

# How Does the New Hemodynamic Definition Affect the Prevalence of Pre-capillary PH?

Ümit Yaşar Sinan, Kemal Engin, Mehmet Serdar Küçüköğlü

Istanbul University-Cerrahpaşa Institute of Cardiology, Department of Cardiology, İstanbul, Turkey

## Abstract

**Objectives:** The current 2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) pulmonary hypertension (PH) guidelines suggest mean pulmonary artery pressure (mPAP) >20 mmHg, pulmonary vascular resistance (PVR) >2 Wood Unit (WU), and pulmonary arterial wedge pressure (PAWP) ≤15 mmHg as the new hemodynamic definition of pre-capillary PH. In this study work, we aimed to analyze how the new ESC/ERS 2022 PH definition would affect the prevalence of pre-capillary PH in daily practice.

**Materials and Methods:** We searched the right heart catheterization (RHC) procedure performed at our institution between 2017 and 2023. When defining pre-capillary PH, both 2015 and 2022 ESC/ERS PH guidelines were used.

**Results:** One hundred and twenty-three catheter procedures were performed over in a 6-year period. Most of them were female (72.4%). Right heart catheterization (RHC) was clinically indicated for various reasons, with 43.9% of patients exhibiting suspicion of idiopathic pulmonary arterial hypertension (PAH), 32.5% having congenital heart disease-associated pulmonary arterial hypertension PAH (APAH-CHD), 17.9% presenting with PH due to left heart disease, and 5.7% diagnosed with chronic thromboembolic pulmonary hypertension PH (CTEPH). The mean age of the study population was 53.1±16.6 years. The RHC results revealed a mean PAP of 35.4±17.8 mm Hg, PAWP of 13.3±6.0 mm Hg, and PVR of 5.2±6.3 WU. According to the previous guidelines, the number of patients diagnosed with pre-capillary pulmonary hypertension PH was 35 (28.5%), whereas while with the new definition, this number increased to 47 (38.2%). Almost 10% of patients had pre-capillary PH according to the new hemodynamic PH definition criteria that who was not



**Address for Correspondence:** Ümit Yaşar Sinan, İstanbul University-Cerrahpaşa Institute of Cardiology, Department of Cardiology, İstanbul, Turkey

**e-mail:** drumityasar@hotmail.com **ORCID:** orcid.org/0000-0002-4837-7099

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## Abstract

able to be classified as having pre-capillary PH according to previous guideline. There was 24.4% patients (n=30) had combined pre and post-capillary PH according to current guideline. Finally, 15.4% of patients had undefined PH, defined as mPAP >20 mmHg, but PVR <2 WU, which was a novel definition for the first-time mentioned in 2022 guideline.

**Conclusion:** The current ESC/ERS guidelines for the diagnosis and treatment of PH is going to increase almost 10% in our pre-capillary PH population.

**Keywords:** Pre-capillary PH, hemodynamic definition, ESC/ERS PH guideline, current evidence, PAH

## Introduction

Increased right ventricle (RV) afterload due to pulmonary vascular injury associated with negative remodeling is the underlying mechanism of pulmonary hypertension (PH), and if it is not diagnosed and treated early, it is characterized by increased mortality risk due to RV failure<sup>(1)</sup>. The World Heart Organization suggested 5 PH groups that classified disease with similar pathophysiology, clinical presentation, and treatment strategy under same umbrella<sup>(2)</sup>. Among these groups, left heart disease (group 2), lung disease (group 3), and chronic thromboembolism (group 4) are the most common pathologies that might be associated with PH<sup>(3)</sup>. Group 1 PH, which is called pulmonary arterial hypertension (PAH), is the most rare group, but drugs tested in randomized clinical trials and approved for this indication are used only in this group. Early diagnosis and quick initial up-front combination therapy according to the patient's risk strata prevent RV function and improve survival.

PH has been defined as a mean pulmonary artery pressure (mPAP) is  $\geq 25$  mmHg at rest in the supine position during right heart catheterization (RHC) since the 1<sup>st</sup> World Symposium of PH (WSPH)<sup>(4)</sup>. This definition was maintained without any change until the 6<sup>th</sup> WSPH (2018)<sup>(2)</sup>. Data accumulated from healthy individuals showed that a normal mPAP at rest is  $14.0 \pm 3.3$  mmHg. Therefore, during the 6<sup>th</sup> WSPH, the revised mPAP threshold for defining PH was set at >20 mmHg.

