ERJ Express. Published on July 7, 2011 as doi: 10.1183/09031936.00019911

The association between resting and mild-to-moderate exercise pulmonary artery pressure.

An invasive study in "non-pulmonary hypertensive" subjects aged less than 50 years

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Key Words : Pulmonary hypertension.

Abstract

The mean pulmonary artery pressure (mPAP) achieved on mild-to-moderate exercise is age-related and its hemodynamic correlates remain to be documented in patients free of pulmonary hypertension (PH).

Our retrospective study involved patients free of PH investigated in our centre for possible pulmonary vascular disease between 01.01.2007 and 31.10.2009, who underwent right heart catheterization at rest and during supine exercise up to 60 watts. The 38/99 patients aged <50 years were included and a mPAP of 30 mmHg was considered the upper limit of normal on exercise.

The 24 subjects who developed mPAP>30 mmHg on exercise had higher resting mPAP (19±3 vs 15±4 mmHg) and indexed pulmonary vascular resistance PVRi (3.4±1.5 vs 2.2±1.1 WU.m²) ($P<0.05$) than the remaining 14 subjects. Resting mPAP > 15 mmHg predicted exercise mPAP>30 mmHg with 88% sensitivity and 57% specificity. The 7 patients with resting mPAP 22-24 mmHg all had exercise mPAP>30 mmHg.

In subjects aged <50 years investigated for possible pulmonary vascular disease and free of PH, patients with mild-to-moderate exercise mPAP>30 mmHg had higher resting PVRi and higher resting mPAP, although there was no resting mPAP threshold value that could predict normal response on mild-to-moderate exercise. The clinical relevance of such findings deserves further long-term follow-up studies.

For the last 30 years, the diagnosis of pulmonary hypertension (PH) depended on either a resting mPAP of > 25mmHg or an increase in mPAP on exercise to >30mmHg, with the pulmonary capillary wedge pressure ≤ 15 mmHg in the subgroup of precapillary PH. Since the 4th World Conference on PH, new guidelines have recommended that the exercise criterion should be eliminated (1, 2), given both the marked age-dependency of "normal" mPAP threshold on exercise (3) and the paucity of robust data supporting its clinical relevance (1, 2). The age-dependency of mPAP is much less at rest (3-7) such that a common 20.6 mmHg upper limits of normal (ULN) was suggested in supine healthy subjects (3). Though a mPAP of ≥ 21 mmHg is beyond the normal range (mean + 2 standard deviations) and may be suspicious of pulmonary vascular disease, a small but significant proportion of apparently normal individuals will have a mPAP ≥21mmHg and they will outnumber the previously documented proportion of patients with PH (3). As a result, new guidelines have defined pulmonary hypertension by a mPAP at rest ≥ 25mmHg (mean + 3 standard deviations), and have also highlighted the fact that studies focusing on patients with resting mPAP of 21 to 24 mmHg are especially needed (1-3).

Numerous studies have documented the high percentage of patients at high risk for PH exhibiting elevation of mPAP on exercise > 30 mmHg while their mPAP was normal at rest (8-16), and this may be considered as an early manifestation of pulmonary vasculopathy (12, 14, 17, 18). Most of these studies had been carried out in middle-aged patients, at a time when normal mPAP values during exercise have not yet been defined. Recently, the review of the range of pulmonary haemodynamic responses to exercise in normals by Kovacs et al. was timely in alerting the community to the huge amount of available data supporting the "classical" definition of exercise induced PH in patients aged < 50 years, while the ULN of 30 mmHg was not always supported by the available data in older patients (3). Thus, the precise relationship between resting mPAP and the age-related mPAP responses during mild-to-moderate exercise still deserve further studies in patients free

of PH, and this may have implications for improving our understanding of PH pathophysiology.

The present study examined the range of hemodynamic responses in individuals aged < 50 years with resting mPAP < 25 mmHg being investigated for possible pulmonary vascular disease in our institution who underwent measurement of pulmonary hemodynamic responses to mild-to-moderate exercise while supine.

