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Early View

Original article

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"Take home" message. In postcapillary and precapillary pulmonary hypertension patients, our study favors comparing pulmonary arterial compliance (PAC) at fixed mean pulmonary artery pressure level (isobaric PAC) rather than at fixed pulmonary vascular resistance level.

ABSTRACT (250)

Pulmonary hypertension (PH) is associated with stiffening of pulmonary arteries which increases right ventricular pulsatile loading. High pulmonary artery wedge pressure (PAWP) in postcapillary PH (Pc-PH) further decreases PA compliance (PAC) at a given pulmonary vascular resistance (PVR) compared to precapillary PH, thus responsible for a higher total arterial load. In all other vascular beds, arterial compliance is considered as mainly determined by the distending pressure, due to non-linear stress-strain behavior of arteries. We tested the applicability, advantages and drawbacks of two comparison methods of PAC depending on the level of mean PA pressure mPAP (isobaric PAC) or PVR.

Right heart catheterization data including PAC (stroke volume/pulse pressure) were obtained in 112Pc-PH (of whom 61 had combined postcapillary and precapillary PH) and 719 idiopathic pulmonary arterial hypertension (iPAH).

PAC could be compared over the same mPAP range (25-66mmHg) in 792/831 patients (95.3%) and over the same PVR range (3-10.7 WU) in only 520/831 patients (62.6%). The main assumption underlying comparisons at a given PVR was not verified as the PVR×PAC product (RC-time) was not constant but on the contrary more variable than mPAP. In the 788/831 (94.8%) patients studied over the same PAC range (0.62-6.5mL/mmHg), PVR and thus total arterial load tended to be higher in iPAH.

Our study favors comparing PAC at fixed mPAP level (isobaric PAC) rather than at fixed PVR. A reappraisal of the effects of PAWP on the pulsatile and total arterial load put on the right heart is needed, and this point deserves further studies.

Pulmonary hypertension (PH) is a group of conditions characterized by an increased mean pulmonary artery pressure (mPAP) at rest due to increased pulmonary vascular resistance (PVR) (precapillary PH), increased left atrial pressure, as reflected currently by pulmonary artery wedge pressure PAWP (postcapillary PH), or increased cardiac output (hyperkinetic PH) (1-3). While the abnormally high mPAP reflects the increased steady load put on the right heart, PH is also associated with a stiffening of pulmonary arteries which leads to an increased pulsatile load (4-8). Total pulmonary arterial compliance (PAC = 1/PA stiffness) is defined as the relation between changes in arterial volume per unit change in arterial pressure, and it is currently estimated by the stroke volume over PA pulse pressure ratio (SV/PP) (9-11). In patients with PH, increased PVR and reduced PAC may contribute to right ventricular dysfunction and poor prognosis (12-19).

Hemodynamic studies performed nowadays consider as granted that the major determinants of PAC are PVR and PAWP (20-24). There is a curvilinear negative relationship between PVR and PAC in precapillary PH patients (21-23), and this relationship is shifted downwards in postcapillary PH (24, 25). In other words, the elevations in PAWP lead to lower PAC than would be anticipated from elevated PVR alone. It is thus admitted that the total arterial load is higher in postcapillary than in precapillary PH (11, 20, 24). This pathophysiological framework may be viewed as a unique feature of the pulmonary circulation. Indeed, in all other vascular beds, arterial compliance is determined by the interplay between the distending pressure and the intrinsic properties of the arterial wall, not by vascular resistance and downstream pressure (25, 26). The rationale for comparing PAC at a given PVR level is based on the key assumption that PAC is accurately predicted by PVR alone in either group, and this assumption relies on the constancy of the PVR times PAC product (“RC-time constancy”) (20-24).

In the present study performed in precapillary and postcapillary PH patients, we tested the applicability, advantages and drawbacks of two comparison methods of PAC depending on either the

level of PVR or the prevailing distending pressure mPAP (isobaric PAC). We also tested the hypothesis that the combined effects of PVR and PAC result in a higher total arterial load in postcapillary as compared to precapillary PH patients.

