ORIGINAL RESEARCH

Predictors of low exercise cardiac output in patients with severe pulmonic regurgitation

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ABSTRACT

Background and objectives Chronic pulmonic regurgitation (PR) following repair of congenital heart disease (CHD) impairs right ventricular function that impacts peak exercise cardiac index (pCI). We aimed to estimate in a non-invasive way pCI and peak oxygen consumption (pVO_2) and to evaluate predictors of low pCI in patients with significant residual pulmonic regurgitation after CHD repair.

Method We included 82 patients (median age 19 years (range 10–54 years)) with residual pulmonic regurgitation fraction >40%. All underwent cardiac MRI and cardiopulmonary testing with measurement of pCI by thoracic impedancemetry. Low pCI was defined <7 L/min/m^2.

Results Low pCI was found in 18/82 patients. Peak indexed stroke volume (pSVi) tended to compensate chronotropic insufficiency only in patients with normal pCI (r=−0.31, p=0.01). Below 20 years of age, only 5/45 patients had low pCI but near-normal (≥6.5 L/min/m^2). pVO_2 (mL/kg/min) was correlated with pCI (r=0.58, p=0.0002) only in patients aged >20 years. Left ventricular stroke volume in MRI correlated with pSVi only in the group of patients with low pCI (r=0.54, p=0.02). No MRI measurements predicted low pCI. In multivariable analysis, only age predicted a low pCI (OR=1.082, 95% CI 1.035 to 1.131, p=0.001) with continuous increase of risk with age.

Conclusions In patients with severe PR, pVO_2 is a partial reflection of pCI. Risk of low pCI increases with age. No resting MRI measurement predicts low haemodynamic response to exercise. Probably more suitable to detect ventricular dysfunction, pCI measurement could be an additional parameter to take into account when considering pulmonic valve replacement.

INTRODUCTION

Chronic pulmonic regurgitation (PR) is one of the main complications after surgical treatment of right ventricular outflow tract obstruction, resulting in right ventricular (RV) volume overload and dysfunction.[1] This condition exposes the relevant patients to long-term adverse events such as heart failure, arrhythmias and sudden cardiac death.[1 2] In asymptomatic patients, pulmonic valve replacement (PVR) is recommended when indexed RV end-diastolic volume (EDVi) is over 160 mL/m^2 or when indexed RV end-systolic volume (ESVi) is over 80 mL/m^2, or when RV ejection fraction (EF) is decreased, as normalisation of RV volume and function is more likely if done at this stage.[3] However, this strategy is still debated because, apart from improving right ventricular volumes, data to prove the benefits of PVR on clinical outcomes are lacking. PVR is also recommended in patients with cardiovascular symptoms or with reduced exercise tolerance assessed by peak oxygen consumption (pVO_2) because they are suspected to have impaired ventricular function that limits their increase in cardiac output.[3 4] Some authors have shown that right ventricular functional reserve defined as an increase in RV EF (by stress MRI/radionucleotide imaging) may provide information on both RV function and prognosis at an earlier stage compared with resting evaluations.[4–7] In addition to that of the RV, the functional reserve of the left ventricle (LV) may also be decreased in these patients due to RV/LV interaction mechanisms and both may affect cardiac output during exercise.[7–9]

During a cardiopulmonary exercise test (CPET), cardiac output is now easily measured by the thoracic impedancemetry technique. The haemodynamic stress response can be evaluated by the difference between resting cardiac output and peak cardiac output. However, this difference is affected by physiological variations of the resting flow (emotions, blood volume and so on), whereas the peak cardiac output is a parameter for which we have already shown a high reproducibility.[10] We sought to assess cardiac output at peak exercise (as a parameter of haemodynamic response) using thoracic bioelectrical impedance in patients with isolated residual PR, to evaluate correlation with pVO_2 and to determine predictors of haemodynamic response to exercise.

