Patients with PAH may present with relatively few physical signs of PAH, yet have significant cardiovascular abnormalities. These patients, with “compensated right-heart failure,” measure pulmonary capillary wedge (PCW) pressure (and thus left ventricular end diastolic pressure) bears important clinical significance, since it is essential to exclude pulmonary venous hypertension when making the diagnosis of PAH.

The standard definition of pulmonary hypertension is defined by most experts as a mean pulmonary arterial pressure of $\geq 25$ mm Hg, with a concomitant pulmonary capillary wedge pressure of $\geq 15$ mm Hg, and pulmonary vascular resistance of $> 3$ Wood units. These criteria are derived from the National Institutes of Health (NIH) registry of patients with primary pulmonary hypertension, now known as idiopathic pulmonary arterial hypertension (IPAH).

Measurement of hemodynamics in patients with PAH via cardiac catheterization can also provide added prognostic value. For example, in patients with primary pulmonary hypertension whose mean right atrial pressure was less than 10 mm Hg, median survival was nearly 50 months without pulmonary vasodilator therapy, compared with less than 3 months in patients whose mean right atrial pressure was 20 mm Hg or greater (Figure 1).

The Catheterization Procedure

The Catheter

The pulmonary artery (right heart) catheter is designed for use in the intensive care unit (ICU) or in the cardiac catheterization laboratory to measure right-heart and pulmonary arterial hemodynamics, to estimate left ventricular end diastolic pressure, and to measure cardiac output. The catheter is usually 120 cm long and has multiple lumens so that pressure recordings and infusions can be made from various locations in the heart and pulmonary arteries. In addition, a small plastic balloon that is located at the tip of the catheter can be inflated and used to “float” the catheter in the direction of blood flow in order to facilitate catheter advancement. This balloon is also used to occlude the pulmonary artery in order to obtain estimates of left atrial pressure (see below). Finally, a thermistor (temperature indicator) is also located at the tip of the catheter; it is used to detect changes in blood temperature when performing thermodilution cardiac output measurements (see below).

When performing right-heart catheterization specifically for patients with PAH, the catheter used often has several modifications that are designed to facilitate the catheterization process. The catheter is stiffer than the standard rightheart catheter and contains a blind-end port, which allows passage of a guidewire for additional stiffness, if desired. This extra stiffness is often needed because advancing the catheter into the pulmonary artery can be technically difficult in the presence of a dilated right ventricle, elevated pulmonary arterial pressure, and tricuspid regurgitation.

Precautions

When planning cardiac catheterization for a patient with suspected PAH, it is important to understand the risks associated with the procedure and to have an emergency treatment plan in place should these risks occur. In addition, the desired measurements should be planned in advance, with careful consideration of the specific operational procedures that are to be done during the procedure.

Clinicians should be very familiar with how to interpret the measurements obtained at cardiac catheterization and be able to troubleshoot suspected inaccuracies. Anticipation of complications and unexpected findings is essential, so that immediate action can be taken. Finally, the clinician must continuously scrutinize the findings and question the measurements for both accuracy and clinical relevance.

Patients with PAH may present with relatively few physical signs of PAH, yet have significant cardiovascular abnormalities. These patients, with “compensated right-heart failure,”
can easily decompensate when subjected to the stressors of cardiac catheterization. Despite these risks, however, cardiac catheterization is safe if appropriate precautions are carried out.

- **Staff experience.** The physician and nursing and technical staff must all be familiar with the diagnosis and management of PAH and with the catheterization laboratory equipment. The staff must be meticulous about flushing and leveling the pressure transducers and flushing the catheter to ensure that accurate measurements are recorded.

- **Patient sedation.** It is generally recommended that adult patients be kept awake during catheterization. However, it is important that anxiety, which may induce tachycardia and hemodynamic embarrassment, be controlled. Small doses of benzodiazepines are useful for controlling anxiety. Close attention to continuous pulse oximetry is required, however, as hypoxemia during catheterization is not uncommon.

- **Atrial and ventricular ectopy.** As the catheter is manipulatively positioned in the right atrium and ventricle, ectopic electrical activity is common. Usually, atrial premature beats and ventricular ectopic beats are brief and self-limited. Sustained activity including atrial and ventricular tachycardia may occur, however. Immediate repositioning or removal of the catheter is required in these instances, and antarrhythmic therapy should always be available should the arrhythmia persist.