METHODS

Patient population. This was a retrospective comparison of right heart catheterization results prospectively obtained 1) in Pc-PH patients referred to our French PH referral center for known or suspected PH between June 2012 and July 2015 (n=112); and 2) in the previously described 719 idiopathic pulmonary arterial hypertension (iPAH) patients belonging to the French PAH Network 2006-2016 registry (7). Only adult patients with their full hemodynamic data set available (PA pressures, PAWP, cardiac output and heart rate) entered the study. The final diagnosis was according to current guidelines at the time of the study, namely mPAP ≥25 mmHg, PAWP ≤15 mmHg, and PVR >3 Wood units (WU) (iPAH) or mPAP ≥25 mmHg and PAWP >15 mmHg (Pc-PH). Among Pc-PH patients, the isolated Pc-PH patients (Ipc-PH) had PVR ≤3WU while the combined post- and pre-capillary PH patients (Cpc-PH) had PVR >3 WU (2). Atrial fibrillation was documented in 31 (28%) Pc-PH patients, and in 45 (6%) iPAH ($P<0.05$). This study complied with the Declaration of Helsinki. Although French law does not require ethics committee approval or informed consent for retrospective data collection, the data collected were anonymized and complied with the requirements of the Commission Nationale Informatique et Liberté (CNIL). This organization dedicated to privacy, information technology and civil rights in France, approved the methods used to collect and analyze data (May 24, 2003, approval number 842063).

Measurements and data analysis. Pulmonary hemodynamics were acquired with a balloon-tipped, double lumen, fluid-filled 7F Swan Ganz catheter via the jugular or brachial vein approach (7, 27). Zero reference was set at the mid-chest. Pressure measurements were averaged over the respiratory cycle. Cardiac output was measured by thermodilution and three values differing by < 10% were averaged. The transpulmonary pressure gradient TPG was calculated as the mPAP minus PAWP

difference. The PVR was calculated as the TPG/cardiac output ratio. Indexed values of hemodynamic parameters were also calculated using correction for body surface area. The PAC was calculated as SV/PP where SV is the thermodilution stroke volume (cardiac output /heart rate) and PP is PA pulse pressure (systolic PAP minus diastolic PAP). The time constant of PAP decline in diastole (RC-time) was estimated using the empiric product PVR × PAC. The isobaric PAC was the total PA stiffness at a given mPAP level.

Statistics Normality was assessed with the Kolmogorov-Smirnov test. Continuous variables were expressed as median (interquartile range IQR, 25% to 75%) as the vast majority of the variables were non-normally distributed. The data dispersion was quantified using the quartile coefficient of dispersion, the interquartile ratio, and the acceptance range for 95% of the values (27, 28). We considered a claim for the presence of a "near-constant" variable in the database to be at least reasonable if the 95% limits of agreement fall within the clinically acceptable range of up to ±30%, i.e., if 95% of the computed values were located within 30% of the median value (29). The Spearman's rank correlation coefficient (rho) was used as a nonparametric measure of rank correlation. Comparisons were performed using the Mann-Whitney's test (independent samples) and Chi-squared test. All tests were two-sided with a $p<0.05$ considered statistically significant. Statistical analyses were performed using the MEDCALC 8.1.0.0 software (MedCalc Software, Mariakerke, Belgium).

RESULTS

The clinical and hemodynamic characteristics of the study population are given in Tables 1 and 2. As compared to Pc-PH patients, iPAH had higher mPAP, higher PVR and lower PAC (each $P<0.05$). As compared to Ipc-PH patients, Cpc-PH had higher mPAP higher PVR and lower PAC (each $P<0.05$). As compared to Cpc-PH, iPAH had similar mPAP ($P=0.34$), markedly higher PVR (+207%) and slightly lower PAC (-23%) (each $P<0.05$). In Pc-PH, there was no relationship between RAP and PAC ($P=0.47$).

