ERJ Express. Published on November 29, 2006 as doi: 10.1183/09031936.00016806

Pulmonary artery distensibility in pulmonary arterial hypertension: a MRI pilot study

Carlos Jardim [1]

Carlos Eduardo Rochitte [2]

Marc Humbert [3]

Gordon Rubenfeld[4]

Dany Jasinowodolinski [2]

Carlos Roberto Ribeiro Carvalho [1]

Rogerio Souza [1,2,3]

1 – Pulmonary Division – Pulmonary Hypertension Unit – Heart Institute

University of Sao Paulo Medical School – Sao Paulo - Brazil

2 – Fleury Research Institute – Sao Paulo - Brazil

3 – Centre des Maladies Vasculaires Pulmonaires, UPRES EA 2705, Hôpital Antoine Béclère - Université Paris-Sud, Clamart, France

4 – Pulmonary and Critical Care Division – University of Washington

Address for correspondence:

Rogério Souza

R. Afonso de Freitas 451 ap 112

São Paulo – Brazil

04006-052

rgrsz@uol.com.br

Phone / Fax: + 5511 3069-7202

Short title: Pulmonary artery distensibility in PAH

Abstract

Pulmonary arterial hypertension is a disease of the small vessels in which there is substantial increase in pulmonary vascular resistance, leading to right ventricle failure and death.

Invasive hemodynamic evaluation is mandatory not only for diagnosis confirmation but also to address prognosis and eligibility to the use of calcium channel blockers through an acute vasodilator challenge. Non-invasive surrogate response markers to the acute vasodilator test have been sought. In this study, we investigated the relationships between pulmonary artery distensibility (assessed by magnetic resonance imaging) and response to acute vasodilator test.

Nineteen patients diagnosed with idiopathic pulmonary arterial hypertension without any specific treatment were evaluated. In a 48 hours window after pulmonary artery catheterization, patients underwent cardiac magnetic resonance imaging.

Cardiac index, calculated after the determination of cardiac output, invasively and non-invasively have shown excellent correlation($r=0.72;p<0.05$), as well as right atrial pressure and right ventricle ejection fraction ($r=-0.60;p<0.01$). Pulmonary artery distensibility was significantly higher in responders($p=0.01$). A receiver-operating characteristic curve analysis has shown that 10% distensibility was able to distinguish responders from non-responders with 100% sensitivity 56% specificity. These findings suggest that magnetic resonance and pulmonary artery distensibility may be noninvasive useful tools for evaluation of patients with pulmonary hypertension.

Keywords: hemodynamic evaluation, magnetic resonance imaging, pulmonary artery distensibility, pulmonary hypertension, acute vasodilator response.

Introduction

Since the beginning of the last century, there have been substantial contributions to the understanding of the pulmonary circulation [1]. The development of right heart catheterization (RHC) has allowed the recognition of the pulmonary circulation as a low resistance and high compliance system [2]. Pulmonary hypertension is defined by mean pulmonary artery pressure (mPAP) greater than 25 mmHg at rest or 30 mmHg in exercise [3, 4]. There is a myriad of conditions in which pulmonary hypertension develops and there has been a great effort for adequate classification of these diseases [5]. When no associated condition can be identified the diagnosis of idiopathic pulmonary arterial hypertension (IPAH) is established. IPAH is a rare condition with high mortality rates even during the last decades after the development of different treatment strategies including the use of prostanoids, endothelin receptor antagonists, calcium channel blockers and phosphodiesterase inhibitors [6].

A small proportion of IPAH patients present sustained response to calcium channel blockers (CCB). For the identification of these patients, it is necessary to evaluate acute vasodilator response [7, 8]. During RHC, patients are challenged with vasodilators; and if a near-normalization of mPAP and pulmonary vascular resistance (PVR) occurs, the patient is classified as acute responder. The importance of assessing responsiveness is based, primary, on eligibility to CCB therapy [9, 10]. However, response to the acute vasodilator testing may also correlate with better preserved cardiac function, thus, being a possible surrogate for vascular remodeling [11].