- **Bradycardias.** One of the most troublesome complications of cardiac catheterization in patients with PAH is the development of vagally mediated bradycardia and hypotension. Often, an anxious or sensitive patient may develop increased vagal tone 1) on viewing the catheterization instruments or during local anesthetic infusion; 2) on insertion of the catheter; or 3) on removal of the catheter. When these “vagal episodes” occur, profound bradycardia and hypotension often ensue within 30 to 60 seconds. It can be extremely difficult to resuscitate such a patient. Therefore, it is imperative that a vagal episode is anticipated in all patients, and that it is recognized and treated with atropine early in its course. This author always keeps an open vial of atropine at the bedside before, during, and after cardiac catheterization of a patient with pulmonary hypertension.

- **Reliability of measurements.** Cardiac catheterization measurements should be made preferably when the patient is supine, with anxiety minimized (see above), and at steady state. Spontaneous variation in hemodynamics over time is a known shortcoming of cardiac catheterization (Figure 2) and thus great care should be taken to ensure that all measurements are taken in close proximity of each other. In general, waiting at least 15 minutes after catheter insertion is advisable. Hemodynamic measurements should then be obtained as close together as possible.

### Choice of Venous Access Sites

Commonly, the right internal jugular vein is used for insertion of a venous sheath through which the pulmonary artery catheter is passed. For patients in whom it is difficult to advance the catheter into the pulmonary artery because of high pulmonary arterial pressures, the right internal jugular approach may be superior to approaches via the inferior vena cava. This is because the former approach allows the catheter to form a natural curve on the floor of the dilated right ventricle and point upward into the main pulmonary artery, making it easier to advance into the more distal pulmonary arteries. Other sites can be advantageous, depending on the situation (Table 1). Formerly, for a patient’s initial catheterization, use of the femoral veins for catheterization was preferred, because it allowed the greatest flexibility with which the clinician could perform the most thorough evaluation. This was especially important for excluding left heart pathology when direct measurement of left ventricular end diastolic pressure was necessary. The advent of left-sided cardiac catheterization via the radial artery approach has, in patients with adequate radial arterial flow, eliminated the absolute necessity for a femoral approach, and the combination of the right internal jugular venous approach to the right heart and the radial artery approach to the left heart has become a viable and convenient alternative for the patient and clinician.

### Measurements to Record

Standard right-heart catheterization measurements (Figure 3) include:

- right atrial pressure (RAP)
- right ventricular pressure (RVP)
- pulmonary arterial pressure (PAP)
- pulmonary capillary wedge pressure (PCWP)
- systemic arterial pressure (BP) and heart rate
- cardiac output (CO)
- pulmonary arterial vasoreactivity
- pulmonary arterial (PA) (“mixed venous”) saturation
- superior vena cava (SVC) saturation*
- inferior vena cava (IVC) saturation*

Normal pressure waveforms are shown in Figure 3. Pulmonary capillary wedge (PCW) pressure measurements are made when the balloon of the catheter is inflated after the catheter has been properly advanced into the pulmonary artery. The inflated balloon prevents the measurement of any pressure proximal to the balloon, and thus measurements recorded from the tip of the catheter reflect only left atrial pressure, which is commonly used as a surrogate for left ventricular end diastolic pressure.

The PCW pressure tracing should display three waveforms: The a wave represents contraction of the left atrium. The c wave is due to a rapid rise in the left ventricular pressure in early systole, causing the mitral valve to bulge backward into the left atrium, so that the atrial pressure increases momentarily. The v wave is produced when blood enters the left atrium during late systole, the time at which most filling of the left atrium occurs.

It is essential that, in spontaneously breathing (ie, not on ventilatory support) subjects, the pressures be measured at end-expiration, since that is the only instant in the left atrium during late systole, the time at which most filling of the left atrium occurs.

### Hemodynamic Calculations

The following formulas are used to calculate standard hemodynamic parameters derived from the above measurements:

- Heart rate
  
- Mean pressure = diastolic pressure + (pulse pressure/3), where pulse pressure = systolic pressure - diastolic pressure.

