyses were performed using the software program SPSS (version 22.0, Chicago, IL, USA). For continuous variables, data are reported as means \pm standard deviation, or as medians [inter-quartile range (IQR)] if the assumption of normal distribution was not valid. Levene's test was performed to assess for equal variances. Discrete variables are presented as frequencies and/or proportions. Comparison of two means was done by two-tailed Student's *t*-test. Analysis of paired data was done by two-tailed paired Student's *t*-test or by related-samples Wilcoxon signed-rank test, when normality was not assumed. Comparison of several means was done by one-way analysis of variance. Pearson's correlation coefficient and Spearman's rank correlation coefficient were calculated to estimate the correlation between dynamic PVR and PAP or right heart morphometry, respectively. Univariate and multivariate Cox-regression analysis was performed to identify predictors of PAH development. Only those factors that are significant predictors in univariate analysis will be included in multivariate analysis. In case of strong collinearity ($r > 0.5$), only one of the collinear variables was retained for multivariate analysis. All tests were two sided, and a *P*-value of < 0.05 was considered statistically significant.

Results

Patient baseline characteristics

Twenty-eight patients with corrected ASD (mean age at inclusion 41 ± 17 years, 79% female patients) were selected and followed for a median time of 3.7 (IQR 2.9–4.1) years. Forty-five patients with SSc (mean age at inclusion 54 ± 13 years, 76% female patients) were selected and followed for a median time of 2.4 (IQR 0.8–2.9) years. Patient baseline characteristics are summarized in Table 1. None of the patients died during follow-up.

Dynamic PVR in patients with corrected ASD: associated morphometric changes of the right heart

Mean dynamic PVR was 5.6 ± 2.4 mmHg/L/min. No patient developed PAH during follow-up. RA diameter and TR severity evolved significantly during follow-up (Table 2).

Dynamic PVR was only associated with greater RA dilatation grade at latest follow-up, and a trend towards association with RA change over time was noted (Table 3). RA dilated significantly more during follow-up in patients with higher dynamic PVR at inclusion (mean dynamic PVR 5.2 ± 2.1 vs. 6.8 ± 2.7 vs. 10.8 mmHg/L/min, $P = 0.047$) (Figure 1).

Dynamic PVR in patients with SSc: predictor of PAH

Mean dynamic PVR was 7.3 ± 4.2 mmHg/L/min. Thirteen patients (30%) developed PAH during follow-up. No morphometric changes of the right heart were noted.

Dynamic PVR, age at latest follow-up, sPAP at rest and sPAP and total PVR at peak exercise were significantly associated with PAH development (Table 4). Patients with higher dynamic PVR (steeper slopes) and a higher sPAP at rest developed PAH. Because bivariate correlation analysis showed a strong correlation between dynamic

Table 1 Patient baseline characteristics

	Corrected ASD (n = 28)	SSc (n = 45)
Age at inclusion (years)	41 ± 17	54 ± 13
Age at SSc diagnosis (years)		49 ± 15
Age at ASD closure (years)	34 ± 20	
ASD defect size (mm)	17 ± 5	
Shunt ratio prior to ASD closure (Qp : Qs) ^a	1.9 (1.5–2.5)	
sPAP prior to ASD closure (mmHg) ^a	26 ± 8	
Gender (male : female)	6 : 22	11 : 34
BMI (kg/m ²)	26 ± 5	24 ± 5
SBP rest (mmHg)	119 ± 16	131 ± 22
DBP rest (mmHg)	71 ± 11	75 ± 11
HR rest (bpm)	63 ± 10	73 ± 13
RA dilatation (x/3)	0 (0–0)	0 (0–0)
RV dilatation (x/3)	0 (0–1)	0 (0–0)
TR (x/4)	1 (0–1.5)	1 (0–1)
sPAP rest (mmHg)	27 ± 6	25 ± 7
Total PVR rest (mmHg/L/min)	6.3 ± 1.7	6.9 ± 2.4
Total PVR peak exercise (mmHg/L/min)	5.8 ± 1.6	6.5 ± 2.5

Continuous variables are presented as mean ± standard deviation, discrete variables as ratio or as median (inter-quartile range).

ASD, atrial septal defect; SSc, systemic sclerosis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RA, right atrium; RV, right ventricle; TR, tricuspid regurgitation; sPAP, systolic pulmonary artery pressure; PVR, pulmonary vascular resistance.

^aInvasive measurement.