Meanwhile, the cut-off points for pre-capillary PH remained unchanged, with pulmonary capillary wedge pressure (PCWP) <15 mmHg and pulmonary vascular resistance (PVR) >3 WU<sup>(2)</sup>. The upper limit of normal PVR in healthy volunteers, and the lowest prognostically relevant threshold for PVR, is approximately  $\sim 2$  WU. Consequently, the definition of pre-capillary PH was once again updated in the 2022 European Society of Cardiology (ESC)/European Respiratory Society (ERS) PH guidelines as mPAP >20 mmHg, PCWP  $\leq 15$  mmHg, and PVR >2 WU<sup>(3)</sup>.

In this study, we analyzed how the new ESC/ERS 2022 PH definition would affect the prevalence of pre-capillary PH in daily practice.

## Materials and Methods

The results of RHC performed using various clinical indications at our institution between 2017 and 2023 were analyzed. The most common indication of RHC was differential diagnosis among various PH etiologies. RHC was performed via the right femoral vein route under local regional anesthesia. For all incident patients, coronary angiography and left heart catheterization were also performed using the same procedure. Swan-Ganz balloon catheter, multipurpose, and pigtail catheters are the most preferred catheters during procedures according to availability. All hemodynamic data were obtained in the supine position at rest. Medical reports were examined to record patient demographics, clinical history, and

comorbidities. Hemodynamic data (mPAP, PAWP, PVR) were collected from RHC reports. Both 2015 and 2022 ESC/ERS PH guidelines were used to identify patients with PH. This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients before the procedure. The retrospective study was approved by the Istanbul University-Cerrahpasa Institute of Cardiology Ethic Committee (number: E-96241115-904-6852, date: 11.01.2023).

### Statistical Analysis

For statistical analyses, we used SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). If the variable is continuous mean  $\pm$  standard deviation or median (minimum-maximum), it was used. Categorical variables are expressed as counts and percentages. Normality was tested with the Kolmogorov-Smirnov test. While Student's t-test or the Mann-Whitney U test were used to compare continuous variables, for categorical data, the chi-square test was used. A p-value  $<0.05$  was set as significant.

### Results

One hundred and twenty-three RHC procedures were performed over a 6-year period. Most were female (72.4%). The mean age was  $53.1 \pm 16.6$  years. After initial diagnostic evaluation, patients with intermediate or high probability of PH underwent RHC. It was clinically indicated for various reasons, with 43.9% of patients exhibiting suspicion of idiopathic PAH, 32.5% having congenital heart disease-associated PAH, 17.9% presenting with PH due to left heart disease, and 5.7% diagnosed with chronic thromboembolic PH (Figure 1) (5). The RHC results revealed a systolic PAP of  $54.2 \pm 26.3$  mmHg, mPAP of  $35.4 \pm 17.8$  mmHg, diastolic PAP of  $23.8 \pm 14.0$  mmHg PAWP of  $13.3 \pm 6.0$  mmHg, PVR of  $5.2 \pm 6.3$  WU and cardiac index of  $2.8 \pm 1.2$  L/per minute/ $m^2$  (Table 1).

According to the previous guidelines, the number of patients diagnosed with pre-capillary PH was 35 (28.5%), whereas with the new definition, this number increased

to 47 (38.2%). Almost 10% of patients had pre-capillary PH according to the new hemodynamic PH definition criteria that could not be classified as having pre-capillary PH according to previous guidelines. There were 24.4% patients (n=30) had combined pre and post-capillary PH according to current guidelines. Finally, 15.4% of patients had undefined PH, defined as mPAP  $>20$  mmHg, but PVR  $<2$  WU, which was a novel definition for the first-time mentioned in 2022 guideline (Table 2)(5).

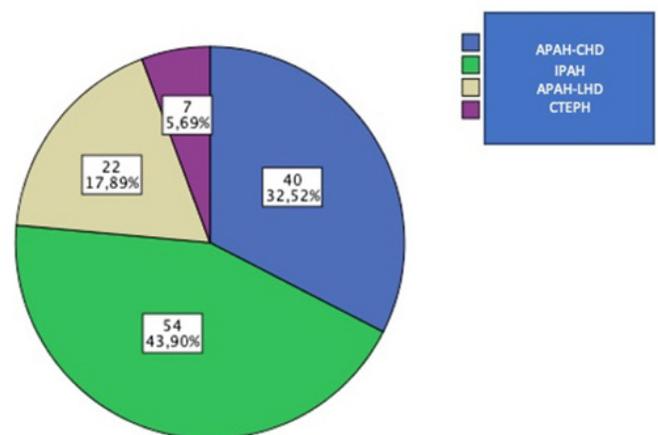
### Discussion

Data collected from healthy individuals suggest  $14.0 \pm 3.3$  mmHg as a normal mPAP at rest and 0.3-2.0 WU as a normal PVR. First during 6<sup>th</sup> WSPH the cut-off mPAP value for PH definition was updated as  $>20$  mmHg(2). Then, the PVR threshold for the diagnosis of

