Available online at www.rajournals.in

RA JOURNAL OF APPLIED RESEARCH
ISSN: 2394-6709
DOI:10.47191/rajar/v9i4.01
Volume: 09 Issue: 04 April-2023

International Open Access

Impact Factor- 8.174

Page no.- 156-163

Hemodynamical Approach to Pulmonary Hypertension

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ARTICLE INFO

Published Online:
01 April 2023

ABSTRACT

Pulmonary hypertension (PH) is a pathophysiological disorder characterized by a vascular obstruction leading to increased right ventricular overload. It can be caused by multiple conditions that we classify into 5 clinical groups. PH is defined hemodynamically and the role and indications of cardiac catheterization are increasingly important. The subject includes a panoply of pathologies with great complexity at the same time physio-pathological, histo-etiopathogenic, genetic... which are gathered under one chapter: the pulmonary vascular pathology. Right heart catheterization (RHC) is crucial and allows to measure and calculate variables to determine patients hemodynamics that are necessary for positive, etiological and severity diagnosis. It can also have therapeutic purpose: vasoreactivity test (APVT), pre-gesture assessment.

Materiel and Methods: retrospective cross-sectional study of 143 patients with suspicion of pulmonary hypertension whom underwent RHC (±left heart) performed between January 2017 and December 2021 in cardiology A department within Ibn Sina university hospital center.

Results: In terms of the results of our study, we have a very diverse review in which PH is assessed at different levels for all groups and subgroups using a multitude of hemodynamic parameters. Our population is characterized by a clear predominance of women

The average age of all 143 cases is 38 years. In terms of hemodynamic classification, isolated pre-capillary PH is the most common (52%). 64% of our cases had PVRs >2 Wu indicating the prevalence of pulmonary vasculopathy. Group 3 represents the population with the most preserved hemodynamical severity parameters. The main vasoreactivity test performed was the NO test.

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KEYWORDS: Pulmonary hypertension, cinical groupe, hemodynamics, right heart catheterization.

INTRODUCTION

Pulmonary hypertension (PH) is a pathophysiological disorder characterized by a vascular obstruction leading to increased right ventricular overload. It can be caused by multiple conditions that we classify into 5 clinical groups. PH is defined hemodynamically by a mean pulmonary arterial pressure (mPAP) above 20mmHg. Right heart catheterization (RHC) is crucial and allows to measure and calculate variables to determine patients hemodynamics that are necessary for positive, etiological and severity diagnosis. It can also have therapeutic purpose: vasoreactivity test, pre-gesture assessment.

MATERIEL & METHODS

We conducted a retrospective cross-sectional study of 143 patients with suspicion of pulmonary hypertension whom underwent RHC (±left heart) performed between January 2017 and December 2021 in cardiology A department within Ibn Sina university hospital center. Collected data included clinical informations, ultrasound, biological markers and hemodynamics. We included patients with intermediate to high probability of PH, patients having disorders with high risk of PH such as scleroderma, patients under specific or non-specific treatment who need hemodynamic reevaluation and patients with cyanotic CHD (congenital heart disease) candidate for cavo-pulmonary diversion. We chose to exclude patients who had catheterism intervention such as closure of atrial defect or ductus arteriosus.

The goal of our study is to precise epidemiological, etiological and hemodynamics aspects of patients who benefited from catheterization to evaluate pulmonary hemodynamics and to compare them to literature.

Our procedure aims to determine hemodynamics including pressures (pulmonary arterial pressure, wedge pressure, right atrial pressure, right ventricular pressure, systemic pressures), cardiac output, pulmonary and systemic vascular resistance, gradients (diastolic and transpulmonary) and differents levels of oxygen blood saturation… For that purpose, we usually use

a 6F Swan-Ganz balloon catheter inserted in the right femoral vein. We retain the PH diagnosis if the mPAP is above or equal to 20mHg. To obtain PAWP, the balloon is inflated and the measure is taken at the end of expiration. Cardiac output is measured using the direct Fick method.