Table 2 Changes in echocardiographic variables of the corrected ASD group

	Baseline	Latest follow-up	P-value
RA diameter (mm)	45 ± 5	48 ± 6	0.013
RA dilatation (x/3)	0 (0–0)	0 (0–1)	0.058
RV dilatation (x/3)	0 (0–1)	0 (0–1)	0.317
TR (x/4)	1 (0–1.5)	1 (1–2)	0.005
sPAP rest (mmHg)	27 ± 6	28 ± 7	0.427

Continuous variables are presented as mean ± standard deviation, discrete variables as median (inter-quartile range).

For abbreviations, see Table 1.

Significant P-values ($P < 0.05$) are indicated in bold.

Table 3 Bivariate correlation analysis with dynamic PVR in the corrected ASD group

	Spearman's correlation coefficient	P-value
RA dilatation at latest FU (x/3)	0.509	0.013
RA change during FU (Δ x/3)	0.386	0.069
RV dilatation at latest FU (x/3)	−0.100	0.658
RV change during FU ^a		
TR severity at latest FU (x/4)	−0.067	0.761
TR change during FU (Δ x/4)	−0.084	0.702
sPAP rest at latest FU (mmHg)	0.145 ^b	0.553

FU, follow-up. For the remaining abbreviations, see Table 1.

^aRV dilatation did not change over time.

^bPearson's correlation coefficient.

Significant P-values ($P < 0.05$) are indicated in bold.

PVR and sPAP at peak exercise (Pearson's correlation coefficient 0.595, $P = 0.001$) and between dynamic PVR and total PVR at peak exercise (Pearson's correlation coefficient 0.862, $P < 0.001$), sPAP and total PVR at peak exercise were excluded from the multivariate model. Multivariate Cox-regression analysis showed that dynamic PVR was the only independent predictor of PAH (Table 4). Mean dynamic PVR in the PAH group was significantly higher than in the non-PAH group (11.0 vs. 5.8 mmHg/L/min, $P = 0.002$).

Comparison between both populations

Patients with SSc and corrected ASD were divided based upon the development of PAH or RA change over time, respectively (Figure 2). Whereas mean dynamic PVR differed significantly in the PAH vs. non-PAH group of SSc patients ($P = 0.002$) and in the group of corrected ASD patients with vs. without RA change (7.6 vs. 5.1 mmHg/L/min, $P = 0.042$), there was no significant difference in mean dynamic PVR of SSc patients with PAH vs. corrected ASD patients with RA change ($P = 0.144$). Likewise, mean dynamic PVR of SSc patients without PAH vs. corrected ASD patients without RA change did not differ significantly ($P = 0.487$). This is visually represented in Figure 3.

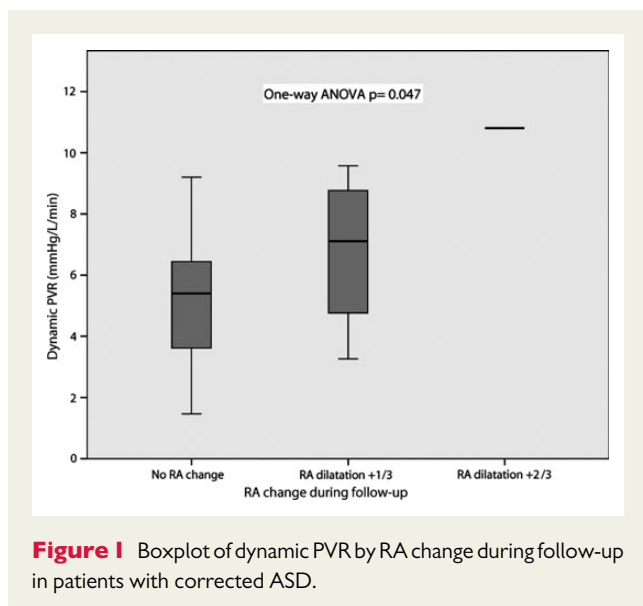


Figure 1 Boxplot of dynamic PVR by RA change during follow-up in patients with corrected ASD.