**Table 1.** Hemodynamic data of study population

Hemodynamic variable	Mean
sPAP (mmHg)	54.2 $\pm$ 26.3
mPAP (mmHg)	35.4 $\pm$ 17.8
dPAP (mmHg)	23.8 $\pm$ 14.0
PCWP (mmHg)	13.3 $\pm$ 6.0
PVR (WU)	5.2 $\pm$ 6.3
CI (L/per minute/ $m^2$ )	2.8 $\pm$ 1.2

CI: Cardiac index, PAP: Pulmonary artery pressure, PCWP: Pulmonary capillary wedge pressure, PVR: Pulmonary vascular resistance



**Figure 1.** Indications of RHC  
RHC: Right heart catheterization

**Table 2.** The comparison of the prevalence of pre, post and combined pre, post-capillary PH patients according to the 2015 and 2022 ESC/ERS PH guideline

Definition	2015 ESC/ERS PH Guideline, n (%)	2022 ESC/ERS PH Guideline, n (%)
Pre-capillary PH	35 (28.5%)	47 (38.2%)
Ipc-PH	0	2 (1.6%)
Cpc-PH	20 (16.3%)	30 (24.4%)
Undefined PH	-	19 (15.4%)
No PH	25 (20.3%)	

*Cpc-PH: Combined pre- and post-capillary pulmonary hypertension, ERS: European Respiratory Society, ESC: European Society of Cardiology, Ipc-PH: Isolated post-capillary pulmonary hypertension, PH: Pulmonary hypertension*

pre-capillary PH in 2022 ESC/ERS guideline on diagnosis and management of PH was redefined as  $>2$  WU, while the PCWP cut-off remained unchanged as 15 mmHg<sup>(3)</sup>. Based on the results of this new hemodynamic definition, it is obvious that the number of pre-capillary PH patients we will diagnose in daily practice will increase. This definition makes it easier for us to diagnose PH early, especially in patients with systemic sclerosis who are at high risk for PAH and have a poor prognosis. Our study showed that the new hemodynamic definition would affect the prevalence of pre-capillary PH by approximately 10%. In our previous study, there was 12.1% increase in our PH patient population after 6<sup>th</sup> WSPH PH definition<sup>(6)</sup>.

Nevertheless, the PH diagnostic algorithm is triggered by clinical suspicion. For individuals exhibiting symptoms, risk factors, and clinical signs indicative of PH, the primary approach in the diagnostic algorithm involves assessing the likelihood of PH through echocardiography. The thresholds for tricuspid regurgitation velocity corresponding to low, intermediate, and high probabilities of PH have not changed ( $<2.8$  m/s, 2.9-3.4 m/s,  $>3.4$  m/s, respectively).

While the incidence of pre-capillary PH diagnoses is on the rise, the randomized controlled trials that led

to the approval of PAH-specific treatments used the old definition. Consequently, these medications have not undergone rigorous testing and approval for both efficacy and safety in individuals falling under this evolving diagnostic category. It is crucial to bear in mind this circumstance. In the future, if PAH-specific drugs receive approval for use in this patient cohort, early detection and swift initiation of initial combination therapy could safeguard RV function and enhance life expectancy.

## Conclusion

After the release of the most recent PH guidelines, our pre-capillary PH population will increase by almost 10%. Although we struggle with more pre-capillary PH patients, we need evidence from randomised clinical trial before treating these patients.

## Ethics

**Ethics Committee Approval:** The retrospective study was approved by the Istanbul University-Cerrahpasa Institute of Cardiology Ethic Committee (number: E-96241115-904-6852, date: 11.01.2023).

**Informed Consent:** Informed consent was obtained from all patients before the procedure.

**Peer-reviewed:** Externally peer-reviewed.

## Authorship Contributions

Surgical and Medical Practices: Sinan ÜY, Concept: Sinan ÜY, Design: Sinan ÜY, Küçükoğlu MS, Data Collection and/or Processing: Engin K, Analysis and/or Interpretation: Sinan ÜY, Literature Search: Sinan ÜY, Writing: Sinan ÜY.

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