Applicability of comparison methods. When PAC values were studied over the same PVR range (3-10.7 WU), only 520/831 patients (62.6%) entered the comparison, namely 61/112 Pc-PH patients (54.5%) and 459/719 iPAH (63.8%) (Figure 1 left panel). By definition, the Ipc-PH (51/112= 45.5% of Pc-PH) had their PVR < 3 WU and thus could not be compared to iPAH at fixed PVR. Furthermore, 260/719 iPAH (36.2%) did not enter the comparison as their PVR exceeded the highest PVR values documented in Cpc-PH (10.7 WU). On the other hand, when PAC values were studied over the same mPAP range (25-66 mmHg), 792/831 patients (95.3%) entered the comparison, namely 112 Pc-PH patients (100%) and 680/719 iPAH (94.6%) (Figure 1 right panel). Only 39/831 iPAH patients (4.7%) could not enter the comparison as their mPAP was > 66 mmHg.

Major dispersion of the PVR × PAC product (RC-time). The main assumption underlying the comparison of PAC at a given PVR level ("RC-time constancy") was not verified. In both Pc-PH and iPAH, the RC-time demonstrated extremely wide limits of agreement (95% confidence interval = ±62%and ±55%, respectively) (Table 3 and Figure 2). In both groups, the dispersion of RC-time was higher than that of mPAP.

Inconsistency of comparing PAC at a given PVR level concerning the total arterial load put on the RV. We first compared PAC at a given level of PVR. In the 62.6% patients in whom the comparison was feasible, PAC values at a given PVR level tended to be shifted downwards in Cpc-PH as compared to iPAH, with a certain amount of overlap (Figure 1 left panel). The tendency towards lower PAC at a given level of PVR implies that total arterial tended to be *lower* in iPAH vs Cpc-PH. We also studied PVR values over the same PAC range. Overall, 788/831 patients (94.8%) entered the comparison, namely 111/112 Pc-PH patients (99.1%) and 677 iPAH (94.2%), with PAC ranging from 0.62-6.5 mL/mmHg. As compared to Ipc-PH, the PVR was, by definition, *higher* in iPAH studied at similar PAC level ranging from 1.14 to 6.5 mL/mmHg. When patients were compared over the same PCA range (0.62 to 3.31 mL/mmHg), PVR and thus total arterial load also tended to be *higher* in iPAH (Figure 3). Finally 43/831 patients (5.2%) did not enter the comparison as their PAC was < 0.62 mL/mmHg (in 42/719 iPAH = 5.8%) or was extremely high (10.5 mL/mmHg in 1/112 Pc-PH).

PAC values studied over the same mPAP range. Isobaric PCA tended to be slightly upwards shifted in Ipc-PH vs iPAH patients studied over the same 25-61 mPAP range, while iPAH and Cpc-PH demonstrated major overlap in their isobaric PAC over the same 29-66 mmHg mPAP range (Figure 3).

DISCUSSION

Pulmonary hypertension is associated with stiffening of pulmonary arteries and enhanced pulsatile arterial load put on the right heart. To compare PAC (1/PA stiffness) between postcapillary and precapillary PH, the chosen method must ideally allow comparison according to a strong physiological rationale and in the vast majority of the patients. The first result of our study was that one must clearly favor comparing PAC at fixed mPAP level (isobaric PAC) rather than at fixed PVR level for the following reasons: 1) there is a strong physiological rationale for comparisons based on isobaric PAC; and 2) mPAP values overlap between postcapillary and precapillary PH in 95.3% of the study population, while PVR values overlap in 62.6% only. This may unify the way in which arterial compliance is studied in the pulmonary vascular bed and that used in all other vascular beds. The second result of our study was that from a fundamental physiological perspective, comparing PAC at each level of mPAP suggests that PAC is not lower in Pc-PH as compared to iPAH. High left atrial filling pressure causes apparent stiffening of the pulmonary arteries by passive increases in mPAP. In Pc-PH patients, elevated left atrial pressure by itself is not associated with further intrinsic stiffening of the PA as compared to iPAH studied at similar mPAP level. Overall, this may lead to a reappraisal of the effects of high PAWP on the pulsatile and total arterial load put on the right heart.