We also perform a left heart catheterization puncturing generally the femoral artery, especially if it's a first procedure or if a left heart disease is suspected. We enclose with pulmonary angiography, necessary for group 4 and also if abnormal pulmonary vein return is suspected.

Concerning reactivity testing, oxygen test is carried out in case of group 3. The most important test in our cath lab is the NO test (nitric oxide), that we achieve in case of idiopathic arterial PH and operable cases of CHD. Positivity criteria are : decrease of more than 10mmHg in PAPm to a value below 40mmHg, with unchanged or increased cardiac output. The third test that we often realise if the filling test, if a left participation is strongly suspected with a PAWP<15mmHg, especially of the PAWP is between 12 and 15mmHg.

RESULTS

General data:

Firstly, from an epidemiological point of view, there is a clear predominance of women (76%), which decreases for groups 3, 4 and 5, while it increases for groups 1 and 2, reaching a percentage of 87% for group 2. The average age of all 143 cases is 38 years. PH was diagnosed in 123 out of 143 cases. From the epidemiological point of view, we noted a clear predominance of group 1 reflecting the particular interest of RHC in this group, followed by group 2, group 3, group 4 and in the last row group 5.

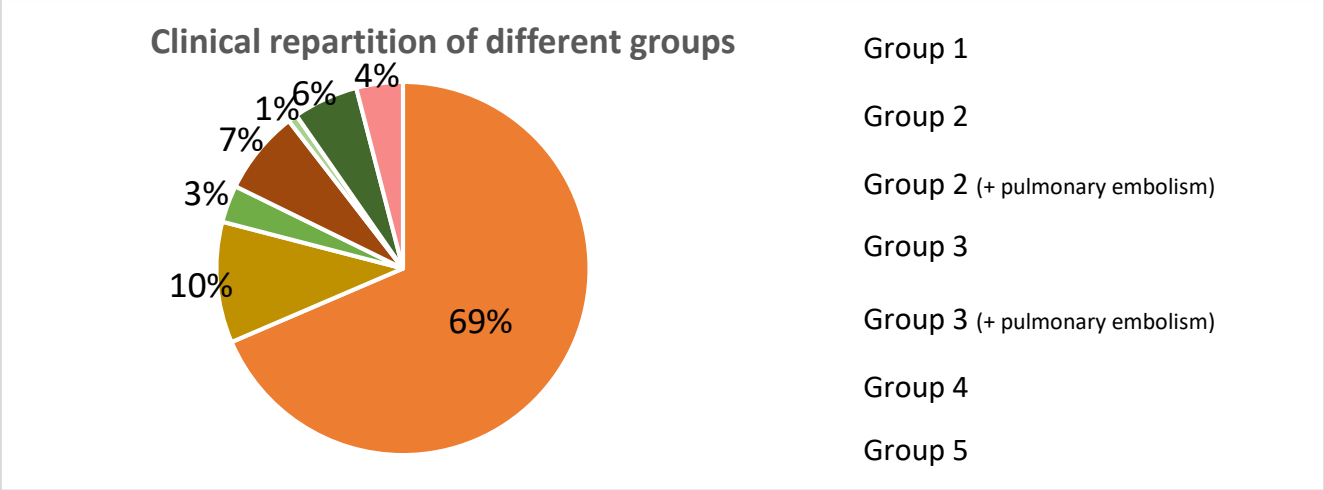
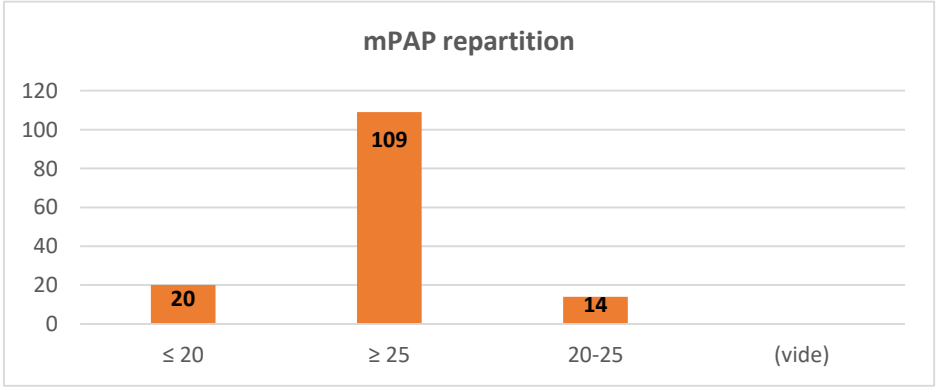