METHODS

This was a retrospective study. We extracted the catheter laboratory records of all patients who underwent diagnostic right heart catheterization at the Centre National de Référence de l'Hypertension Pulmonaire Sévère, Hôpital Antoine Béclère, Assistance Publique Hôpitaux de Paris, Université Paris-Sud, over a 34 month period (01.01.2007-31.10.2009).

We included patients with a mPAP at rest of less than 25mmHg and a pulmonary artery occlusion pressure (Paop) ≤ 15 mmHg who underwent progressive supine exercise test during the right heart catheterisation procedure. Patients with unexplained exertional dyspnoea or an abnormal screening echocardiogram were included, as well as patients with a history of probable or possible pulmonary thrombo-embolic disease being investigated for chronic thrombo-embolic pulmonary hypertension. As our aim was to examine a "real life" patient population undergoing diagnostic right heart catheterization, we did not exclude patients with significant comorbidities, including diseases known to carry a risk of PH (1, 2). We also excluded patients in whom acceptable quality Paop could not be obtained. On exercise, Paop > 20 mmHg was considered as abnormal but the corresponding patients were not excluded *a posteriori*. The six-minute walking distance, and respiratory and biological tests were obtained according to our routine protocol. Our retrospective study was compliant with requirements of the French Commission Nationale de l'Informatique et des Libertés (CNIL), and right heart catheterization with exercise is part of the usual care at our Institute.

Amongst the 99 eligible patients, only patients aged < 50 years (n=38) were included in our final analysis and 30 mmHg was considered the upper limit of normal on mild-to-moderate exercise (ULN) (3). Patients aged ≥ 50 years were excluded given that Kovacs et al. have suggested that an upper limit of 30 mmHg could not be supported by the available data in such subjects (3). The main risk factors and comorbidities were a previous history of thromboembolic pulmonary disease (n=14, 37%), connective tissue disease (n=8, 21%; namely two lupus and six systemic sclerosis) and anorexigens intake (n=5, 13%) (Table 1).

Patients had baseline hemodynamic measurements showing resting mPAP < 25 mmHg and Paop ≤ 15 mmHg. Then they carried out supine bicycle exercise ergometry (19, 20) including baseline measurements with feet in the pedals but no dynamic exercise followed by a step wise increase of load. The number of steps and the pattern of increase in load were determined for each individual by the operator's judgement based on the patient's age, comorbidities and clinical response to initial load. As we have concentrated on examining the hemodynamic response at mild-to-moderate exercise, we examined the data obtained up to 60 watts (3). As our standard protocol was developed before the new guidelines from the 4th World Conference on PH (1, 2), the exercise was terminated in cases where the mPAP was noted to be over 30mmHg. In patients whose exercise was terminated prior to 60W, either due to symptoms or reaching a mPAP greater than 30mmHg, we analysed their response at their highest workload.

Statistics

Data presented are means ± SD. Comparisons at baseline (rest) were performed by using one-way analysis of variance followed by unpaired t test. The hemodynamic effects of exercise were compared between patients with normal and abnormal mPAP on mild-to-moderate exercise by using a two-way Anova (group x time interaction). Correlations were tested by using the least squares method. Frequency distribution of both gender and mPAP responses between subgroups were compared by using the chi-squared test. Receiver

Operating Characteristic (ROC) curves (with 95% CI) were constructed for testing the ability of the resting mPAP to predict mild-to-moderate exercise mPAP > 30 mmHg. A P value < 0.05 was considered statistically significant. The statistical analysis was performed by using the Statview 512 software (Abacus concepts, Berkeley, CA) except for ROC curves analysis performed by using the MedCalc8.1.0.0 software (Mariakerke, Belgium).