METHODS

Population

We retrospectively included 82 consecutive available patients from 2016 to 2018 with isolated severe residual pulmonic regurgitation after congenital heart disease repair, who underwent CPET with cardiac output measurement and cardiac MRI within 6 months. Forty-five patients aged below 20 years were included from a paediatric centre and 37 patients aged above 20 years from an adult centre. Severe PR was defined as regurgitant fraction >40%, using MRI quantification (velocity-encoded phase contrast sequence). Patients with

significant residual right ventricular outflow tract obstruction (peak gradient >40 mm Hg and/or RV pressure >50 mm Hg) on echocardiography, patients with impaired left ventricular function for an identified reason unrelated to PR and patients with pacemaker and/or beta-blockade therapy were excluded. Moreover, patients with aortic regurgitation >grade 1 were excluded because, in the event of significant aortic regurgitation, assessed peak indexed stroke volume (pSVi) by thoracic impedancemetry is not the effective stroke volume that contributes to cardiac output.

Cardiovascular MRI

Data were acquired on local available magnetic resonance systems. Volumes indexed to body surface area (RV and LV EDVi, RV and LV ESVi, LV stroke volume (SVi), LV and RV EF and (RV EDVi)/(LV EDVi) ratio were measured from a stack of short-axis cine images. The PR fraction was calculated with velocity-encoded phase contrast sequence. Values were indexed to body surface.

Cardiopulmonary exercise test

Protocol

CPET was performed to assess the maximum exercise capacity by means of a cycle ergometer as previously described.[10] The effort was considered as maximal if the patient achieved a respiratory exchange ratio >1.1 and/or peak heart rate (pHR) >85% of predicted value (PV) and/or if oxygen uptake reached a plateau. Oxygen pulse at peak is defined as the ratio of pVO_2 to pHR and as the product of peak stroke volume and peak arteriovenous difference in oxygen content according to the Fick equation. VE/VCO_2 slope was also determined. Chronotropic insufficiency was defined as pHR <80% of PV.

Non-invasive stroke volume measurement

Cardiac output and stroke volume were tested and determined non-invasively during exercise using a thoracic bioelectrical impedance device (PhysioFlow, PF-05 Lab1, Manatec Biomedical) in our centre. This method was previously described.[11] We considered an abnormal peak cardiac index (pCI) when it was below 7 L/min/m^2, the value for the fifth percentile of healthy paediatric and adult populations previously evaluated with the same device.[11–14]

Statistical analysis

Normality of each variable was studied using the Kolmogorov-Smirnov test. Comparisons were performed using non-paired t-test or Mann-Whitney U test as appropriate. The Pearson's or Spearman's correlation coefficient was used to determine correlation between continuous or categorical variable and a continuous variable. The χ^2 test was used to compare two groups for nominal variables. The Z-test was used to compare proportions and correlations (r). Significance level was set at $p<0.05$. Explicative variables associated with low pCI with $p<0.25$ were selected to identify the independent predictors of low pCI using multivariable logistic regression analysis with the stepwise method. Correlated variables were included in the analysis if variance inflation factors (VIF) was <5 (moderate collinearity). The goodness of fit of the final model was examined using the Hosmer-Lemeshow test and the discrimination with the area under the receiver operator characteristic (ROC) curve. We modelled the evolution of the risk of low cardiac output with the variables by a logistic regression to check the log linearity of this relationship. We discretised the variable into categories and compare two models where discretised variable was coded by orthogonal polynomial contrasts of order 1 and 3 by a log likelihood ratio test. The distribution of standardised deviance residuals of the model was analysed. Patients with missing data were suppressed for each model. Statistical analysis was performed using XLSTAT (V.2019.3.2; Addinsoft).