Figure 1: clinical classification of our patients

Hemodynamic data:

Concerning the hemodynamic approach, we noted several elements including: vascular site of punction, mostly occluded pulmonary artery (left one), before confirming PH diagnosis and classifying patients into pre-capillary PH, post capillary PH, combined PH and increased flow PH. 14% of all cases had low mPAP. The percentage of low mPAP varies by groups and sub-groups, for example in left heart diseases, given the limited number of indications for RHC, all the catheterization performed confirmed clinically and echocardiographically suspected PH without exception. In the population of connective tissue diseases (CTD) within group 1, the percentage of procedures with low pulmonary pressures is important: 21%, and rises to 23% for scleroderma illustrating the indication for screening in this disease. Also, the rate of cases of CTD in the former grey zone between 20 and 25mmHg is 26%. Lowering the threshold to 20mmHg is therefore particularly important in this population.



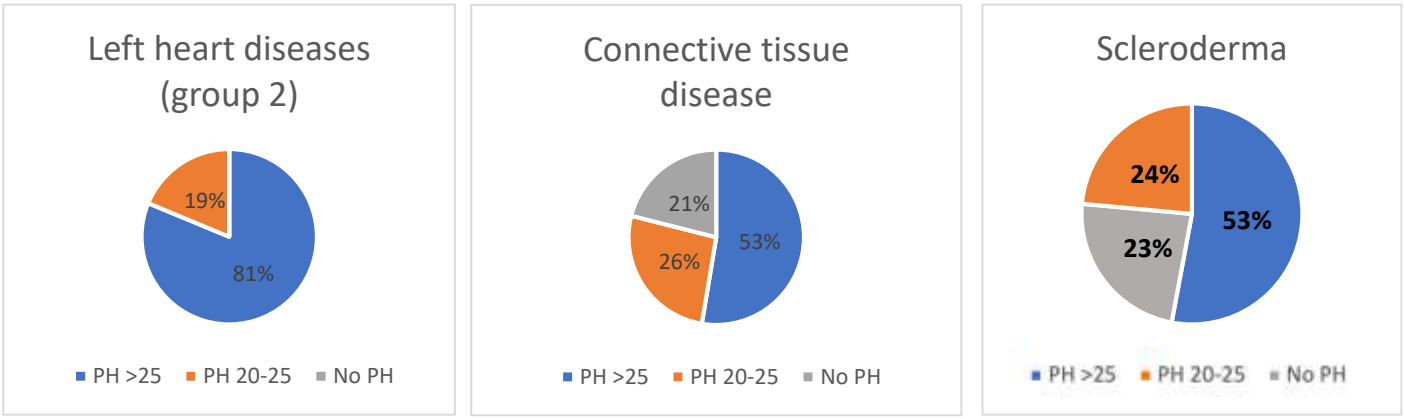


Figure 2: repartition of mPAP in our study (all cases, group 2, CTD, scleroderma)

In terms of hemodynamic classification, isolated pre-capillary PH is the most common (52%), followed by combined PH (31%), isolated post-capillary PH (13%) and finally PH by flow elevation without PVR elevation (14%).