RESULTS

The study population (n=38) comprised 30 women and 8 men (age = 40±8 years) and their clinical characteristics are listed in Table 1. Median workload was 40 watts (mean ± SD = 41 ± 16 watts). Overall 63% of patients (24/38) developed mPAP > 30 mmHg on mild-to-moderate exercise. As compared to the remaining 14 subjects, the 24 patients who developed mPAP > 30 mmHg on mild-to-moderate exercise had lower body surface area, forced expiratory volume in one second, forced vital capacity, diffusing capacity of the lung for carbon monoxide (Table 1). Differences in risk factors and comorbidities were also observed between the two groups (see Table 1). The two groups had similar sex ratio, age, systolic and diastolic arterial pressure, heart rate, and haemoglobin and brain natriuretic peptide blood content. The six-minute walking distance was 478 ± 99 meters in the 24 patients who developed mPAP > 30 mmHg on and 550 ± 100 meters in the remaining 14 patients (P = 0.062) (Table 1).

The hemodynamic characteristics of the study population are listed in Table 2. Individual hemodynamic data are presented as Electronic Supplementary Material. The 24 patients who developed mPAP > 30 mmHg on mild-to-moderate exercise had higher resting mPAP (19±3 vs 15±4 mmHg; P < 0.01) and higher PVRi at rest (3.4 ±1.5 vs 2.2 ±1.1 WU.m²; P < 0.05) as compared to the remaining 14 subjects, (Table 2). They had similar Paop and cardiac index at rest (Table 2), and similar right atrial pressure at rest (4±3 vs 5±3 mmHg; P=NS).

In the overall study population, there was a weak positive relationship between resting mPAP and mild-to-moderate exercise mPAP (r^2=0.39; P <

0.001) (Figure 1). There was no relationship between age and either resting mPAP or mild-to-moderate exercise mPAP.

Hemodynamic responses to mild-to-moderate exercise in the two subgroups are detailed in Table 3 and individual mPAP, Paop and cardiac index values are presented as Electronic Supplementary Material. Cardiac index increased in a similar way and PVRi remained unchanged in the two subgroups (Table 3). Mild-to-moderate differences in Paop changes (P = 0.047) were documented between the two subgroups. On exercise, two patients had their Paop > 20 mmHg (25 and 21 mmHg, see ESM) with > 12 mmHg transpulmonary pressure gradient (24 and 13 mmHg, respectively), and both had their mPAP > 30 mmHg.

Exercise mPAP exceeded 30 mmHg in 15/27 (55%) of the patients with resting mPAP < 21 mmHg and in 9/11 (82%) of the patients with resting mPAP between 21-24 mmHg (P=NS) (Table 4). The 7 patients with resting mPAP 22-24 mmHg all had exercise mPAP > 30 mmHg. ROC curve analysis (Figure 2) indicated that a resting mPAP > 15 mmHg predicted exercise mPAP > 30 mmHg with 88% sensitivity (95% CI = 68-97%) and 57% specificity (95%CI = 29-82%).

DISCUSSION

Our retrospective study was performed in 38 patients aged < 50 years, free of PH (resting mPAP < 25 mmHg), being investigated in our centre for possible vascular disease between 01.01.2007 and 31.10.2009. The main results were as follows: i) patients with mild-to-moderate exercise mPAP > 30 mmHg had higher resting PVRi and higher resting mPAP; ii) it was not possible to reliably set a lower limit of resting mPAP which guarantees normal mPAP at mild-to-moderate exercise loads; and iii) all 7 patients with resting mPAP 22-24 mmHg had exercise mPAP > 30 mmHg. The clinical relevance of such findings deserves further long-term follow-up studies.

The present study was undertaken following recent articles and editorials that stressed the necessity of further research in the area of haemodynamics in patients with pulmonary vascular diseases, with special

focus on the potential link between resting and exercise pulmonary hemodynamics and on the significance of resting mPAP 21-24 mmHg (1-3, 12, 17, 18). Numerous studies (8-16) have documented the so-called "exercise-induced pulmonary hypertension" (12, 13, 15, 17) frequently observed in various populations carrying a high risk of PH while their mPAP was normal at rest. To the best of our knowledge, our study is the first to take into account the recent recommendations made by Kovacs et al., namely that the 30 mmHg ULN for the mPAP achieved on mild-to-moderate exercise fairly applies in patients aged < 50 years only (3). Thus elderly patients (61/99) were not included in our final analysis given that an ULN of 30 mmHg could not be supported by the available data in such patients (3).