Table 1 Characteristics of the populations

Age, years	23.9±12 (10-54, 19)
Weight, kg	57±18 (21-100, 57)
Height, cm	165±12.2 (125-190, 167)
Body surface area, m^2	1.6±0.3 (0.9–2.3, 1.6)
Gender, male (%)	51/82 (62)
Congenital heart diseases, n (%)	
Tetralogy of Fallot	67 (81.7)
Tetralogy of Fallot with pulmonary atresia	5 (6.1)
Pulmonic valve stenosis	6 (7.3)
Pulmonary atresia	3 (3.7)
Transposition of great vessels, VSD, pulmonic valve stenosis	1 (1.2)
Age at repair, years	2.0±3.7 (0–29, 0.5)
NYHA class I/II/III/IV, n	59/21/2/0
CPET	
Load, W	123±40 (51–210, 118)
Load, % of predicted load	73±20 (33–152, 75)
pVO_2, mL/kg/min	20±7.9 (13.2–48.5, 29.9)
pVO_2, % of predicted value	76±17 (43–138, 74)
pHR, min-1	164±22 (107–205, 166)
pHR % theoretical max HR	84±9 (59–105, 83)
O_2 pulse, mL	10±3 (5–19, 9)
O_2 pulse, % of predicted value	91±19 (58–151, 85)
VE/VCO_2 slope	32±6 (20–51, 31)
pSVi, mL/m^2	51±10 (30–75, 50)
pCI, L/min/m^2	8.3±2.0 (3.6–12.9, 8.3)

Data are presented as number and percentage or mean±SD (range, median).
CPET, cardiopulmonary exercise test; NYHA, New York Heart Association; pCI, peak cardiac index; pHR, peak heart rate; pSVi, peak indexed stroke volume; pVO_2, peak maximal oxygen uptake; VCO_2, carbon dioxide production; VE, minute ventilation; VSD, ventricular septal defect.

Patients and public involvement

Patients and public were not involved.

RESULTS

Population

We included 82 patients with a mean age of 23.9±12 years (range 10–54, median 19). Out of the 87 patients initially included, 5 patients were finally excluded due to a poor impedancemetry signal that did not result in a pCI value. Anthropologic data are reported in table 1. The main underlying congenital heart disease was tetralogy of Fallot. We found a negative correlation between pCI and age ($r=-0.43$; $p<0.0001$) as well as between pCI and age at repair ($r=-0.30$; $p=0.007$). Eighteen patients (22%) had low pCI. In patients below 20 years of age, 5/45 patients (11%) had low pCI but near-normal pCI and pSVi (≥6.5 L/m^2 and ≥39 mL/m^2) while 13/37 (35%) patients older than 20 years had low pCI (figure 1).

Determinants of peak cardiac index

Within the 82 patients, the 18 (22%) with low pCI had significantly lower pSVi and pHR (%PV) than others (respectively

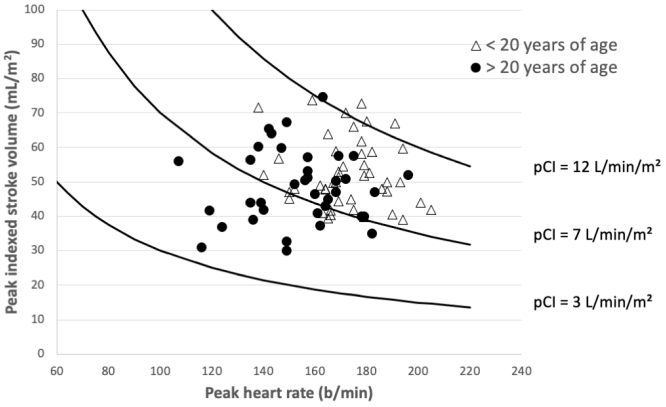

Figure 1 Determinants of pCI in patients aged <20 years and in patients aged >20 years. Isopleths (solid lines) are those calculated from equation: pCI=pSVi×pHR for various pCI values. pHR, peak heart rate; pCI, peak exercise cardiac index; pSVi, peak indexed stroke volume.