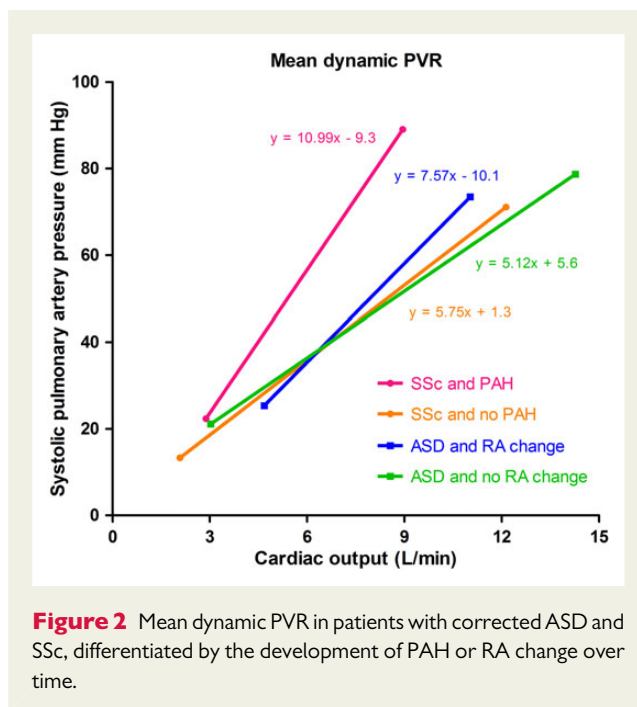


Figure 2 Mean dynamic PVR in patients with corrected ASD and SSc, differentiated by the development of PAH or RA change over time.

Table 4 Cox regression analysis for PAH in patients with SSc

	Hazard ratio	95% CI	P-value
Univariate analysis			
Dynamic PVR	1.23	1.04–1.45	0.015
Age at latest FU	1.06	1.02–1.10	0.007
sPAP rest	1.15	1.07–1.24	<0.001
sPAP peak exercise	1.13	1.07–1.20	<0.001
Total PVR rest	1.25	0.99–1.56	0.054
Total PVR peak exercise	1.67	1.15–2.41	0.006
Gender	2.41	0.53–11.03	0.256
BMI	1.03	0.93–1.14	0.616
SBP rest	1.02	0.99–1.05	0.342
DBP rest	1.01	0.94–1.08	0.842
HR rest	1.01	0.97–1.06	0.587
Multivariate analysis			
Dynamic PVR	1.22	1.01–1.47	0.038
Age at latest FU	1.00	0.95–1.06	0.933
sPAP rest	1.15	0.98–1.35	0.083

All variables refer to baseline measurements, unless otherwise specified. PAH, pulmonary arterial hypertension; SSc, systemic sclerosis; CI, confidence interval; PVR, pulmonary vascular resistance; FU, follow-up; sPAP, systolic pulmonary artery pressure; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate

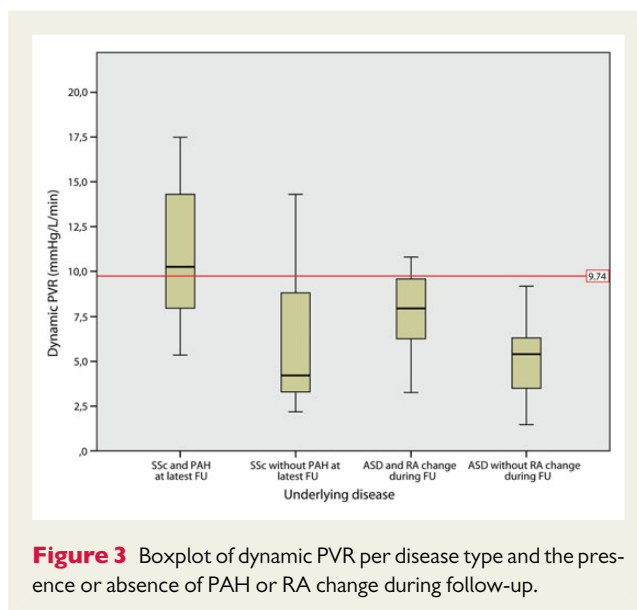


Figure 3 Boxplot of dynamic PVR per disease type and the presence or absence of PAH or RA change during follow-up.

Dynamic PVR in the combined group of corrected ASD and SSc

Dynamic PVR in the combined group of corrected ASD and SSc remained an independent predictor of PAH in multivariate analysis (Table 5). Based on ROC curve analysis (AUC 0.856), a cut-off value for dynamic PVR at 9.74 mmHg/L/min was determined as predictor for PAH development, with sensitivity and specificity of 63 and

93%, positive and negative predictive value of 0.67 and 0.92, respectively (Figure 3). Positive and negative likelihood ratios were 9.33 and 0.40. This cut-off value was validated in the subgroup of SSc patients (AUC 0.837, cut-off value of 9.65 mmHg/L/min, sensitivity 62%, and specificity 90%).