Our study focused on mild-to-moderate exercise only, and this was based on the following rationale. *First*, the literature review made it possible to define reliable ULN for mPAP during mild-to-moderate exercise (3, 5). *Second*, reliable and consistent mPAP, Paop and cardiac output data have been published during mild-to-moderate exercise (4, 5, 21) thus allowing pathophysiological interpretation of our data. *Finally*, light exercise may reflect the daily life physiological stress put on the pulmonary circulation and right ventricle more accurately than maximal exercise (1, 2).

In healthy subjects < 50 years, the resting mPAP is circa 14 mmHg on average (1-3) and the hemodynamic changes on mild-to-moderate exercise while supine slightly differ according to the research team, with either unchanged PVR (5, 22), or slightly decreased PVR (23). Pulmonary capillary pressure may slightly increase (3, 5, 6, 24), although other studies and reference textbooks often indicate unchanged pulmonary capillary pressure during exercise. The 18 mmHg resting mPAP value documented in our study (Table 1) is consistent with that previously reported in populations similar to ours (12-15) and reflects the fact that patients were investigated in our centre for possible vascular disease. It has been suggested that age, gender and resting systolic blood pressure significantly influence mPAP responses to exercise, but all were similar in the two groups (Table 1). The underlying risk factors and comorbidities (Table 1) may contribute to explain, at least in part,

the high percentage (24/38 =63%) of patients exhibiting abnormal mPAP responses (8-16).

The stress put on the right ventricle is minimal at rest and this may in part explain why resting pulmonary hemodynamics do not tightly correlate with exercise pulmonary hemodynamics in patients with established PH (6, 8, 12, 19, 20, 25, 26). In our patients at risk for PH and exhibiting normal mPAP at rest, ROC curve analysis indicated that resting mPAP > 15 mmHg predicted exercise mPAP>30 mmHg with 88% sensitivity and 57% specificity. Interestingly, Saggar et al. have suggested that resting mPAP ≥ 14 mmHg was associated with abnormal mPAP responses on exercise in patients with systemic sclerosis (15). However, in our study, it was not possible to reliably set a lower limit of resting mPAP which guarantees normal mPAP at mild-to-moderate exercise loads

As far as the upper limit which guarantees abnormal mPAP at mild-to-moderate exercise loads is concerned, it may be expected that the closer the resting mPAP lies to the ULN on exercise (30 mmHg) the more likely the exercise mPAP threshold is breached. Consistently, resting mPAP was higher in the 24 patients who developed mPAP > 30 mmHg on mild-to-moderate exercise, and this was explained by the 55% higher levels for resting PVRi as compared to the remaining 14 patients who did not develop mPAP > 30 mmHg on mild-to-moderate exercise (Table 2). This could also explain why exercise mPAP was > 30 mmHg in 88% (9/11) of the patients with resting mPAP 21-24 mmHg and in all 7 patients with resting mPAP 22-24 mmHg.

Significant differences in Paop changes were also documented and contributed to explaining differences in exercise mPAP in the two subgroups (Table 2). Amongst the 24 patients with mPAP > 30 mmHg on exercise, 2 (8%) had their exercise Paop > 20 mmHg (see ESM), thus confirming that acute left ventricular dysfunction could also contribute, e.g., diastolic dysfunction (27, 28). Conversely, similar cardiac output responses on exercise were documented in the two subgroups, and similar PVRi responses as well (Table 2). In summary, in patients aged < 50 years and free of PH, the increased PVRi at rest resulting in higher resting mPAP was the main factor

likely to explain abnormally high mPAP on mild-to-moderate exercise. Additionally, further exercise-related increases in capillary wedge pressure also played a role.