In vascular beds of the body, arterial compliance is considered as mainly determined by the mean distending pressure, due to non-linear stress-strain behavior of arteries. One exception is the pulmonary vascular bed, where it is widely admitted that PAC depends on vascular resistance (PVR) and downstream pressure (PAWP) (20-24). The present study points to several inconsistencies in this approach. *First*, the comparison of PAC at a fixed PVR level was only feasible in less than two-thirds of the study population. By definition the comparison excluded the Ipc-PH patients, and it was feasible in only 63.2% iPAH. This lack of universal applicability appears to be a major limitation. *Second*, the classic belief that PAC may be accurately predicted by PVR alone in either group (20-24)

was not verified. The RC-time was not constant but, on the contrary, highly variable and, in fact, as variable as mPAP in both groups. To continue to support the RC-time constancy or near-constancy would be as unrealistic as supporting that mPAP is constant or near-constant in PH states. We have previously discussed (7, 30) the reasons why earlier studies have supported the opposite. *Third*, although it was confirmed that PAC studied at a given PVR level tended to be lower in Cpc-PH vs iPAH, there was a major overlap in PVR/PAC individual values. This was probably due to the natural heterogeneity of the various hemodynamic phenotypes encountered in PH (12-19) resulting in an extremely variable RC-time. *Fourth*, concerning the total arterial load put on the right heart, no clear conclusion could be reached from the analysis of the PVR vs PAC relationships. Indeed, when patients were compared at a given PVR level (520/831 = 62.6%), it was concluded that total arterial load tended to be *lower* in iPAH than Cpc-PH, while when patients were compared at a given PAC level (788/831 = 94.8%), it was concluded that total arterial load tended to be *higher* in iPAH than in both Ipc-PH and Cpc-PH. In an attempt to explain this aporia, the following points must be stressed: i) there are numerous limitations of the classic approach relying on the PVR vs PAC relationship, as detailed above; ii) it is likely that the contributions of PVR and PAC to total arterial load are overlapping rather than additive as they share SV and PA pressures in their formalism, thus leading to a major, problematic mathematical coupling (30); and iii) the concept of total arterial load, which lumps the influences of PVR and PAC, seems questionable in our opinion, because for a given right ventricular geometry and in the absence of outflow tract obstruction, it is PAP which loads the right heart, not PVR nor PAC.

Comparing PAC values at fixed mPAP level (isobaric PAC) has strong physiological rationale and was feasible in the vast majority of the patients, namely all Pc-PH and 94.6% iPAH. In our opinion, this is clearly a major advantage over the other method. Due to non-linear stress-strain behavior of arteries (5, 6, 25, 26), arterial stiffness has to be measured under isobaric conditions to document potential intrinsic (i.e., pressure-independent) properties of the arterial wall. To quote the

international recommendations in the field: “Be aware of the pressure dependence of arterial stiffness. If BP [blood pressure] differs between populations being studied, arterial stiffness has to be measured under isobaric conditions (26)”. As mPAP increases, there is greater recruitment of relatively inelastic collagen fibers and, consequently, an increase in stiffness / a reduction in elasticity of the pulmonary arterial wall (5, 6, 31-33). The two other reasons explaining the increased PA stiffness in PH are the chronic stiffening due to wall thickening and vascular remodeling of the extracellular matrix, with loss of elastin and increase in collagen content; and stiffening due to smooth muscle cell responses (5, 6, 34). Impedance studies have shown that there was a direct correlation between vessel stiffness and mPAP (4). As far as the inverse relationship between PVR and PAC is concerned, Milnor *et al.* concluded that the main mechanism by which increased PVR would alter PA stiffness is by raising mPAP (4). Our study is consistent with milder intrinsic changes/remodeling of the arterial wall in Ipc-PH than in iPAH patients, while the same limits of compliance may well have been reached in Cpc-PH vs iPAH, and this point deserves further studies.