There is a great effort to find non invasive markers that reflect not only the hemodynamic parameters but also the acute responsiveness to vasodilators. [12]. Imaging techniques, such as echocardiography, computerized tomography (CT) and magnetic resonance imaging (MR) may also help the assessment of IPAH patients not only with anatomical, but also with functional data [13]. It is known that echocardiography is useful for estimation of systolic and mean pulmonary artery pressures, but it may lack reliability for measurement of right atrial pressure (RAP) and is not able to accurately estimate cardiac index (CI) [14]. Chest CT, especially if performed with intravenous contrast, may provide data on right ventricular performance and may predict early

death in acute pulmonary embolism [15]. Moreover, MR may be used to estimate mPAP, PVR, ventricular volumes and cardiac output, thus allowing calculation of cardiac index [16-18].

The distensibility of main pulmonary artery (mPAD) by MR has been addressed in other studies to assess pulmonary hemodynamics and diagnose pulmonary vascular disease in specific settings [19, 20]. It is believed that mPAD may reflect the degree of vascular remodeling, thus being a very interesting marker for evaluation of IPAH patients [21]. However, one aspect of mPAD that has not been evaluated to date is its relationship to the acute vasodilator test response.

The main objective of the present study was to investigate whether mPAD assessed by MR could be a non-invasive marker of acute vasodilator responsiveness in IPAH patients. We have also evaluated whether MR could reflect or substitute part of the hemodynamic parameters obtained through right heart catheterization.

.

Material and Methods

Study Subjects:

We prospectively evaluated hemodynamic measurements and MR data of twenty consecutive patients diagnosed with IPAH between January and December 2004. Our sample size was based on an expected prevalence of responders to be around 15% [8] and on an standard deviation and effect size for mPAD of 4% and 7%, respectively[21]. Pulmonary arterial hypertension (PAH) was defined by a mean pulmonary artery pressure in excess of 25mmHg and a normal pulmonary artery occlusion pressure (PAOP) < 15 mmHg at rest. Secondary causes were excluded on the basis of clinical examination, laboratory studies, chest X-ray, computerized tomography, echocardiography and pulmonary angiography, if necessary [5]. All patients signed an informed consent approved by our local ethics committee. One patient was excluded from the study due to inadequate image quality at MR.

Hemodynamic measurements

All patients underwent RHC with a triple-lumen balloon-tipped catheter through the internal jugular vein (Swan-Ganz, Model 131F7; Baxter, Edwards Critical-Care Division, Irvine, CA). Hemodynamic data were collected at baseline and after administration of inhaled NO (20ppm for 10 minutes) [10].

The following hemodynamic variables were recorded: RAP, cardiac output, PAOP, mPAP and pulmonary vascular resistance. Cardiac index (CI) and indexed pulmonary vascular resistance (PVRi) were obtained after adjustment to body surface area (BSA).

Patients were classified as responders or non-responders according to a decrease in mPAP of at least 10mmHg to a level lower than 40mmHg with a maintained or increased cardiac index [8].

MR analysis

MR was performed within 48 hours after RHC, without any change in clinical status or treatment. All patients underwent a MR study in a 1.5 T Signa Horizon EchoSpeed (General Electric,

Milwalkee, WI, USA). The protocol included cine-MR images using an ECG-gated steady-state free precession gradient-echo pulse sequence (SSFP) that allowed for dynamic evaluation of cardiovascular morphology and function. The parameters of this sequence were as follows: repetition time 3.6msec; echo time 1.6msec, 45^{o} flip angle, receiver bandwidth of +/- 125 kHz, 34-36cm field of view, 256x160 matrix, 20-30 cardiac phases, 8-14 views per segment, depending on heart rate to allow temporal resolution of 40 msec. This sequence provided images with intense bright-blood and high definition of vascular and cardiac structures. Short-axis images (8.0mm slice thickness, 2.0mm gap) from the apex to the base of the heart and a set of parallel four-chamber long-axis views (6.0mm slice thickness, no gap) from RV inferior wall to the RVOT were also acquired. Additionally, a long-axis RVOT view and LVOT views were also acquired. From those 2 planes a set of 2 to 3 transverse short axis-view (perpendicular to the long-axis) of the aortic root and main pulmonary artery were imaged using SSFP technique and also a gradient-echo with phase-contrast reconstruction to assess blood flow velocities. The SSFP images were used to measure maximal and minimal sectional area during cardiac cycle, from which the main PA distensibility was calculated as follows:

mPAD = [SA – DA] / SA and expressed in percentage variation (figure 1).