Our study did not involve healthy subjects but patients with symptoms and a certain risk of PH. Accordingly, the results cannot be used to create novel thresholds of physiologic changes during exercise and may not be compared with studies examining healthy individuals. The clinical heterogeneity of the study group reflects the current "real life" experience of a reference PH centre. Other limitations include the retrospective study design and the lack of extensive assessment of left ventricular function at rest (e.g., detailed echocardiography to detect diastolic and/or systolic dysfunction). The intrinsic limitations related to the exercise protocol must also be discussed. We have examined mPAP responses on mild-to-moderate exercise as best as we could, with the understanding that we do not measure oxygen consumption during our right heart studies. We could not determine the slope and pressure axis intercept of the mPAP-cardiac output relationship, as the number of data points and pattern of exercise varied between individuals. The determination of multipoint mPAP-cardiac output plots provides more accurate insight into the nature of PVR than the single point PVR, as the intercept may be higher than pulmonary capillary pressure (6, 7, 19, 20, 29, 30). Thus the observed pattern of increased transpulmonary pressure gradient and increased cardiac output together with unchanged or decreased single-point PVR does not necessarily reflects unchanged or decreased resistive properties of the pulmonary circulation (7, 20, 29, 30). Similarly, we cannot exclude the possibility that our results reflect averaging patients with various patterns of mPAP-cardiac output relationship on exercise (20). The two patients with exercise Paop > 20 mmHg were included in our final analysis as our aim was to study the relationship between resting and mild-to-moderate exercise mPAP in patients at risk of PH but free of PH at rest (mPAP < 25 mmHg) and with normal filling pressure at rest (Paop ≤ 15 mmHg). Finally, elderly subjects could not be studied for the above-mentioned reasons and further studies focusing on this population are thus needed.

The implications of our study must be carefully considered. First of all, we wish to emphasise the fact that our study did not intend to challenge the 4th World Conference proposal that exercise test must be abandoned in the definition of PH (1, 2). However, we remain concerned by the fact that the new consensus does sometimes leave clinicians faced with a patients that have symptoms suggestive of pulmonary vascular disease but with resting mPAP < 25 mmHg (12, 14, 18). Interestingly, our study pointed to major redundancy between resting and mild-to-moderate exercise mPAPs in the subgroup of patients < 50 years with resting mPAP 22-24 mmHg. The 22-24 mmHg range of resting mPAP may help clinicians to recognize patterns consistent with abnormal hemodynamic responses on mild-to-moderate exercise. Elsewhere, our study demonstrates a lack of tight correlation between resting and exercise hemodynamics in non-PH patients. In other words, our data would suggest that it is not possible to reliably set a lower limit of resting mPAP which guarantees that pulmonary hemodynamic responses to exercise will be normal at mild-to-moderate exercise loads in patients <50yrs.

In conclusion, in subjects aged < 50 years and free of PH, patients with mild-to-moderate exercise mPAP > 30 mmHg had higher resting PVRi and higher resting mPAP. Although all patients with resting mPAP 22-24 mmHg had exercise mPAP > 30 mmHg, there was no resting mPAP threshold value that could reasonably predict normal/abnormal response on mild-to-moderate exercise. The clinical relevance of such findings deserves further long-term follow-up studies.

Acknowledgements and footnote.

The authors thank the nurses of the catheterization lab for their helpful work. Part of the study has been presented at the ERS 2010 meeting held in Barcelona, and consequently appears as an abstract (#204: Whyte K et al. Relationship between mean pulmonary artery pressure at rest and on mild-to-moderate exercise in subjects aged < 50 years and free of pulmonary hypertension).

Legends of the figures.

Figure 1. Linear relationship between exercise mPAP (ex_mPAP) and resting mPAP. N=38; r^2= 0.39; P < 0.001.

Figure 2. Receiver Operating Characteristic (ROC) curve. A resting mPAP > 15 mmHg predicted exercise mPAP > 30 mmHg with 88% sensitivity (95% CI = 68-97%) and 57% specificity (95%CI = 29-82%).