40±6 mL/m^2 vs 54±9 mL/m^2 and 79±11% vs 85.2±8.2%, p<0.0001). The influence of pSV on pCI (r^2=0.299) tended to be higher than the influence of that of pHR (%PV) (r^2=0.146) but this difference did not reach significance (p=0.07). In patients with normal pCI, pSVi was negatively correlated with pHR (r=−0.31, p=0.01), while this correlation did not reach significance in patients with low pCI (p=0.07).

Peak cardiac index in relation to CPET and symptoms

There was significant correlation between pVO2 (mL/kg/min) and pCI (r=0.44, p<0.0001) but not between pVO2 and pSVi. These respective correlations were both significant in patients older than 20 years of age (r=0.58, p=0.0002; r=0.39, p=0.02)

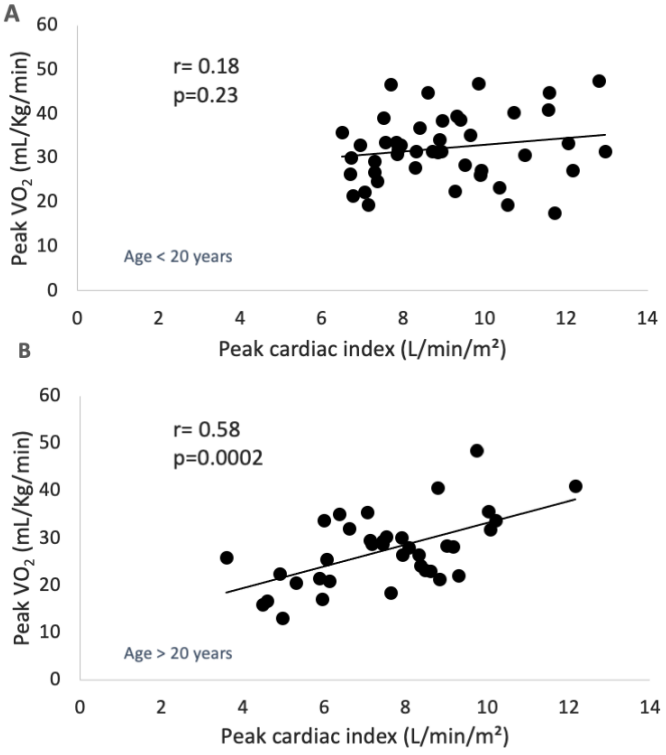

Figure 2 Relationship between pCI and pVO2 in patients aged <20 years (A) and in patients aged >20 years (B). pCI, peak exercise cardiac index; pVO_2, peak maximal oxygen uptake.

while they were not in younger patients (figure 2). In the whole population and in subgroups of age, VE/VCO_2 slope did not significantly correlate with pCI. Likewise, oxygen pulse (%PV) was not significantly correlated with pSVi. New York Heart Association class was not correlated with pCI, did not predict low pCI and was only slightly correlated with pVO2 (mL/kg/min) (r_s=−0.24, p=0.03).

Peak cardiac index in relation to cardiac MRI measurements

Apart from a significant correlation between LV SVi in MRI and pSVi (r=0.53, p=0.02) in patients with low pCI, there was no significant correlation between MRI parameters and pSVi or pCI (table 2). Within the 18 patients with low pCI, 9/18 had RV EDVi <150 mL/m² and RV ESVi <80 mL/m². Within the 64 patients with normal pCI, 28/64 had RV EDVi >150 mL/m² or RV ESVi >80 mL/m².

