

EDITORIAL

# Clearing Our Vision for Discerning Precapillary From Postcapillary Pulmonary Hypertension With the OPTICS Risk Score

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One of the key components of the evaluation of pulmonary hypertension (PH) is distinguishing precapillary PH from postcapillary PH. Treatments are predicated on this distinction and when misapplied can harm patients instead of the intended benefit. Drawing the line between precapillary and postcapillary PH is a challenging task: many patients present with multiple comorbidities,<sup>1–3</sup> and a normal pulmonary artery wedge pressure (PAWP) at rest may not completely exclude group II PH as a result of heart failure with preserved ejection fraction (HFpEF).<sup>4–6</sup> Thus, the concept of developing a pretest probability of high PAWP in patients referred for PH is quite important to assist clinicians in their decision-making process. As a single variable will unlikely be sufficient for an accurate differential diagnosis, composite scores integrating clinical and nonclinical features is the way forward.<sup>6</sup> This is why, 5 years ago, Jacob and colleagues developed a noninvasive score to identify left-sided heart failure in a population suspected of pulmonary arterial hypertension.<sup>7</sup>

patients referred for PH evaluation at a leading European center.<sup>8</sup> The OPTICS score was derived from a population referred to the Vrije Universiteit Medical Center in Amsterdam between 1998 and 2012 for evaluation of PH. Patients with more than mild left valvular disease on echocardiography and a left ventricular ejection fraction <50% were excluded. The definition of postcapillary PH was a PAWP >15 mm Hg at rest or >18 mm Hg immediately after fluid challenge of 500 mL of saline infused for 5 minutes. In the derivation cohort, independent predictors of postcapillary PH were the following: body mass index  $\geq 30$  kg/m<sup>2</sup>, diabetes mellitus, paroxysmal or persistent atrial fibrillation, dyslipidemia, prior valvular surgery without residual left valvular disease, the presence of left atrial dilation on echocardiography (defined as left atrial volume index >34 mL/m<sup>2</sup> or a qualitative description) and the sum of the S wave in V1 and the R wave in V6 on electrocardiography (SV1+RV6, in millimeters, as a continuous variable). A point scoring system (the so-called OPTICS risk score) was then developed for each of these predictors. Using a cut off value of  $\geq 104$ , the test characteristics for predicting postcapillary PH in the derivation cohort were a sensitivity of 23%, specificity of 100%, positive predictive value of 100%, and a negative predictive value of 86%. This cut off was chosen to ensure that no precapillary PH patients were predicted as having postcapillary PH, for example, limiting false positives.

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## See Article by Jansen et al.

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In this issue of the *Journal of the American Heart Association*, Jansen and colleagues now present the performance of an adaptation of the previous score (now called OPTICS) to predict an elevated PAWP in

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The validation cohort derived from a more recent group of patients in community hospitals referred for right heart catheterization for signs of PH on echocardiography. These patients were older than the derivation cohort, with more males represented. The specificity and positive predictive value remained 100% (so no false positives), and the negative predictive value dropped to 49%, so there were more false negatives (predicted to not have postcapillary PH, but did by right heart catheterization). The authors compared the performance of the OPTICS risk score with the H<sub>2</sub>FPEF score, recently developed to assess the probability of HFpEF in patients with unexplained dyspnea.<sup>9</sup> Both scores appear to have a rather similar performance when the H<sub>2</sub>FPEF score  $\geq 6$ , although there were a few false positives in the latter (ie, high HFPEF probability in some precapillary PH).

The authors must be commended for their important effort to build a noninvasive tool helping busy clinicians to determine a pretest (ie, preinvasive assessment) probability of PH, as recently suggested by an expert consensus.<sup>6</sup> One of the strengths of the work of Jansen and colleagues is, for the first time, an external validation of a score derived from a single center analysis. More important, the score was applied to a population of patients referred from non-PH expert centers. In other words, the OPTICS risk score may be applicable to identify patients in whom an elevated PAWP may account for the presence of PH and be assessed accordingly.