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Table 1. Characteristics of the study population

	Overall population n=38	mPAPex ≤ 30 mmHg n=14	mPAPex > 30 mmHg n=24	P value
Demographic and clinical data				
Female gender, n (%)	30 (80)	10 (71)	20 (83)	NS
Age, y	40±8	40±8	40±8	NS
BSA, m²	1.72±0.22	1.86±0.22	1.63±0.18	< 0.01
SAP, mmHg	118±17	123±18	116±16	NS
DAP, mmHg	76±10	77±9	75±10	NS
Heart rate, bpm	76±11	74±12	78±10	NS
Hemoglobin, g/dL	13.3±2.0	13.7±1.7	13.2±2.1	NS
BNP, pg/mL	31±21	30±8	32±24	NS
6MWD, m	505±104	550±100	478±99	0.062
FEV1, predicted %	86±22	98±20	81±21	0.048
FVC, predicted %	85±21	94±19	80±21	0.110
DLCO, predicted %	62±20	74±18	56±19	0.030
Risk factors and comorbidities				
History of thromboembolic disease.	14	6	8	
CTD	8	1	7	
Anorexigens	5	5	0	
Miscellaneous	7	1	6	
None	4	1	3	

Values are means ± SD. BSA: body surface area. SAP: systolic arterial pressure. DAP: diastolic arterial pressure. BNP: brain natriuretic peptide. 6MWD: six-minute walking distance. FEV1: forced expiratory volume in one second. FVC: forced vital capacity. DLCO: diffusing capacity of the lung for carbon monoxide. CTD: connective tissue diseases. NS = not significant.

Table 2. Hemodynamics at rest and at mild-to-moderate exercise (n=38).

	Rest	**Mild-to-moderate exercise**
RAP, mmHg	4 (3)	not recorded
mPAP, mmHg	18 (4)	31 (8)
Paop, mmHg	8 (3)	12 (5)
TPG, mmHg	10 (5)	19 (7)
CI, L/min/m²	3.49 (0.54)	6.34 (1.13)
PVRi, W.U.m²	2.9 (1.5)	3.1 (1.5) [NS]

Values are means (SD).

RAP: right atrial pressure. mPAP: mean pulmonary artery pressure. Paop: pulmonary artery occlusion pressure. TPG: transpulmonary pressure gradient. CI: cardiac index. PVRi: pulmonary vascular resistance index. W.U. Wood Units. Each $P < 0.001$ except where indicated. NS = not significant.

Table 3. Rest and exercise hemodynamic data according to the normal/abnormal response of mPAP on mild-to-moderate exercise (mPAPex).

	mPAPex ≤ 30 mmHg n=14		**mPAPex > 30 mmHg n=24**		**2-way Anova**
	Rest	Exercise	Rest	Exercise	**P**
mPAP, mmHg	15(4)	23(5)	19(3)**	36(5)	0.0001
Paop, mmHg	8(4)	10(4)	8(3)NS	13(5)	0.047
TPG, mmHg	8(4)	13(5)	11(4)*	22(6)	0.0001
CI, L/min/m²	3.62 (0.56)	6.26 (1.24)	3.41 (0.52) NS	6.38 (1.09)	0.30
PVRi, W.U.m²	2.2 (1.1)	2.1(1.0)	3.4(1.5) *	3.7(1.5)	0.25

Values are means (SD).

mPAP: mean pulmonary artery pressure. Paop: pulmonary artery occlusion pressure. TPG: transpulmonary pressure gradient. CI: cardiac index. PVRi: pulmonary vascular resistance index.

NS not significant * $P < 0.05$ and ** $P < 0.01$

versus resting values in the mPAPex $\leq$ 30 mmHg subgroup.

Table 4: Summary of resting mPAP/exercise mPAP in the 38 patients.