Prediction of low pCI by explicative variables

No MRI parameters were associated with low pCI. Age and age at repair were significantly different between patients with normal versus those with low pCI (table 3). Correlation between age and age at repair was significant r=0.54 (p<0.0001) and VIF=1.4. In the multivariable logistic regression analysis, we included the two variables age and age at repair. Only age was a significant predictor of low pCI (p=0.001) with an OR=1.082 (95% CI 1.035 to 1.131). The multivariable model showed a good fit (Hosmer-Lemeshow test; p=0.445). Discriminating ability is fair, as shown by the area under the ROC curve (0.734) (figure 3). In this model, the age of 38.5 had a positive and negative predictive value of 65% and 89%, respectively. Age was discretised into 10 years age categories to model the evolution of risk of low pCI. In both models where discretised age was coded by orthogonal polynomial contrasts of order 1 and 3, only the linear components of age were significantly associated with the risk of low cardiac output (first-order model p=0.0005; third-order model p=0.0002). Moreover, the likelihood ratio test between order 1 and 3 models was not significant (p=0.347), thus we retained the more parsimonious model (ie, the order one model) and conclude that there is no significant departure to the log-linearity relationship between age and the risk of low pCI. The distribution of standardised deviance residuals was centred around zero. The distribution of pCI according to age is shown in the figure 4.

DISCUSSION

We non-invasively assessed cardiac output at peak exercise in patients with isolated residual PR, to evaluate the correlation with pVO2 and to determine predictors of the haemodynamic response to exercise. Cardiac output response to exercise was poor in 22% of our patients with isolated PR due to either chronotropic insufficiency and/or a decrease in pSVi. During submaximal exercise, an increase in left ventricular filling (preload/starling mechanism) is predominant in regulating the left ventricular stroke volume in a normal heart.[15] At maximal effort, an increase in inotropy maintains stroke volume despite a decrease in tachycardia-dependent preload.[15] Both mechanisms, preload/starling and inotropy, are dependent on calcium pathway and sarcomere proteins and were known to be impaired in heart failure.[15] We found that weight of pSVi tended to be greater than pHR (%PV) in the explanation of pCI value. Interestingly, we observed that some of our patients with low pHR were able to maintain normal cardiac output by a compensatory increase in stroke volume as already seen in children without

Table 2 Relationship between haemodynamic response (ie, pCI and pSVi) and cardiac MRI measurements

	Total population				Patients with normal pCI				Patients with low pCI			
	pCI (L/min/m²)		pSVi (mL/m²)		pCI (L/min/m²)		pSVi (mL/m²)		pCI (L/min/m²)		pSVi (mL/m²)	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
RV EDVi, mL/m²	−0.02	(0.83)	−0.03	(0.83)	−0.01	(0.93)	−0.02	(0.86)	−0.08	(0.77)	−0.07	(0.78)
RV ESVi, mL/m²	−0.08	(0.51)	−0.06	(0.57)	−0.04	(0.73)	−0.07	(0.56)	−0.03	(0.90)	−0.14	(0.58)
RV EF, %	0.06	(0.59)	0.06	(0.59)	0.04	(0.75)	0.08	(0.53)	0.01	(0.97)	0.14	(0.57)
LV EDVi, mL/m²	0.07	(0.56)	0.02	(0.86)	0.11	(0.42)	0.01	(0.97)	0.41	(0.09)	0.35	(0.15)
LV ESVi, mL/m²	−0.07	(0.54)	−0.001	(0.99)	0.06	(0.66)	0.002	(0.97)	0.21	(0.4)	−0.06	(0.81)
LV EF, %	−0.05	(0.69)	0.07	(0.96)	0.05	(0.68)	−0.004	(0.98)	0.02	(0.95)	0.36	(0.14)
LV SVi, mL/m²	0.04	(0.74)	0.03	(0.78)	0.12	(0.38)	0.01	(0.96)	0.36	(0.14)	**0.53**	**(0.02)**
RV EDVi/LV EDVi	−0.13	(0.27)	−0.09	(0.45)	−0.07	(0.60)	−0.01	(0.92)	−0.41	(0.09)	−0.31	(0.21)

EDVi, indexed end-diastolic volume; EF, ejection fraction; ESVi, indexed end-systolic volume; LV, left ventricular; pCI, peak cardiac index; pSVi, peak indexed stroke volume; RV, right ventricular; SVi, indexed stroke volume.

residual cardiac lesions.[16] Preservation of normal pCI by an adaptation of the pSVi to a low heart rate (excluding severe chronotropic insufficiencies) could therefore characterise patients with normal biventricular function. The negative correlation between pHR and pSVi observed with pCI ≥7 L/min/m² supports this hypothesis.