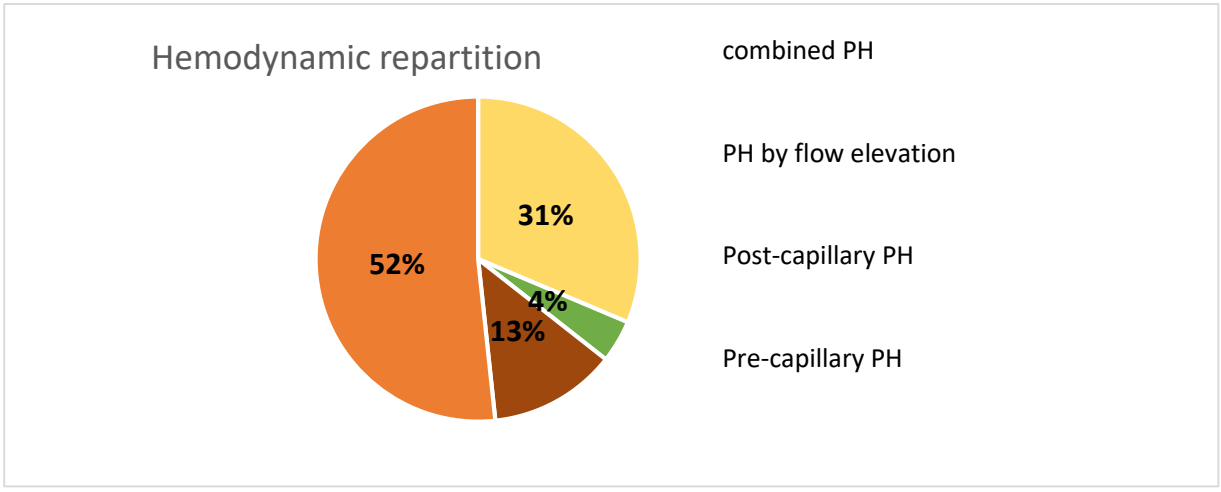
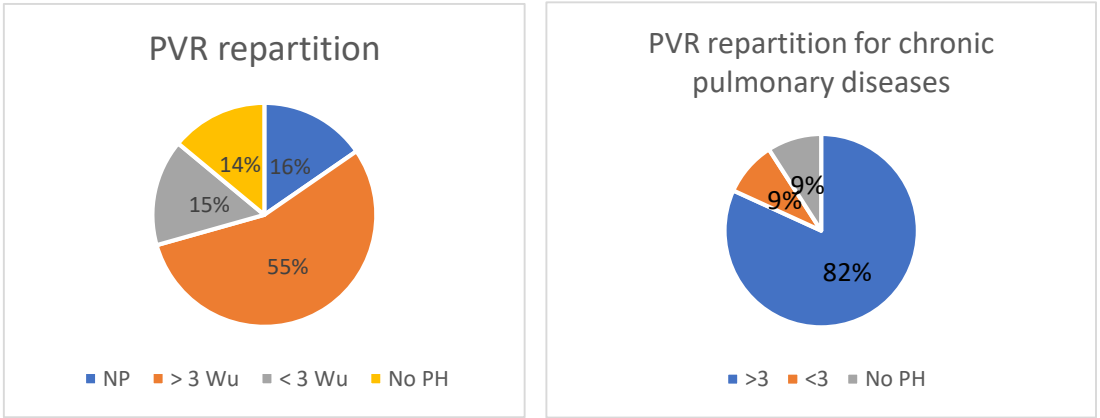


Figure 3: hemodynamic reparition of our review

For the distribution of high PVRs, we will compare this distribution according to the old cut-off of PVR fixed at 3 Wu to the new cut-off according to the last recommendations ESC/ERS 2022 fixed at 2 Wu. 64% of our cases had PVRs >2 Wu indicating the prevalence of pulmonary vasculopathy. According to the old cut-off, 55% had PVR >3 Wu (this is still more than half). We found a significant high PVR rate for chronic lung disease of 91% (82% old cut-off), which explains the need to introduce the PVR parameter in the definition of this group