Exercise mPAP	Resting mPAP <21 mmHg	Resting mPAP 21-24 mmHg	Total (n)
≤ 30mmHg (n)	12	2	14
> 30mmHg (n)	15	9	24
Total (n)	27	11	38

Figure 1

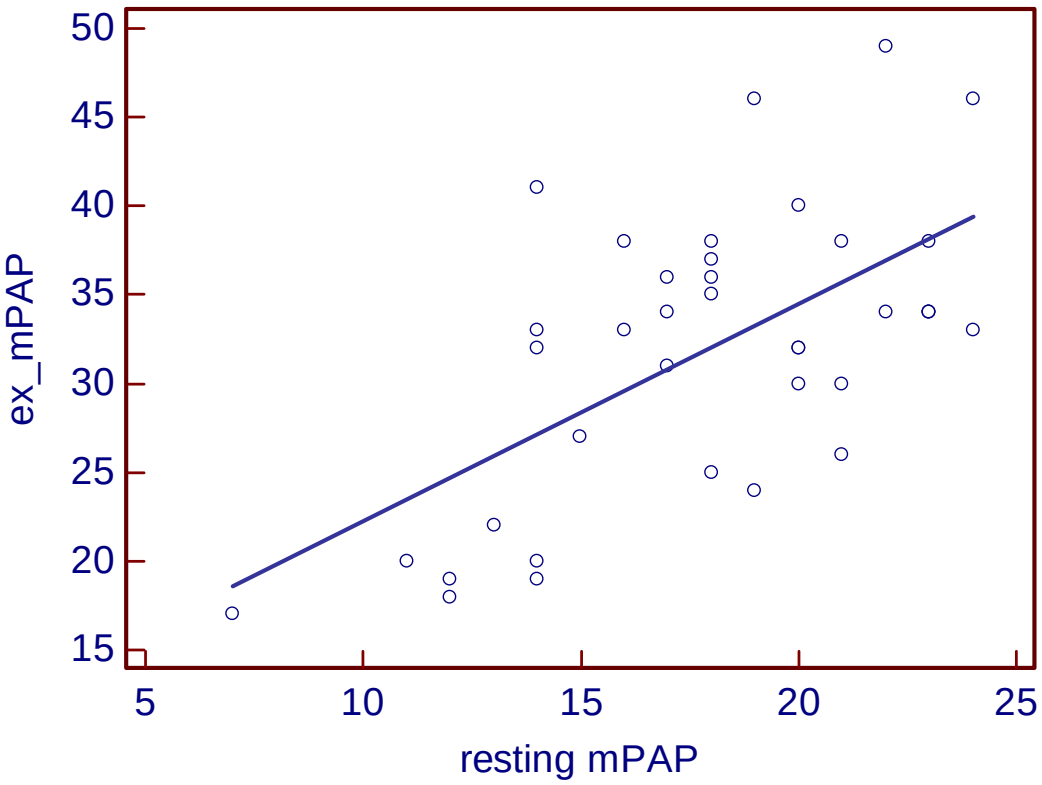
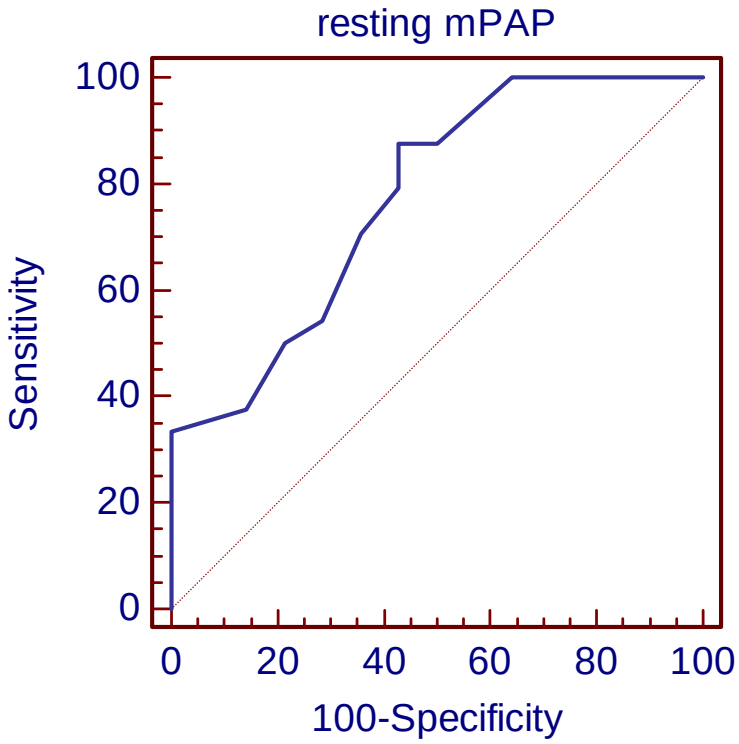