In our patients, only age predicted a low cardiac output at effort. The influence of age (and thus the time during which the right ventricle is exposed to the volume overload) on haemodynamic response has been already suggested by Kipps *et al*. The authors have shown that pVO2 of patients with repaired tetralogy of Fallot tended to decrease over time more than in the healthy population and this deterioration was primarily related to a decrease in oxygen pulse, a common surrogate of pSVi.[17] Similarly, RV functional reserve (by exercise-MRI) and pVO2 in patients on average 15 years of age with tetralogy of Fallot were comparable to healthy controls while RV functional reserve (by dobutamine stress MRI) was impaired in adult patients.[6 7] Unlike what is observed in older patients, the correlation between pCI and pVO2 present in patients by 20 years of age was not observed in young patients. This should be interpreted while being mindful of the fact that older patients had poorer pCI, pHR and pSVi than patients under 20 years of age. Thus, in younger patients, the differences in pVO2 depend mainly on differences in peripheral O2 transport and/or utilisation. Although the pCI significantly correlated with pVO2 in adults, a low pVO2 does not necessarily indicate an insufficient rise in cardiac output during exercise. Several studies have shown that pVO2 can be lowered due to poor ventilatory adaptation, or significant peripheral muscle deconditioning in these patients.[16 18] The lack of correlation between oxygen pulse and pSVi and between VE/VCO_2 slope and pCI illustrates the difficulty in apprehending the haemodynamic response from standard CPET parameters.[16]

No MRI parameters have predicted a low pCI in our patients. Similarly, previous studies have shown that biventricular functional reserve (normal in children and decreased in adults) was not predicted by resting MRI parameters.[6 7] In patients with significant PR, Uebing *et al* evidenced by conductance catheter, that impaired end-systolic elastance (intrinsic load-independent myocardial contractility) was predicted by resting RV ESVi. Under dobutamine, end-systolic elastance rose, and this correlation was still present.[19] The only significant relationship that we

Table 3 Differences in explicative variables between patients with normal pCI and patients with low pCI

	Normal pCI (≥7 L/min/m²) n=64	Low pCI (<7 L/min/m²) n=18	P value
Age, years	21.2±10.3 (10–54, 17)	33.5±14 (10.4–53, 39)	<0.0001
Gender, male (%)	40 (68)	11 (61)	0.91
Congenital heart diseases, n (%)			
Tetralogy of Fallot	52 (81.2)	15 (83.3)	1
Tetralogy of Fallot with pulmonary atresia	3 (4.7)	2 (11.1)	0.65
Pulmonic valve stenosis	5 (7.8)	1 (5.6)	1
Pulmonary atresia	3 (4.7)	0	0.82
Transposition of great vessels, VSD, pulmonic valve stenosis	1 (1.6)	0	0.92
Age at repair, years	1.4±2 (0–7.2, 0.5)	4.3±6.6 (0.1–28.6)	0.003
MRI measurements			
RV EDVi, mL/m²	147±29 (99–237, 145)	149±30 (99–215, 149)	0.765
RV ESVi, mL/m²	75±18 (39–125, 73)	78±23 (46–124, 76)	0.55
RV EF, %	49±6 (38–64, 49)	48±9 (30–64, 46)	0.606
LV EDVi, mL/m²	72±12 (47–101, 71)	74±16 (41–93, 77)	0.570
LV ESVi, mL/m²	31±7 (19–47, 30)	31±10 (16–46, 32)	0.903
LV EF, %	57±5 (46–67, 57)	59±9 (42–79, 58)	0.356
LV SVi, mL/m²	41±8 (26–66, 41)	43±12 (24–71, 43)	0.543
RV EDVi/LV EDVi	2.1±0.4 (1.5–3.0, 2.0)	2.1±0.6 (1.3–4.2, 2.0)	0.742

Data are presented as number and percentage or mean±SD (range, median).
EDVi, indexed end-diastolic volume; EF, ejection fraction; ESVi, indexed end-systolic volume; LV, left ventricular; pCI, peak cardiac index; pHR, peak heart rate; pSVi, peak indexed stroke volume; RV, right ventricular; SVi, indexed stroke volume; VSD, ventricular septal defect.