Ancien cut-off



Nouveau cut-off

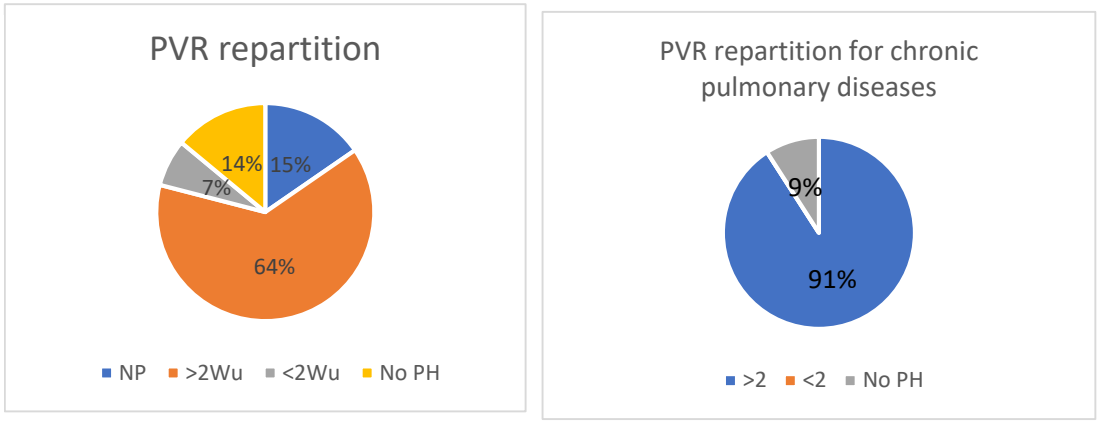


Figure 4: PVR repartition in our review (all cases, groupe 3)

Severity diagnosis:

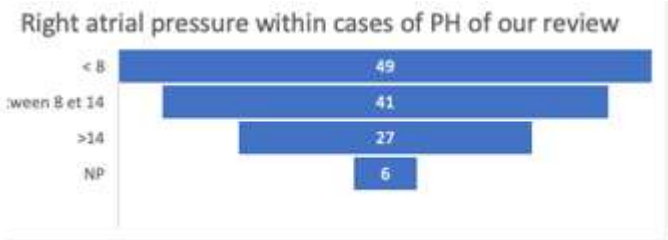
We selected as severity parameters: RAP, CI and SvO_2 measured at the TVI.

- For RAP 22% had a high RAP >14.
- For CI, except for congenital cases, 40% had a low CI <2.4.

Group 4 constitutes the group with the most altered CI and RAP averages.

- Regarding mixed venous saturation, 25% had a low SvO2 <60%. Idiopathic PH followed by connective tissue diseases constitute the entities with the most low saturations.

Group 3 represents the population with the most preserved hemodynamical severity parameters.



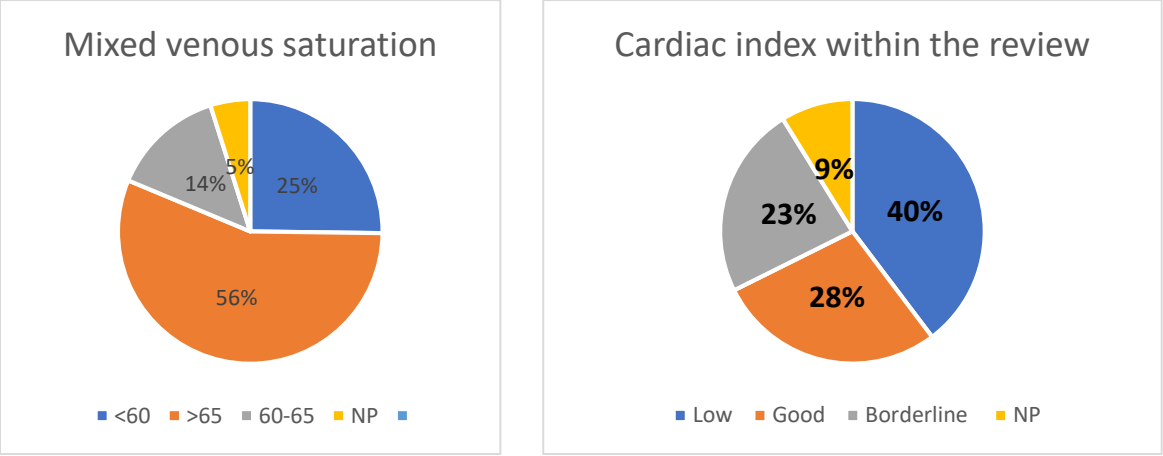


Figure 5: severity hemodynamics parameters in our review (RAP, SvO2, CI)