In PAH, major abnormalities have been reported at the vascular tissue and cellular level and may contribute to PA stiffening (35, 36). In Pc-PH patients, it is likely that the physiological explanation is that high left atrial pressure (which occurs as a consequence of systolic or diastolic dysfunction of the left ventricle and/or left atria) leads to higher mPAP by passive backward transmission of pressure. This results in lower PAC because of higher prevailing mPAP. With sustained elevation of pulmonary venous pressure, alterations in pulmonary vasoreactivity and structural damage at the arteriolar level ensue, responsible for a superimposed precapillary PH component (Cpc-PH) (2, 16, 18, 34). Our results are consistent the classic notion that elevated left heart filling pressures directly increase mPAP thus necessarily reducing PAC; and secondarily increase PVR through acute vasoconstriction and chronic vascular remodeling, which may further decrease PAC (16, 18). In our study, iPAH patients with similar mPAP as Cpc-PH patients exhibited a slightly lower PAC while PVR was markedly higher. Impedance studies performed in PH have shown that *for*

a given elevation of distending pressure, the stiffening of larger arteries in the patients with high resistance is greater than in the patients with normal resistance (4).

The Pc-PH patients had a mean RAP of 13 mmHg suggesting that many of them were decompensated at the time point of right heart catheterization. However, PAC was not associated with RAP, thus suggesting that the potential beneficial effects of decongestive therapy (eg, diuretics), if observed, would be rather related to the treatment-induced decreases in mPAP.

The limitations of our retrospective study must be discussed. PA load is at best assessed by the arterial input impedance in the frequency domain, but this is a complex approach, and as most clinical studies in this field, we used a time-domain approach. The new definition of PH based on mPAP > 20 mmHg (37) will not change our results as mPAP values in the 21-24 mmHg range will still overlap between pre and postcapillary PH. Although a PVR threshold of 2.2 WU may be more clinically relevant for risk stratification (19), PVR ≥ 3 WU remains the standard for defining PH patients with a precapillary component. Finally, given the more than six-fold size difference between the two groups, we did not perform matching procedures. Although a clear-cut conclusion emerges, the study results were mainly qualitative, and further studies are needed to refine comparisons depending on the patient's hemodynamic phenotypes in the two PH states.

The implications of our study should be discussed. Bearing in mind that the right ventricular function is a leading outcome determinant in patients with PH, our study challenges the classic notion that PAC is lower in postcapillary PH leading to more compromised right ventricular function than in precapillary PH. The great variability of the PVR × SV/PP product (RC-time) implies that PVR and PA stiffness were differently affected by the disease process and thus may be potentially modified separately by therapeutic interventions. The analysis of isobaric PAC may help unify the way arterial compliance is studied in all vascular beds including the pulmonary circulation.

In conclusion, our study favors comparing PAC at fixed mPAP level (isobaric PAC) rather than at fixed PVR level. This may unify the way arterial compliance is studied in all vascular beds including that of the lungs. In Pc-PH, elevated left atrial pressure by itself was not associated with further intrinsic stiffening of the PA as compared to iPAH. A reappraisal of the effects of high PAWP on the pulsatile and total load put on the right heart is needed, and this point deserves further studies.

Legends of the figures

Figure 1. Scatter diagram showing the total pulmonary arterial compliance (PAC) plotted against overlapping pulmonary vascular resistance (PVR) (left panel) or overlapping mean pulmonary artery pressure (right panel). Open circles in red: patients with idiopathic pulmonary arterial hypertension (iPAH). Open squares in blue: patients with isolated postcapillary pulmonary hypertension (Ipc-PH). Closed squares in blue: patients with combined postcapillary and precapillary pulmonary hypertension.

Figure 2. Box-and-whisker plots showing major dispersion of the pulmonary vascular resistance times total arterial compliance product (RC-time, left) and of mean pulmonary arterial pressure (mPAP, right) in precapillary pulmonary hypertension (Pc-PH) (upper) and idiopathic pulmonary arterial hypertension (iPAH) (lower).