Measurements of left and right ventricular volumes, ejection fraction and mass were performed using the cine-MR short-axis views and MASS plus software analysis package (MEDIS, Leiden, the Netherlands). The calculations used by this software are based on the true Simpson´s rule for volumes measurements. Measurements of the flow-velocities through aorta were performed using CV-Flow (MEDIS, Leiden, the Netherlands). Both softwares were part of the Advantge Windows Workstation 4.0 (GEHealthcare). MR was performed without supplemental NO because the intention was to assess patients in their basal condition.

Two independent observers blinded to the results of hemodynamic measurements performed all image analyses. Cardiac index was obtained after adjustment of cardiac output to body surface area (BSA).

Statistical analysis

Variables are presented as mean ± SD. Comparison of the continuous variables between groups was conducted using Mann-Whitney U test. Inter-observer agreement was assessed by the Bland Altman method, as well as the comparison between the CI assessed by magnetic resonance (CI-MR) and CI assessed by right heart catheterization (CI-RHC). The correlation of the hemodynamic variables and the MR measurements was assessed through Pearson's correlation coefficient. In order to evaluate the capability of mPAD in distinguishing responders from non-responders we used a receiver operating characteristic (ROC) curve, which was generated by plotting sensitivity against 1-specifity for all possible cutoff values.

Results

Baseline hemodynamic and clinical characteristics of the 19 IPAH patients enrolled in the study are listed in table 1. The hemodynamic variation during NO inhalation is summarized in table 2. Four patients (21%) were identified as responders after the acute challenge with NO inhalation.

Functional and hemodynamic data obtained by MR images analyses are shown table 3. We have found our data to be consistent to previous reports of patients with chronic *cor pulmonale,* concerning diminished right ventricle function and elevated right ventricle mass and end diastolic volume with normal left ventricular function [22, 23].

The interobserver agreement for the cardiac index estimation, assessed by the Bland-Altman method, evidenced a mean error of 0.004 ± 0.03 L/min/m^2. For the PAD, the mean error was of 1.33 ± 5.70 %.The Bland-Altman analysis for agreement between the two techniques for CI measurements (RHC *versus* MR) has shown a mean error of 0.33 ± 0.69 L/min/m^2 (Figure 2).

The mPAD differed significantly in responders and non-responders as shown in figure 3 (p=0.01). Based on the ROC curve, we arbitrarily chose 10% mPAD as a cutoff value which is able to distinguish responders from non-responders with 100% sensitivity (95% confidence interval of 61% to 100%) and 56% specificity (95% confidence interval of 33% to 77%). We also found a positive predictive value of 36% (95% confidence interval of 15% to 65%) and a negative predictive value of 100% (95% confidence interval of 77% to 100%).

We have not found significant relationship between mPAD and mPAP (r = - 0.25; p = 0,28), PVRi (r = 0.02; p = 0.91) and CI (r = - 0.14; p = 0.54). In two patients, the image quality obtained was not sufficient to allow a proper estimation of ventricular volumes and masses; even though, a significant correlation between right atrial pressure (RAP) and RV ejection fraction was found (n=17, r = - 0.60, 95% confidence interval from 0.17 to 0.84; p < 0.01), as well as PAOP and LV ejection fraction (n = 17, r = - 0.59, 95%CI from 0.18 to 0.83; p = 0.01).

Ejection fractions from LV and RV, assessed by MR, have also shown significant correlation (n=17, r = 0.51, 95%CI from 0.03 to 0.80; p < 0.05). Correlation between RV mass /

LV mass ratio and mPAP was significant as well (n=17, r = -0.62, 95%CI from 0.20 to 0.85; $p < 0.05$).