Figure 2


resting mPAP
Sensitivity
100
80
60
40
20
0
0
20
40
60
80
100
100-Specificity

ESM: Individual hemodynamic data at rest and on mild-to-moderate exercise (n=38)

Patient n°, initial	Age y	Sex	BSA m²	mPAP rest mmHg	mPAP ex mmHg	Paop rest mmHg	Paop ex mmHg	CI rest L/min/m²	CI ex L/min/m²
1.KE	43	F	1.74	19	24	7	12	4.84	8.22
2.FI	45	F	1.75	17	31	3	12	4.04	7.86
3.GU	46	F	1.43	18	35	11	18	3.57	7.38
4.KI	46	F	1.50	23	38	4	6	3.17	4.57
5.RU	48	F	1.73	14	33	9	18	4.41	7.43
6.DO	38	F	1.34	14	32	2	14	2.59	5.07
7.GE	44	F	1.53	22	34	8	10	3.73	6.57
8.FR	45	F	1.89	17	30	1	8	3.81	7.14
9.TA	28	M	1.66	18	32	12	17	3.33	6.42
10.ME	48	F	1.69	16	32	8	12	3.53	7.15
11.GU	45	F	1.50	24	46	6	7	3.60	6.03
12.BR	27	F	1.73	24	33	7	8	3.03	5.55
13.PI	27	F	1.39	23	34	10	10	4.68	6.65
14.LA	38	F	1.69	14	41	11	17	3.43	8.61
15.YE	37	F	1.53	20	32	10	11	3.51	5.96
16.KR	46	F	2.28	14	20	7	12	3.77	5.35
17.SE	35	F	1.74	18	25	13	16	3.97	7.21
18.DA	47	F	1.63	19	46	6	19	2.85	5.77
19.MO	37	F	2.15	20	30	7	8	3.19	4.72
20.BE	36	M	1.92	18	32	13	17	3.30	6.85
21.BU	46	F	1.51	22	49	8	25	3.11	5.76
22.PA	42	M	1.95	21	30	14	16	2.65	4.44
23.HO	35	F	1.42	17	34	6	9	3.38	7.25
24.BR	47	F	1.97	12	19	5	10	3.54	5.81
25.MO	38	M	2.13	15	26	12	15	3.78	5.31
26.RI	38	F	1.54	18	36	8	13	3.20	5.03
27.MI	41	M	1.65	12	18	9	12	4.00	7.42
28.RO	49	F	1.54	20	40	6	9	2.21	4.61
29.LA	22	F	1.66	16	33	11	14	3.42	6.48
30.FR	36	F	1.55	11	20	5	5	2.82	7.48
31.BE	29	F	1.86	21	35	11	13	3.17	7.39
32.RE	46	F	2.05	23	34	10	21	3.90	6.93
33.LE	41	M	1.69	20	32	8	11	3.41	7.10
34.JU	47	F	1.83	7	13	3	4	4.17	6.80
35.CA	19	F	1.67	13	22	5	5	3.47	6.29
36.DE	45	F	1.64	21	26	11	9	3.41	6.98
37.HO	46	M	1.93	23	34	8	12	3.20	4.77
38.BE	33	M	1.80	14	19	8	12	3.28	4.47

BSA: body surface area. ex: mild-to-moderate exercise. mPAP: mean pulmonary artery pressure.

CI: cardiac index; Paop: PA occlusion pressure.