Vasoreactivity test:

The main vasoreactivity test performed was the NO test. First notice: within our 143 cases, the NO test was not performed in 80 procedures. There was initial vasoreactivity in 21KT. Two patients were classified as chronic responders to CI. For cases of idiopathic PH, NO testing was always performed except in control catheterisms when the former was negative. In this idiopathic population, apart from the two chronic responders to calcium antagonists whose NO test remained positive on the control catheterisms, none of the rest of the patients of the review (14 patients) met the criteria for NO testing positivity and 2 patients had a reverse response with worsening pulmonary pressure numbers. We note that the NO test is repeated in the control catheterism when the first one reveals a positive NO test in order to verify that it is indeed a chronic responder.

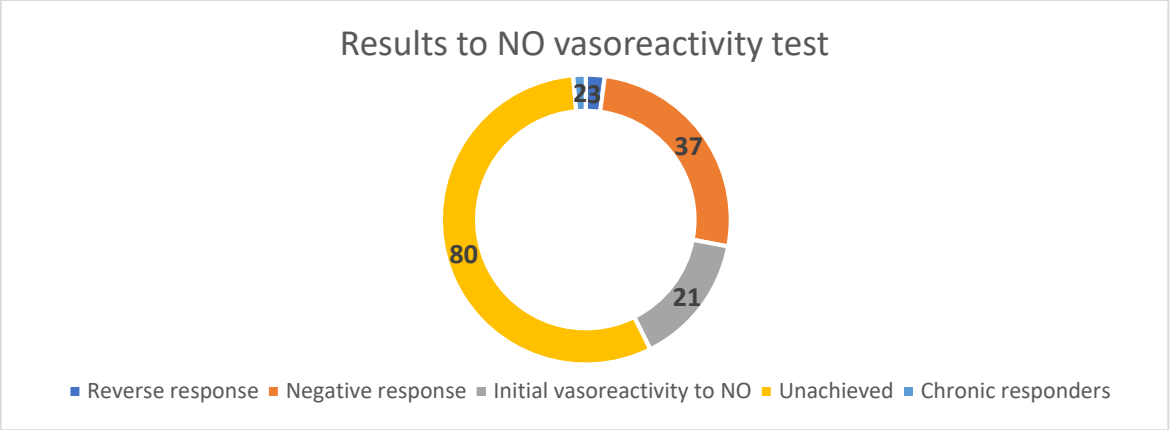


Figure 6: vasoreactivity testing results of all our cases

Side effects:

On another note, complications identified in our series are few and mostly benign.