Neither the correlation between the variation of mPAP (mPAP before / mPAP after NO) and mPAD (n=19; r = 0.37; p = NS), nor the correlation between mPAD and mPAP at rest (n=19; r = - 0.25; p = NS) has been found to be statistically significant.

Discussion

Our results show that there is a significant difference in the mPAD of responders and non-responders and that this parameter could be used as a tool to differentiate these two groups of patients through a baseline MR.

Distensibility measurements between the two observers have shown an excellent agreement. Previous MR studies for anatomical investigation have found similar results [21]. The mPAD was significantly higher in acute NO responders, in comparison to non-responders (27.3% ± 18.4% and 11.0 ± 6.8%, respectively; $p<0.05$). There are interesting data on the literature regarding right pulmonary artery distensibility and its relation to pulmonary artery pressure [13], but, to our knowledge, no other study has evaluated this parameter as a noninvasive predictor of acute NO response. There are known differences in mPAD in PAH patients when compared to normal individuals as stated by Bogren et al (mPAD 8% in PAH patients) [19] and Casalino et al (mPAD in HIV-associated pulmonary hypertension patients was 18% *versus* 26% in control group, $p < 0.05$) [21]. In normal individuals the average mPAD was reported to be around 25% [24]. The fact that mPAD in responders is similar to mPAD in normal individuals of other studies suggests that elevation in mPAP is not the main factor involved in mPAD reduction.

This hypothesis was addressed in our study and no correlation was found between mPAP and the pulmonary artery distensibility. We have also tested the correlation between variation in mPAP (mPAP before / mPAP during NO) and mPAD, to see whether pressure variation would bring a variation in distensibility; again, no significant correlation was found. Pulmonary circulation assessment through analysis of proximal vessels may have limitations and is a matter of debate. It is known that there is an inverse correlation between PA compliance and pressure levels [25], however, when mPAP reaches 40 mmHg this relation tends to flatten and become stable [26] and thus the proximal part of the system would better reflect the behavior of the distal arteries, particularly in PAH where changes in elastic arteries lead to a diminished compliance of the whole vascular system [26, 27]. Considering these concepts together with our findings, the mPAD may be a marker of pulmonary vascular remodeling process and not a consequence of the

hemodynamic pattern. Although interesting, this hypothesis would require the analysis of pathology lung specimens to be confirmed.

In order to further address mPAD use in the clinical setting, we sought to determine by a ROC curve analysis which value would distinguish acute NO responders from non-responders. We found an area under the curve of 0.83 ($p < 0.05$) and we have arbitrarily chosen the value of 10% mPAD as a cutoff point. We are aware that this cutoff value determines high sensitivity and low specificity. We based our decision on the fact that it is of major importance to recognize the larger population of patients that should not be treated with calcium channel blockers instead of accurately recognize the small proportion of responders. Thus, the use of a cutoff value with high sensitivity will avoid the need of a significant number of acute vasodilator tests at baseline; this could be particularly important when considering patients that already underwent right heart catheterization before being referred to a pulmonary hypertension center.

The high negative predictive value of mPAD, considering this cutoff value for the differentiation between responders and non-responders brings up the perspective for the use of mPAD as a noninvasive marker of acute response. This might be of interest not only for ruling out the use of CCBs in non-responders, but also as a follow up tool in the evaluation of the cardiovascular system in the setting of the available therapies for PAH treatment. With the development of 64 detectors CT, gated-CT images might also enable the estimation of PAD at the screening for thromboembolic disease during PAH investigation. However, this hypothesis should be addressed in prospective studies comparing MR and CT images.

Our results, however, should be scrutinized considering the small number of patients enrolled in this pilot study. Even though the clinical and hemodynamic characteristics of those patients were similar to the previously described data from IPAH patients [28] and that baseline hemodynamic data did not differ significantly between responders and non-responders; the proportion of responders is higher than previously described for this response criteria [8].