Discussion

This study showed an association between dynamic PVR and PAH development in patients with SSc, whereas dynamic PVR in corrected ASD patients was associated with right heart morphometric changes.

Table 5 Cox regression analysis for PAH in the combined group of corrected ASD and SSc

	Hazard ratio	95% CI	P-value
Univariate analysis			
Dynamic PVR	1.35	1.14–1.60	0.001
Age at latest FU	1.07	1.02–1.11	0.003
Disease type	63.82	0.70–5798.61	0.071
sPAP rest	1.10	1.02–1.19	0.009
sPAP peak exercise	1.06	1.02–1.11	0.004
Total PVR rest	1.36	1.08–1.70	0.009
Total PVR peak exercise	2.03	1.39–2.97	<0.001
Gender	2.09	0.46–9.47	0.339
BMI	0.99	0.89–1.10	0.804
SBP rest	1.04	1.01–1.07	0.015
DBP rest	1.03	0.97–1.10	0.324
HR rest	1.05	1.00–1.09	0.034
Multivariate analysis			
Dynamic PVR	1.44	1.01–2.05	0.045
Age at latest FU	1.02	0.91–1.14	0.768
sPAP rest	1.00	0.85–1.18	0.980
SBP rest	1.02	0.96–1.08	0.583
HR rest	1.09	0.95–1.25	0.237

All variables refer to baseline measurements, unless otherwise specified. ASD, atrial septal defect. For the remaining abbreviations, see Table 4.

The choice for dynamic PVR in the prediction model

Right heart catheterization is the gold standard for PAH diagnosis. However, non-invasive assessment techniques such as stress echocardiography and cardiac magnetic resonance imaging are evolving as useful tools for early PAH detection.^{8,27} Although the sensitivity of transthoracic echocardiography at rest for early PAH diagnosis is rather limited, stress echocardiography could be more promising to predict PAH development through detection of mild PVD. In addition, exercise capacity correlates with outcome in patients with moderate to severe PAH.²⁸

Our research group already developed a standardized technique for the detection of mild PVD by bicycle stress echocardiography (by measuring dynamic PVR) in patients with ASD and normal PAP at rest.⁶ Some studies were able to show that PAP measurements during rest and stress echocardiography correlated sufficiently well with haemodynamic invasive measurements.^{7,17,29,30}

Therefore, we focused more on dynamic PVR in our study. We believe that dynamic PVR may better represent PVD than total PVR at peak exercise.¹¹ Dynamic PVR integrates more information about patient haemodynamics (sPAP and cardiac output throughout the entire exercise). Moreover, PVR at peak exercise is flow dependent, whereas dynamic PVR is not.¹⁶ Furthermore, it is difficult to measure sPAP at peak exercise instead of immediately after because of the rapid decline during recovery.³¹ Dynamic PVR will be less influenced by delayed measurement. In addition, in a recently published

study of patients with SSc, sPAP at peak exercise was not predictive of PAH development.²⁴

Dynamic PVR: association with PAH and right heart morphometric changes

In patients with corrected ASD, dynamic PVR was significantly associated with RA dilatation at latest follow-up. Long-standing volume overload of RV and pulmonary circulation in patients with secundum ASD causes PVD in the long run.³² After late ASD closure, mild PVD may even persist. We hypothesized that mild PVD, identified by high-dynamic PVR, related to morphometric changes of the right heart. We showed earlier that high PVR during exercise is related to persistent TR after ASD closure.³³ The present data fit with the morphometric hypothesis. However, a longer follow-up time could have showed greater morphometric changes and maybe PAH development.³⁴ No ASD patients developed PAH during follow-up. However, high-dynamic PVR could be an early sign of PAH development, before evident RV remodelling has taken place and symptoms occur. Moreover, by excluding patients with a history of or current arrhythmias, we might have induced a selection bias. The risk of arrhythmia is indeed increased in patients with late ASD closure, and this subgroup of ASD patients could be at greater risk of PVD and PAH.