In contrast with previous reports, the authors excluded patients with more than mild valvular disease. This is an important exclusion, which accounted for 11% of the cohort. In addition, a history of valve surgery was the single strongest predictor of postcapillary PH, and indeed we know that treating this group as precapillary PH is detrimental based on the SIOVAC (Sildenafil for Improving Outcomes after Valvular Correction) trial.<sup>10</sup>

Another apparent strength is that, for the first time, the H<sub>2</sub>FPEF score<sup>9</sup> has been applied to a prediction of postcapillary PH. However, there are significant limitations to the interpretation that the latter performs less well than OPTICS. The H<sub>2</sub>FPEF score was developed to establish a probability of HFpEF in patients with unexplained dyspnea. By no means should it be applied to establish a probability of PH even in this context. In addition, it should be noted that 24% of patients in the current study did not have Doppler echocardiographic E/e' available, so this was assumed to be  $>9$  for the purposes of calculating a H<sub>2</sub>FPEF score (1 extra point higher). Therefore, this should not be considered a complete evaluation of the H<sub>2</sub>FPEF score for predicting postcapillary PH. Despite this significant limitation, both the OPTICS and H<sub>2</sub>FPEF scores both included body mass index  $\geq 30$  kg/m<sup>2</sup> and a history of atrial fibrillation,

which speaks to the association of these risk factors with postcapillary PH and HFpEF and the high prevalence of PH associated with HFpEF. As it was not designed for the workup of PH, it is not surprising that intermediate H<sub>2</sub>FPEF scores can be associated with either precapillary PH or postcapillary PH. This also brings up the potential for confounding based on unique causes of PH such as chronic thromboembolic disease, congenital heart disease, and pulmonary veno-occlusive disease and is a reminder that such conditions must be carefully considered in the PH evaluation.

Regarding the hemodynamic definition of postcapillary PH, one should remember that the response of the PAWP to fluid challenge is dependent on age and sex and that there is yet no consensus on this definition, although the definition used by the authors does have data to support it.<sup>11,12</sup> Similarly with evaluating the PAWP response to exercise, a rise in PAWP  $>2$  mm Hg per 1 L/min rise in cardiac output seems to have the clearest evidence, but aging may induce an early rise that may be misleading.<sup>13,14</sup> This may be particularly relevant in the systemic sclerosis population, which seems to have a high prevalence of occult left ventricular diastolic dysfunction as well as pulmonary arterial hypertension (precapillary PH).<sup>15</sup>

Some other notable limitations in the study include the following. First, it was developed in a homogenous White population, so it would be important to validate the OPTICS score in other groups and societies, such as those with a high prevalence of obesity and the metabolic syndrome that predisposes to HFpEF and group II PH (and indeed hyperlipidemia was an independent predictor in this study). Second, this derivation cohort included data collected during the course of 25 years, over which time echocardiography technology and methodology has evolved and thus some of the data were limited, particularly surrounding the evaluation of left ventricular diastolic function, such as E/e', left ventricular mass, and left atrial volume, which can be very helpful in raising suspicion of HFpEF as a cause of PH. Overall, missing data prevented calculation of the OPTICS risk score in 10% of patients in the validation cohort, reminding us that a risk score is only as useful as the data you can obtain to calculate it. It should also be kept in mind that although the score held up to evaluation in a second cohort, the number of patients with a scores  $\geq 104$  was small, so this does need to be further validated to determine how it may fit into the PH evaluation algorithm.

So here is where we stand...

Can risk scores such as the OPTICS score help us in evaluating PH? Surely. However, we need further, broader validation. It certainly helps clinicians keep in mind the critical issue of distinguishing precapillary PH from postcapillary PH. Could one exclude high-scoring patients from further evaluation such as right heart catheterization? Surely not. Patients with precapillary PH must not be missed because we have effective therapies for them

when pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension is established. A missed diagnosis depriving patients from appropriate treatment may be as bad as prescribing drugs in the wrong individuals, as emphasized by the authors. Would such a score be helpful to plan for provocative testing during right heart catheterization? Maybe. Actually, many centers may not pursue a provocative maneuver, such as fluid challenge or exercise, if not ordered ahead of time, sometimes necessitating a separate procedure or referral. One application of these scores may be to further stratify patients if a resting PAWP of  $\leq 15$  is present but no provocative testing results are available, although this remains to be demonstrated.

The work presented by Jansen and colleagues confirms that a multiparametric analysis may predict which patient may present with an elevated PAWP when referred for PH assessment. It does not neglect the importance of right heart catheterization in the diagnostic process. Looking at the workup for PH through the lens of the OPTICS risk score may improve our diagnostic accuracy. Instead of remaining blinded by the light, future work will tell if this vision is correct(ed).

## ARTICLE INFORMATION

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