Although not the primary objective of our study, the use of MR also allowed the non-invasive estimation of hemodynamic data such as the cardiac index. The interobserver agreement for the estimation of cardiac index was excellent probably due to the fact the CI was

calculated from aorta flow measurements and once aorta is a extremely regular vessel, there is little room for involuntary measurement misjudgment at the semi-automatic contour detection used for the flow analysis [19, 21, 24].

The mean error found when analyzing the agreement between CI measured by MR and by RHC show that although MR seems to be an interesting non-invasive method for hemodynamic assessment [16] CI-MR cannot be used as a substitute for CI-RHC at present time. Nevertheless, the potential use of CI-MR as a follow-up tool, in order to demonstrate the trend of CI towards improvement or deterioration during treatment, remains to be addressed.

The limited number of patients studied did certainly influence the magnitude of the mean error between the two methods; moreover, RHC using thermodilution for CI determination may not be the ideal gold-standard as many factors, including tricuspid regurgitation, affect the accuracy of CI measurements [7]. Future studies should compare cardiac output measurements using thermodilution, MR and the Fick method.

Other data obtained by MR image analysis also set interesting perspectives for their use. Significant correlations between RAP and RVEF, as well as PAOP and LVEF, show the relationships between ventricular pumps and upstream pressures emphasizing the potential ability of a non-invasive technique, such as MR, in reflecting important prognostic markers in PAH patients, as RAP .

Another interesting finding was the significant correlation between RV and LV ejection fractions. Previous studies in PAH patients have shown relationships between right and left ventricle volumes [18] and interventricular interdependence [29]. We believe that our findings regarding right and left ventricular functions relationships reinforce these pathophysiologic findings previously reported.

In conclusion, this pilot prospective monocenter study indicates that noninvasive assessment of PAD by MR reflect the acute response pattern in IPAH patients These encouraging results, together with the perspective of using MR for hemodynamic measurements, should be confirmed in a larger prospective multicenter study.

Acknowledgment

This study was possible thanks to an educational grant received from CAPES – Ministry of Education – Brazil

References

1. Fishman AP. Primary pulmonary arterial hypertension: a look back. *J Am Coll Cardiol* 2004;43:2S-4S.
2. Dawson CA, Krenz GS, Karau KL, Haworth ST, Hanger CC, and Linehan JH. Structure-function relationships in the pulmonary arterial tree. *J Appl Physiol* 1999;86:569-83.
3. Farber HW and Loscalzo J. Pulmonary arterial hypertension. *N Engl J Med* 2004;351:1655-65.
4. Barst RJ, McGoon M, Torbicki A, Sitbon O, Krowka MJ, Olschewski H, and Gaine S. Diagnosis and differential assessment of pulmonary arterial hypertension. *J Am Coll Cardiol* 2004;43:40S-47S.
5. Simonneau G, Galie N, Rubin LJ, Langleben D, Seeger W, Domenighetti G, Gibbs S, Lebrec D, Speich R, Beghetti M, Rich S, and Fishman A. Clinical classification of pulmonary hypertension. *J Am Coll Cardiol* 2004;43:5S-12S.
6. Humbert M, Sitbon O, and Simonneau G. Treatment of pulmonary arterial hypertension. *N Engl J Med* 2004;351:1425-36.
7. Chemla D, Castelain V, Herve P, Lecarpentier Y, and Brimioulle S. Haemodynamic evaluation of pulmonary hypertension. *Eur Respir J* 2002;20:1314-31.
8. Sitbon O, Humbert M, Jais X, Ioos V, Hamid AM, Provencher S, Garcia G, Parent F, Herve P, and Simonneau G. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation* 2005;111:3105-11.
9. Sitbon O, Brenot F, Denjean A, Bergeron A, Parent F, Azarian R, Herve P, Raffestin B, and Simonneau G. Inhaled nitric oxide as a screening vasodilator agent in primary pulmonary hypertension. A dose-response study and comparison with prostacyclin. *Am J Respir Crit Care Med* 1995;151:384-9.
10. Sitbon O, Humbert M, Jagot JL, Taravella O, Fartoukh M, Parent F, Herve P, and Simonneau G. Inhaled nitric oxide as a screening agent for safely identifying responders to oral calcium-channel blockers in primary pulmonary hypertension. *Eur Respir J* 1998;12:265-70.
11. Costa EL, Jardim C, Bogossian HB, Amato MB, Carvalho CR, and Souza R. Acute vasodilator test in pulmonary arterial hypertension: evaluation of two response criteria. *Vascul Pharmacol* 2005;43:143-7.
12. Souza R, Bogossian HB, Humbert M, Jardim C, Rabelo R, Amato MB, and Carvalho CR. N-terminal-pro-brain natriuretic peptide as a haemodynamic marker in idiopathic pulmonary arterial hypertension. *Eur Respir J* 2005;25:509-13.