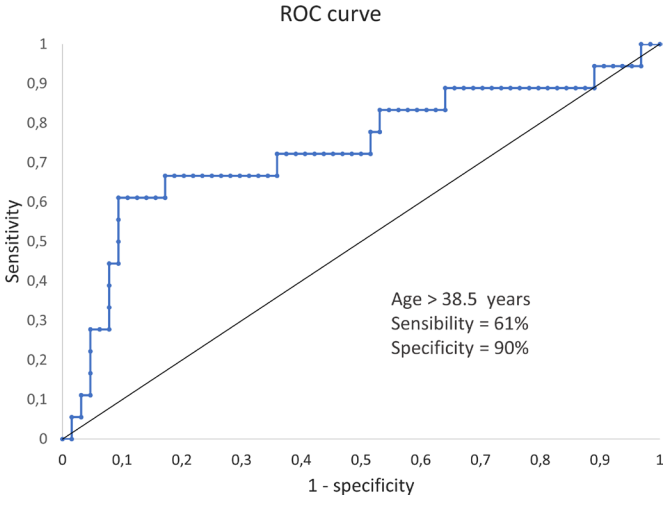

Figure 3 Receiver operating characteristic (ROC) curve. Sensitivity and specificity of age at cardiopulmonary exercise test (CPET) in predicting low peak cardiac index (pCI).

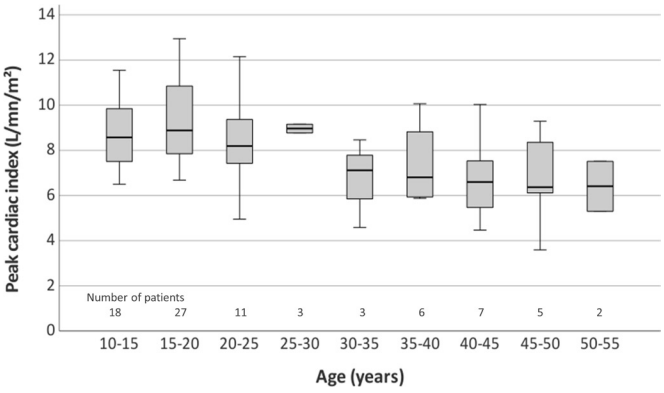

Figure 4 Distribution of peak cardiac index (pCI) as a function of age (box represent the minimum value, first quartile, median, third quartile and the maximum value of the sample of each age group).

observed between haemodynamic response and MRI parameters was between MRI LV SVi and pSVi. This relationship existed only in the low pCI group. Presence of additional pathophysiological mechanisms may explain this result. First, an impairment of the diastolic function of the left ventricle due to severity of preoperative hypoxaemia has been reported.[20] Moreover, some authors observed that the increase of left ventricular stroke volume during exercise is associated with a decrease of the PR (partially attributed to the fall of the pulmonary vascular resistance at effort) which contributed to improve the LV filling.[21] This mechanism could be altered over time by the progressive appearance of diastolic dysfunction of the left ventricle and thus limits the increase in cardiac output on effort. In addition to the scarring fibrosis, T1 mapping cardiac MRI evidences diffuse infiltration of intramyocardial fibrosis with a prognostic impact in these patients.[22] This fibrosis is associated with stiffer ventricles and diastolic dysfunction, reaches both the RV and the LV and seems more favoured by the overload in volume than in pressure.[22–24] The non-significant trend found in the low pCI group—that is, the smaller the LV EDVi, the lower their pCI was—is consistent with this hypothesis.