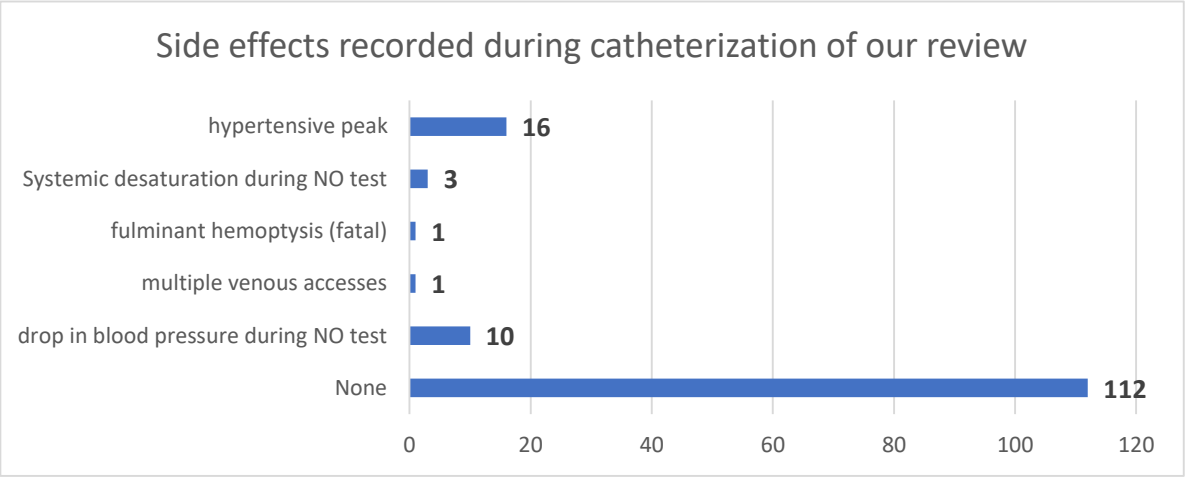


Figure 7: Complications and side effects recorded during catheterization of our review

DISCUSSION

Pulmonary hypertension is characterized by a great clinical disparity with innumerable etiologies and a great heterogeneity of its affections which are differentiated and classified according to clinical, hemodynamic and histo-pathological, but also molecular, genetic and humoral data.

First difficulty we encountered is classifying all patients. In fact, it can be easy and logical for some populations, as CHD found in children where the simple left-right shunt is classified as group 1. But in contrast, finding a CHD in adults (such as aged atrial septal defects) gives a lot of trouble since classifying it in one group is more difficult. Same for connective tissue disease where the pulmonary vasculopathy can be multi-factorial: respiratory, cardiac, thrombo-embolic… We were confronted to this difficulty of classification for several patients, so we had to focus on their medical history, comorbidities, hemodynamic profile... to be able to draw a predominant character. We chose to discuss each group separatly.

Group1 : For group 1, the comparison of epidemiological data with the literature (1) shows a more marked female predominance in our population, as well as a younger population of about 10 years, except for CTD whose average age is close to the literature.

Concerning hemodynamics, by analyzing our series and the French registry (1), we noticed: the highest average of mPAP is found in congenital, the lowest in CTD ; PVRs of our review are on average lower (13 versus 20). The most preserved values of RAP and CI are found in the congenital ones, the most altered in the idiopathic ones.

Table 1: Comparison of hemodynamic results of group 1 (our serie vs. French registry)

	Average mPAP (mmHg)		**Average indexed PVRs** (Wu/m²)		**Average RAP** (mmHg)		**Average CI** (l/min/m²)	
	Our review	French study	**Our review**	French study	**Our review**	French study	**Our review**	French study
Group 1 and Idiopathic chronic responders to CCBs	**59,15**	55 ±15	**13,76**	20,5 ±10,2	**9,67**	8 ±5	**2,45**	2,5 ±0,8
Connective diease tissue (group 1)	**56,27**	56 ±14	**18,84**	22,8 ±10	**11,86**	9 ±5	**2,06**	2,3 ±0,7
Congenital heart disease (group 1)	**40,53**	45 ±14	**22**	16,5±8,8.	**9,33**	8 ±6	**2,37**	2,5 ±0,7
	66,29	68 ±18	**11,96**	26 ±15,2	**8,71**	6 ±4	**2,76**	2,7 ±1,1

Concerning vasoreactivity test since it concerns group 1: we note that it was not performed in more than half of our cases given its limited indication to suspected idiopathic, heritable, or drug-related PH. Also, the main vasoreactivity test performed is the NO testing following recent recommandations. The hyperoxia testing is less crucial and has no place in predicting response to calcium channel blockers (CCBs).