13. Vonk-Noordegraaf A, Marcus JT, Holverda S, Roseboom B, and Postmus PE. Early changes of cardiac structure and function in COPD patients with mild hypoxemia. *Chest* 2005;127:1898-903.
14. Bossone E, Bodini BD, Mazza A, Allegra L. Pulmonary arterial hypertension: the key role of echocardiography. *Chest* 2005;127:1836-1843.
15. Schoepf U, Kucher N, Kipfmueller F, Quiroz R, Costello P, Goldhaber S. Right ventricular enlargement on chest computed tomography: a predictor of early death in acute pulmonary embolism. *Circulation* 2004;110:3276.
16. Saba TS, Foster J, Cockburn M, Cowan M, and Peacock AJ. Ventricular mass index using magnetic resonance imaging accurately estimates pulmonary artery pressure. *Eur Respir J* 2002;20:1519-24.
17. Mousseaux E, Tasu JP, Jolivet O, Simonneau G, Bittoun J, and Gaux JC. Pulmonary arterial resistance: noninvasive measurement with indexes of pulmonary flow estimated at velocity-encoded MR imaging--preliminary experience. *Radiology* 1999;212:896-902.
18. Boxt LM, Katz J, Kolb T, Czegledy FP, and Barst RJ. Direct quantitation of right and left ventricular volumes with nuclear magnetic resonance imaging in patients with primary pulmonary hypertension. *J Am Coll Cardiol* 1992;19:1508-15.
19. Bogren HG, Klipstein RH, Mohiaddin RH, Firmin DN, Underwood SR, Rees RS, and Longmore DB. Pulmonary artery distensibility and blood flow patterns: a magnetic resonance study of normal subjects and of patients with pulmonary arterial hypertension. *Am Heart J* 1989;118:990-9.
20. Berger RM, Cromme-Dijkhuis AH, Hop WC, Kruit MN, and Hess J. Pulmonary arterial wall distensibility assessed by intravascular ultrasound in children with congenital heart disease: an indicator for pulmonary vascular disease? *Chest* 2002;122:549-57.
21. Casalino E, Laissy JP, Soyer P, Bouvet E, and Vachon F. Assessment of right ventricle function and pulmonary artery circulation by cine-MRI in patients with AIDS. *Chest* 1996;110:1243-7.
22. Vincent JL. What is right ventricular (dys)function? *Crit Care Med* 1994;22:2024-6.
23. Saito H, Dambara T, Aiba M, Suzuki T, and Kira S. Evaluation of cor pulmonale on a modified short-axis section of the heart by magnetic resonance imaging. *Am Rev Respir Dis* 1992;146:1576-81.
24. Paz R, Mohiaddin RH, and Longmore DB. Magnetic resonance assessment of the pulmonary arterial trunk anatomy, flow, pulsatility and distensibility. *Eur Heart J* 1993;14:1524-30.
25. Harris P, Heath D, and Apostolopoulos A. Extensibility of the human pulmonary trunk. *Br Heart J* 1965;27:651-9.