Figure 3. Scatter diagram showing pulmonary vascular resistance (PVR) plotted against overlapping total pulmonary arterial compliance (PAC). Open circles in red: patients with idiopathic pulmonary arterial hypertension (iPAH). Open squares in blue: patients with isolated postcapillary pulmonary hypertension (Ipc-PH). Closed squares in blue: patients with combined postcapillary and precapillary pulmonary hypertension. Note that PVR is rightwards shifted in iPAH patients as compared to Pc-PH patients studied at a similar level of PAC.

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Table 1. Demographic and hemodynamic characteristics of the patients with postcapillary pulmonary hypertension (Pc-PH) and idiopathic pulmonary arterial hypertension (iPAH).

	iPAH (n=719)	Pc-PH (n=112)
Age, years	66 (51-75)	70.5 (64-79)
Female gender, n (%)	376 (54)	72 (64) NS
Body surface area, m²	1.77 (1.63-1.94)	1.92 (1.79-2.06)
Cardiac output, L/min	4.18 (3.38-5.00)	5.49 (4.33-6.29)
Cardiac index, L/min/m²	2.35 (2.90-2.79)	2.77 (2.29-3.35)
HR, bpm	79 (68-88)	78 (63-88) NS
Stroke volume, mL	54 (42-69)	70 (55-93)
Stroke volume index, mL/m²	30 (24-38)	37 (29-48)
mPAP, mmHg	46 (39-54)	38 (33-48)
PA pulse pressure, mmHg	45 (36-53)	36 (26-43)
PAWP, mmHg	9 (6-11)	21 (17-25)
TPG, mmHg	38 (31-46)	18 (12-25)
RAP, mmHg	7 (4-11)	13 (10-18)
PVR, WU	9.1 (6.6-12.5)	3.3 (2.4-4.7) NA
PAC, mL/mmHg	1.20 (0.88-1.68)	2.18 (1.46-3.07)
RC-time, ms	650 (546-767)	396 (321-489)

Values are expressed as median (IQR) except for gender in n (%). HR: heart rate. mPAP: mean pulmonary artery pressure. PA: pulmonary artery. PAC: total pulmonary arterial compliance. PAH: pulmonary arterial hypertension. PAWP: pulmonary artery wedge pressure. PH: pulmonary hypertension. PVR: pulmonary vascular resistance. RAP: right atrial pressure. RC-time: the PVR times PP/SV product. sPAP: systolic pulmonary artery pressure. TPG: transpulmonary pressure gradient (mPAP – PAWP). WU: Wood units. Each $P < 0.05$ except HR (NS: not significant) and PVR (N.A. not applicable). Each $P < 0.05$ except where indicated NS (not significant) or NA (not applicable).

Table 2. Demographic and hemodynamic characteristics of the patients with isolated postcapillary pulmonary hypertension (Ipc-PH) and combine post- and precapillary PH (Cpc-PH).

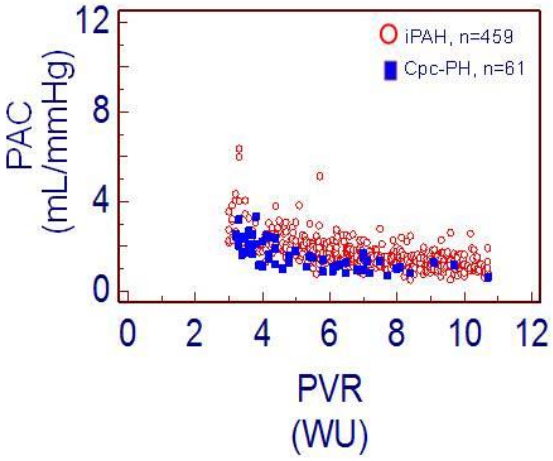
	Ipc-PH (n=51)	Cpc-PH (n=61)
Age, years	69 (64-76)	72 (63-79) NS
Female gender, n (%)	31 (61)	41 (67) NS
Body surface area, m²	1.95 (1.84-2.04)	1.90 (1.74-2.07) NS
Cardiac output, L/min	6.00 (5.18-7.48)	4.63 (3.94-5.71)
Cardiac index, L/min/m²	3.15 (2.74-3.73)	2.44 (2.14-2.92)
HR, bpm	73 (62-85)	80 (64-92) NS
Stroke volume, mL	86 (68-108)	61 (48-86)
Stroke volume index, mL/m²	45 (36-54)	31 (26-40)
mPAP, mmHg	34 (29-37)	46 (37-52)
PA pulse pressure, mmHg	30 (21-36)	39 (33-48)
PAWP, mmHg	21 (17-25)	20 (17-24) NS
TPG, mmHg	11 (9-16)	23 (19-28)
RAP, mmHg	12 (10-15)	14 (11-20)
PVR, WU	2.0 (1.6-2.5)	4.4 (3.6-6.5) NA
PAC, mL/mmHg	3.08 (2.32-4.03)	1.55 (1.11-2.06)
RC-time, ms	345 (276-424)	448 (363-520)