The prognostic value of pCI is yet unknown in this specific population even though it was proven that pCI is an independent prognostic factor in patients with heart failure.[25] In the logistic regression model, we observed that the age of 38.5 years had a positive and a negative predictive value of low cardiac output of 65% and 89%, respectively. The age of 40 years has been shown by an Australian study to be the time when serious event-free survival declined markedly as mortality, ventricular arrhythmia and/or heart failure required hospitalisation.[26] Equally, this clinical course was proven to be independent of RV dilatation.[26] Factors for recovery of normal pCI after PVR are also unknown. However, a previous study has already shown that improvement in left ventricular filling and resting cardiac output after PVR is seen in younger patients before 17.5 years of age as opposed to older patients, possibly because left ventricular fibrosis may not be significant enough at this age.[27]

Half of patients with low cardiac output had ventricular volumes below the PVR indication thresholds. Conversely, slightly less than half of those who had normal pCI had RV dilatation above 150 mL/m^2. The significance of this parameter in the monitoring and timing of PVR is questionable given the difficulties of the current strategy based on resting volumes.[28] Aerobic capacity is one of the criteria for PVR, as a decrease in aerobic capacity is indicative of a decrease in haemodynamic response. However, pVO_2 only partially reflects pCI. Thus, pCI is probably a more relevant endpoint than pVO_2, even though its prognostic value has not been studied in this population. Although age is a predictor of low pCI in our series, this result does not allow us to dispense with its measurement. We believe that at this time we may discuss the indication of PVR in patients with low pCI even if they have not met the required MRI volume criteria.

LIMITATIONS

Our study presents some limitations, as it is a retrospective study and included a relatively small number of patients due, in part, to the choice to study patients with homogenous residual lesion. Moreover, we counted some missing data but they did not depend on characteristics and measurements of the patients and we believe that they had no significant impact on our results. Another limit is that the cardiac output was measured by a non-invasive method. The chosen device has shown good accuracy during exercise compared with the Fick and the thermo-dilution method.[29] We demonstrated high reliability of this device in children and young adults with CHD. We noticed that the reliability was similar to stress echocardiography and MRI reported in the literature.[10 30] Furthermore, these investigations do not permit maximal effort, and unavailability of stress MRI equipment, a limited acoustic window and difficulties in Doppler alignment limit their use in the clinic. This PhysioFlow device has the advantages of enabling evaluation of pSVi in an upright position, portability, lower costs and it also requires low technical expertise to acquire the results.[30]

CONCLUSION

In conclusion, in patients with severe PR, peak oxygen consumption and symptom intensity poorly reflect haemodynamic response to exercise. Risk of low pCI increases with age. The lack of prediction of MRI measurements suggests the interplay of several pathophysiological mechanisms in addition to impaired RV contractility, such as diastolic right and left ventricular dysfunction by progressive diffusion of myocardial fibrosis.

Key questions

What is already known on this subject?

- Compared with MRI measurements, the ventricular functional reserve (that affects cardiac output on effort) appears to provide additional information on ventricular function and prognosis to monitor patients with severe pulmonic regurgitation.

What might this study add?

- Assessed by thoracic impedancemetry, cardiac index at peak exercise (pCI) is poorly reflected by cardiopulmonary testing or symptom intensity.
- Risk of low pCI (with lower heart rate and stroke volume) increases with age, independently of MRI measurements.

How might this impact on clinical practice?

- Non-invasive measurement of the haemodynamic response to exercise by thoracic impedancemetry is an easily accessible additional tool for early detection of ventricular damage related to chronic volume overload and could be an additional measurement to take into account (in addition to MRI measurements) to determine the right time for pulmonic valve replacement.

Probably more suitable to detect biventricular dysfunction, pCI could be an additional parameter to be considered when making decisions regarding PVR. Its prognostic value in this population remains to be determined as well as the conditions of recovery after PVR.

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