26. Reuben S. Compliance of the human pulmonary arterial system in disease. *Circ Research* 1971;29:40-50.
27. Reeves JT, Linehan JH, and Stenmark KR. Distensibility of the normal human lung circulation during exercise. *Am J Physiol Lung Cell Mol Physiol* 2005;288:L419-25.
28. Rich S, Dantzker DR, Ayres SM, Bergofsky EH, Brundage BH, Detre KM, Fishman AP, Goldring RM, Groves BM, Koerner SK, and et al. Primary pulmonary hypertension. A national prospective study. *Ann Intern Med* 1987;107:216-23.
29. Pinsky MR. Recent advances in the clinical application of heart-lung interactions. *Curr Opin Crit Care* 2002;8:26-31.

Table 1

Baseline clinic and hemodynamic characteristics (RHC)

	n=19
Age (years)	38 ± 11
Gender (M/F)	6 /13
NYHA functional class (I-II / III-IV)	5 /14
Mean Pulmonary arterial pressure (mmHg)	69 ± 21
Indexed pulmonary vascular resistance (dyn.s.cm^{-5}.m $^{-2}$)	2312 ± 1635
Cardiac Index (L.min^{-1}.m^{-2})	2.39 ± 1.06
Pulmonary artery occlusion pressure (mmHg)	9 ± 5
Right atrial pressure (mmHg)	12 ± 6
Body surface area (m^2)	1.80 ± 0.17
Heart rate (bpm)	84 ± 9

Data presented as mean ± SD

Table 2 - Hemodynamic data according to acute NO testing (RHC)

	Responders (n=4)*		Non-responders (n=15) *	
	Baseline	NO	Baseline	NO
Mean pulmonary artery pressure (mmHg)	60 ± 6	31 ± 8	72 ± 23	63± 21
Indexed pulmonary vascular resistance (dyn.s.cm^{-5}.m $^{-2}$)	2314 ± 919	1219 ± 1172	2311±1793	1840±1126
Cardiac Index (L.min^{-1}.m^{-2})	2.04 ± 0,66	2.88 ± 0.68	2.47 ± 1.14	2.45 ± 1.08
Pulmonary artery occlusion pressure (mmHg)	10 ± 2	9 ± 1	8 ± 2	9 ± 1
Right atrial pressure (mmHg)	7 ± 6	5 ± 4	13 ± 6	12± 6

Data presented as mean ± SD

*There are no statistically significant differences in baseline hemodynamics between responders and non-responders

Table 3

Functional data (MR)

	n=19
CI (L. $min^{-1}.m^{-2}$)	1.98 ± 0.71
Ejection fraction LV (%)*	58 ± 13
Ejection fraction RV (%)*	32 ± 16
Left Ventricular mass (g)*	75 ± 25
Right Ventricular mass (g)*	42 ± 19
Left Ventricle end diastolic volume (mL)	69 ± 24
Right Ventricle end diastolic volume (mL)	108 ± 41
Pulmonary Artery systolic area (mm^2)	1407 ± 600
Pulmonary Artery diastolic area (mm^2)	1259 ± 605
Mean Pulmonary Artery Distensibility (%)	14 ± 11

Data presented as mean ± SD

* n = 17; In two patients, the estimation of ventricular volumes and masses was not performed

Figure 1 – Cross-sectional image of pulmonary artery used for mPAD determination according to the following formula: mPAD = (SA-DA) / SA, where SA = systolic area (marked area in panel A) and DA = diastolic area (marked area in panel B).