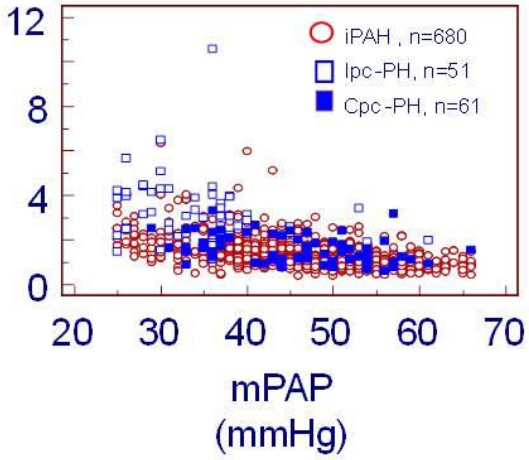
Values are expressed as median (IQR) HR: heart rate. mPAP: mean pulmonary artery pressure. N.A.: not applicable. PA: pulmonary artery. PAC: total pulmonary arterial compliance. PAH: pulmonary arterial hypertension. PAWP: pulmonary artery wedge pressure. PH: pulmonary hypertension. PVR: pulmonary vascular resistance. RAP: right atrial pressure. RC-time: the PVR times PP/SV product. sPAP: systolic pulmonary artery pressure. TPG: transpulmonary pressure gradient (mPAP – PAWP). WU: Wood units. Each $P < 0.05$ except where indicated NS (not significant) or NA (not applicable).