In contrast, no morphometric changes could be detected in SSc patients, but PAH developed in 30%. This could be explained by the rapid PAH development in SSc patients, probably before right heart morphometric changes are observed.¹⁹ Dynamic PVR was identified as an independent predictor of PAH development. Recent studies in patients with SSc without clinically suspected PAH or elevated PAP at rest analogously showed that an inappropriate PAP increase during exercise was related to PAH development.^{10,24}

Interestingly, Figure 2 showed that mean dynamic PVR in SSc patients with PAH development and in corrected ASD patients with RA change over time were within the same range. Moreover, SSc patients without PAH and corrected ASD patients without RA change during follow-up also presented similar mean dynamic PVR. This suggests a different predictive value for dynamic PVR depending on the underlying disease type. However, our data suggest that a more severe underlying predisposing risk factor for PAH development (connective tissue disease vs. shunt-related CHD) *per se* is not enough to develop PAH, but that a certain degree of PVD, represented by a steeper dynamic PVR slope, is needed.

Future challenges

Dynamic PVR aetiology can be considered multicausal, including demographic variables (age, obesity, and physical health status), genetic predisposition (gender), and environmental factors (pulmonary vascular overload and vasoconstriction, left ventricular dysfunction, and pulmonary vascular distensibility).^{8,9,16,23,32,35–40} Therefore, clear threshold values for exercise-induced PAP and dynamic PVR for the prediction of PAH development are needed. The next step would be the treatment of pathologically high dynamic PVR to prevent PAH development and its (morphometric related) complications.⁴¹

Limitations

We simplified the way of slope calculation, which was based on two measurement points (rest and peak exercise), to enable an equal

slope calculation in both populations. More measurement points per patient, as methodologically examined earlier by our research group,⁶ probably gives a more precise estimation of dynamic PVR. However, multipoint sPAP-flow plots were well described by a linear or slightly curvilinear approximation in earlier studies.^{16,31,42} In addition, there was a strong linear correlation between the slopes of the corrected ASD group, measured with 2 vs. 5 measurement points per patient (slope-2-points = $1.26 \times$ slope-5-points + 0.4; $P < 0.001$). Furthermore, echocardiographic measurements were not confirmed by right heart catheterization. Therefore, it is not excluded that some patients had combined precapillary and post-capillary pulmonary hypertension. Moreover, analyses were limited by the relatively small sample size, possibly resulting in a lack of power. Lastly, no control group was implemented because of the difficulty to match with both patients with corrected ASD and SSc (lack of homogeneity). For the corrected ASD group, data of a control group are available.⁶

Conclusions

Dynamic PVR was identified as an important predictor for PAH development in patients with SSc, whereas dynamic PVR was associated with morphometric changes of the right heart in patients after secundum ASD closure. Dynamic PVR might have a different predictive value depending on the underlying disease type or as a result of a different pace of disease progression in patients with SSc opposed to corrected ASD. Larger studies are needed to confirm these findings and to clearly define a diagnostic and prognostic relevant cut-off of dynamic PVR.

Conflict of interest: None declared

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IMAGE FOCUS

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Three-dimensional echocardiography guidance in case of papillary fibroelastoma complicating transaortic valve implantation

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A 77-year-old man with severe aortic stenosis presented for transcatheter aortic valve replacement (TAVR). His clinical history was significant for severe chronic obstructive lung disease (COPD) and prior treatment of lung cancer with surgery and chest radiation. Given his co-morbidities and frailty, he was classified as prohibitive risk for surgical aortic valve replacement. Given the anaesthesia risks in the setting of COPD, the plan was for a transesophageal echocardiogram (TEE) prior to implantation in the cardiac catheterization laboratory.

On initial pre-procedure TEE images, a large mobile echodensity was noted near the aortic valve, with a stalk at the base of the non-coronary cusp (Panel A, Supplementary data online, Videos S1 and S2), the appearance most consistent with a fibroelastoma.

The decision was made to proceed with TAVR implantation, using 3-dimensional TEE guidance to avoid excessive manipulation in the aortic root so there would be minimal disruption to the fibroelastoma. Under 3D TEE guidance, the wire was visualized as it was advanced through the aortic valve (Panel B, Supplementary data online, Video S3). A Medtronic 31 mm CoreValve (Minneapolis, MN, USA) was maneuvered into position and deployed with the valve 'waist' at the level of the fibroelastoma, essentially trapping the fibroelastoma in the non-coronary cusp (Panel C, Supplementary data online, Video S4). It could be visualized with minimal mobility after TAVR implantation. Minimal paravalvular regurgitation was noted (Panel D). The patient was uneventfully discharged 6 days later. This case illustrates the use of real-time 3-dimensional TEE to aid in a complex cardiac catheterization procedure treating both severe aortic stenosis and a fibroelastoma in a patient who was not a surgical candidate.

Supplementary data are available at *European Heart Journal – Cardiovascular Imaging* online.

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