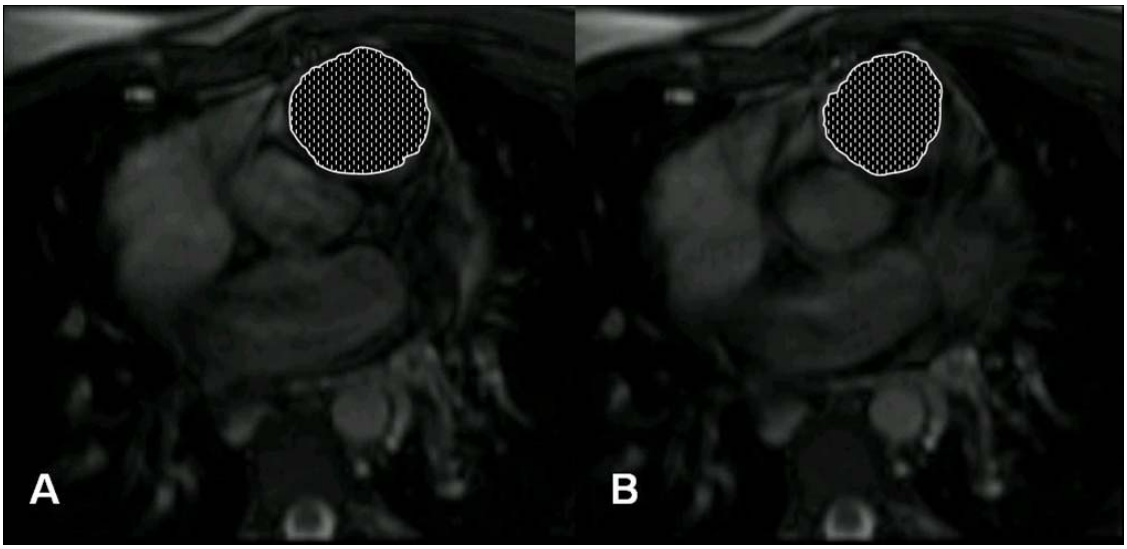

Figure 2 – Bland-Altman analysis of cardiac index estimated by MR and by RHC

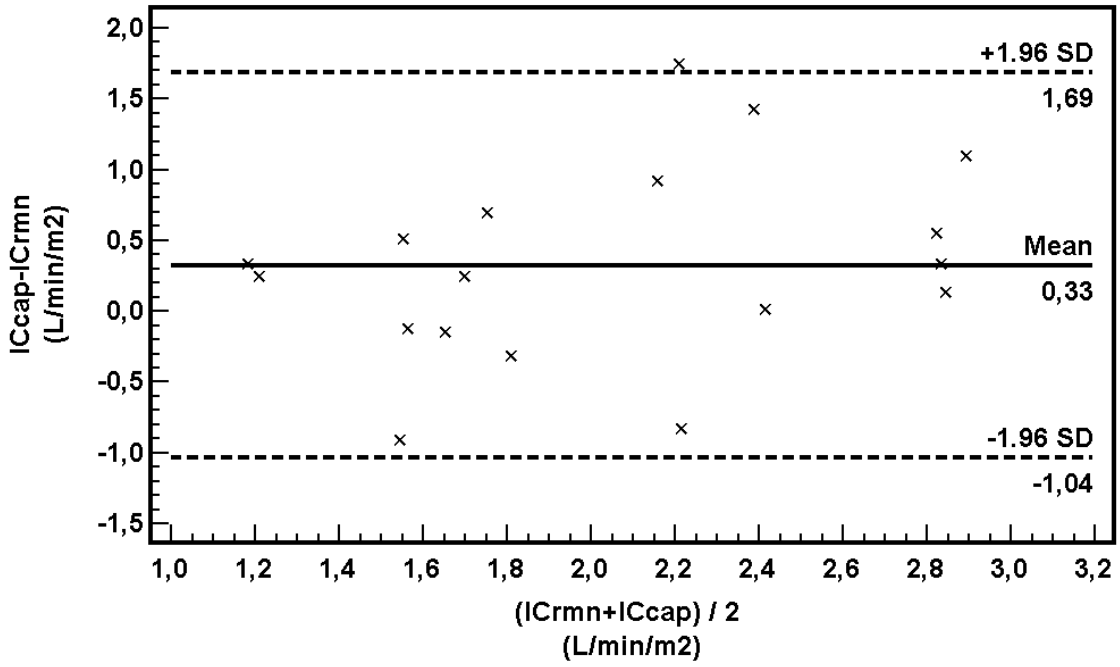

Figure 3 – Mean Pulmonary Artery Distensibility (mPAD) in responders and non-responders (p=0.01)