Group 2:

This is the most frequent form of PH, most often affecting women of advanced age with co-morbidities and especially a metabolic syndrome (2). In our review, these different risk factors and co-morbidities are more frequently found in group 2 patients than in the other groups. Diabetes and hypertension were found in almost half of our patients, obesity or dyslipidemia in 27%. We subdivided this group into 2 hemodynamic profiles: isolated and combined postcapillary. 62% of our patients were isolated and 37% were combined, with the cut-off point of PVR being 3 Wu. When the cut-off point is 2, the trend is strangely reversed, with 68% combined and 31% isolated. This is intended to introduce many more patients into pulmonary vasculopathy, which may be of therapeutic interest.

Indeed, the objective of this isolated/combined distinction is that, in the first profile, it is necessary to optimize the treatment of the heart disease in question by correcting the risk factors. The second type of profile could benefit from specific PAH treatments. Concerning the hemodynamic severity: Combined PH presents more altered figures whatever the parameter studied.

Table 2: Severity hemodynamics in group 2 PH of our review

Group 2 PH of the review		
Hemodynamics of severity	**Isolated**	**Combined**
Average RAP (mmHg)	13,5	14,2
Average CI (l/min/m²)	2,61	1,77
Average SvO_2 (%)	65,22	56,16
PVR (Wu)	1,43	7,17

Group 3:

The sex ratio of this group is close to 1. Moderate PH is a common complication of chronic and hypoxemic lung diseases, however, severe PH is rare in the literature (3). The definition of severe PH has been modified in the latest guidelines (4). The new definition of severity depends on PVRs: a group 3 PH is severe when PVRs are higher than 5 uW.

Considering the new definition, severe PH is not that rare, we found in our review 50% of moderate PH and 50% of severe PH with more marked hemodynamic alterations for CI and SvO2. Based on the old definition of severity (a first category of moderate PH with mPAP between 20 and 35 mmHg and a second category of severe PH with mPAP>35 or low CI), the rate of severity was still 50% but with no difference in hemodynamic alterations. Thus, this new definition is of great interest.

Table 3: Severity hemodynamics in group 3 PH of our review

Group 3 PH of our review		
Hemodynamics of severity	Moderate PH (PVR <5 uW)	Severe PH (PVR >5 uW)
Average RAP (mmHg)	9,2	8,6
Average CI (l/min/m²)	2,75	1,99
Average SvO_2 (%)	70,8	48,8
Average PVR (Wu)	3,55	9,11

Group 4:

Systematic screening for PH after a pulmonary embolism episode is not supported to date, especially since a significant number of CTEPH develop in the absence of previous acute episode. Chronic thrombo-embolic PH or CTEPH is an important indication for RHC despite the technical complexity and the high risk of bleeding during manipulation. The only death in our serie during the procedure corresponds to a case of CTEPH. The interest is also in the realization of the pulmonary angiography which can show impressive images.

On the hemodynamic level, a large international registry (5), including 679 CTEPH patients reported the following data: Severe precapillary PH with a mean mPAP of 47 mmHg and PVR of 8.9 Wu. According to this registry, in these patients, for even a moderate elevation of mPAPs (20 to 24 mmHg), PVRs were generally high. In our series, the mean PAPm of patients in group 4 was 59.5 mmHg with a mean PVR of 17.95 Wu, which is consistent with, and even more severe than, the literature.

Table 4: Hemodynamics in cases oh CTEPH of our review

	CTEPH in our review		
Hemodynamics of severity	**CTEPH**	**Isolated pre-capillary PH**	**Predominant pre-capillary PH with a post-capillary component**
Average RAP (mmHg)	13	9	15,6
Average CI (l/min/m²)	1,73	3,95	1,54
Average SvO_2 (%)	54	62	46
Average PVR (Wu)	17,95	10,05	25,85

CONCLUSION

PH has a hemodynamical definition and the role and indications of cardiac catheterization are increasingly important. The subject includes a panoply of pathologies with great complexity at the same time physio-pathological, histo-etiopathogenic, genetic... which are gathered under one chapter: the pulmonary vascular pathology.

In terms of the results of our study, we have a very diverse review in which PH is assessed at different levels for all groups and subgroups using a multitude of hemodynamic parameters.

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