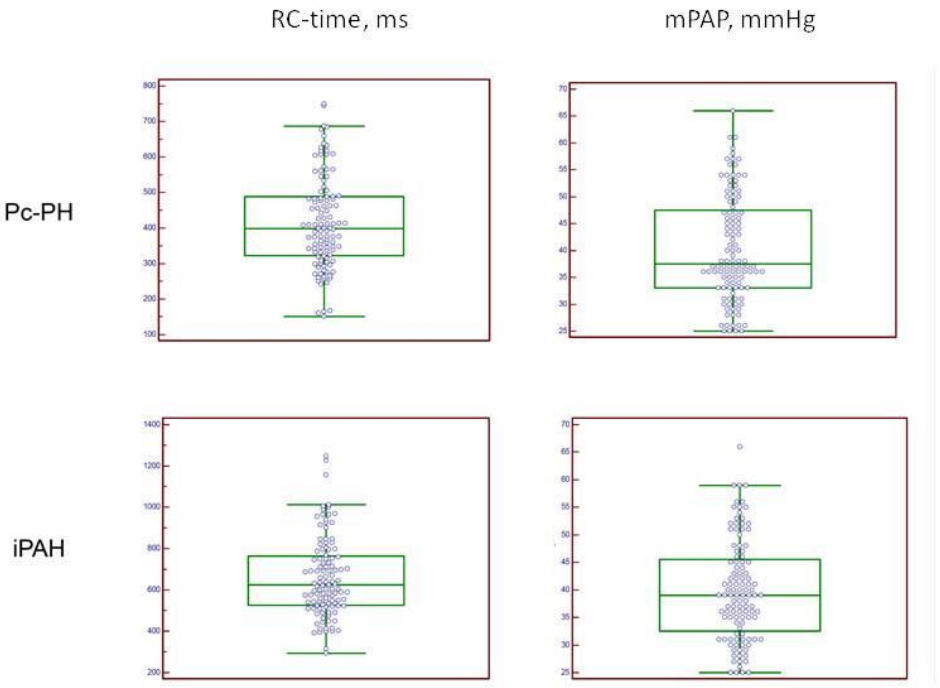
Table 3. Data dispersion indices

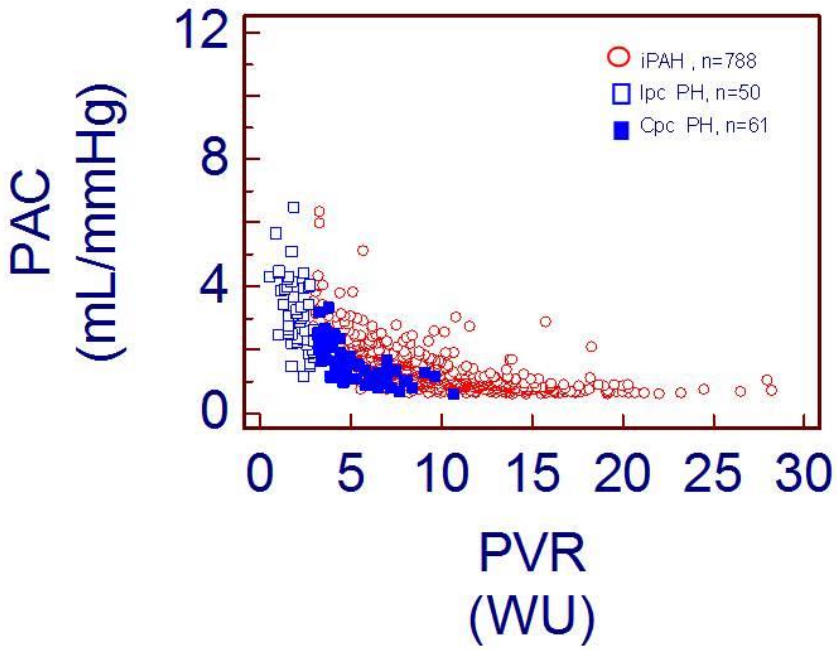
Variable	QCD	IQR	95% limits of agreement
Pc-PH (n=112)			
Body surface area	0.07	0.14	±24%
Age	0.10	0.21	±32%
mPAP	0.18	0.39	±48%
RC-time	0.21	0.42	±62%
iPAH (n=719)			
Body surface area	0.09	0.18	±25%
Age	0.19	0.36	±60%
mPAP	0.16	0.33	±50%
RC-time	0.17	0.34	±55%

The data dispersion was quantified using the quartile coefficient of dispersion (QCD), the interquartile ratio (IQR), and the acceptance range for 95% of the values. IQR = (Q3-Q1)/median. QCD = (Q3-Q1) / (Q3+Q1). mPAP: mean pulmonary artery pressure. RC-time: PVR × C product.
The 95% limits of agreement (acceptance range for 95% of the values) correspond to median ± %error. we considered a claim for the presence of a "near-constant" variable in the database to be at least reasonable if the 95% limits of agreement fall within the clinically acceptable range of up to ±30%, i.e., if 95% of the computed values were located within 30% of the median value, (acceptance range from 0.7 × median to 1.3 × median)


PAC
(mL/mmHg)
12
8
4
0
0
2
4
6
8
10
12
PVR
(WU)
iPAH, n=459
Cpc-PH, n=61


12
8
4
0
20
30
40
50
60
70
mPAP
(mmHg)
iPAH , n=680
Ipc-PH, n=51
Cpc-PH, n=61


RC-time, ms
mPAP, mmHg
Pc-PH
iPAH


PAC
(mL/mmHg)
12
8
4
0
0
5
10
15
20
25
30
PVR
(WU)
iPAH , n=788
Ipc PH, n=50
Cpc PH, n=61