- Systemic vascular resistance (SVR) = (mBP – RAP)/CO

- Pulmonary vascular resistance index (PVRI) = (mPAP – mean PCW pressure)/Cardiac output (CO)

<table>
<thead>
<tr>
<th>Site</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right internal jugular vein</td>
<td>Facilitates pulmonary artery access; proximity to heart; may not need fluoroscopy</td>
<td>Cautious access can be difficult</td>
<td>Hematoma, pneumothorax, tracheal obstruction</td>
</tr>
<tr>
<td>Left subclavian vein</td>
<td>Facilitates pulmonary artery access; proximity to heart</td>
<td>Vascular control of bleeding difficult</td>
<td>Pneumothorax, hemothorax</td>
</tr>
<tr>
<td>Femoral veins</td>
<td>Easiest to cannulate; easiest for vascular control of bleeding</td>
<td>Most problematic for pulmonary artery access; small risk of infection; limits patient mobility; fluoroscopy required</td>
<td>Hematoma</td>
</tr>
</tbody>
</table>

*When indicated.*
studies suggest that it be performed only in selected subgroups of PAH. Measurement of pulmonary vasoreactivity has an extremely important role in the diagnosis and management of patients with PAH, especially in the context of vasodilator testing. These issues are beyond the scope of this article.

The minimum exercise load and target end point during exercise during catheterization has not been established. In addition, factors such as wider swings in intrathoracic pressure during rapid breathing with exercise, and the patient's inability to maintain peak exercise during the entire hemodynamic registration, may render interpretation of the systemic vasoreactivity index (SVR) = SVR/BSA

Cardiac output measurements. There are two standard methods for determining cardiac output. Both methods measure pulmonary blood flow, which in the absence of an intracardiac shunt is equal to systemic blood flow.

The thermodilution method for determining cardiac output uses the indicator dilution principle, where the indicator is cold saline infused as a bolus injection into the proximal port of the right-heart catheter. The thermistor at the distal end of the catheter then measures the appearance and disappearance of indicator over time, and a cardiac output is then calculated. This method can be inaccurate at very high or very low cardiac outputs, and can underestimate cardiac output when significant valve regurgitation is present.

When using this technique, the clinician must ensure that the proximal right atrial port for injection is actually in the right atrium, since the port can be in the right ventricle when the catheter is wedged.

The Fick method for determining cardiac output is based on the principle that consumption of a substance (oxygen in this case) must equal blood flow to the organ multiplied by the difference between the arterial and venous concentrations of the substance. For this method, the formula for cardiac output is as follows:

\[
CO = \frac{\text{oxygen consumption per minute (VO2)}}{\text{arterial oxygen content - venous oxygen content}}
\]

where oxygen content is calculated as: 1.34 x [Hb] x oxygen saturation/100.

In this case, the oxygen consumption can either be estimated or directly measured using standard techniques. Arterial oxygen saturation is usually determined by arterial blood gas analysis, while venous oxygen saturation is determined by mixed venous (pulmonary arterial) blood gas analysis.

Note: In order to measure systemic arterial oxygen saturation for determining cardiac output using the Fick method, caution should be exercised when relying on pulse oximetry, since both overestimation and underestimation can lead to significant errors in cardiac output calculations. Additionally, pulse oximetry may not be reliable in patients with Raynaud’s phenomenon, a common finding in patients with PAH.

Shunt measurements. An abnormally high pulmonary arterial saturation suggests a right-to-left shunt due to congenital heart disease and requires further evaluation and testing to identify and quantitate the shunt. Quantitation of left-to-right and/or right-to-left shunting is an integral part of right-heart catheterization. However, these calculations are beyond the scope of this article.

Left-heart catheterization. Left-heart catheterization is not absolutely required in all patients with suspected PAH, although many PAH specialists prefer to perform left-heart catheterization in all patients with suspected PAH as part of their initial (diagnostic) evaluation, to assure that the exclusive workup of PAH is complete.

Left-heart catheterization should be considered a mandatory part of the evaluation of pulmonary hypertension in the following instances:

- validation of abnormal pulmonary capillary wedge pressure/evaluation of left ventricular diastolic dysfunction
- suspected left-to-right shunt
- suspected left-to-right shunting
- suspected coronary artery disease

Special Considerations

Exercise

Special consideration is required when obtaining right-heart hemodynamics during exercise. Unfortunately, there is no consensus on the modality of exercise, nor the exercise protocol recommended for exercise right-heart catheterization. Many clinicians employ arm exercise, placing weights such as 1L saline bags in each arm and having the patient perform over-the-head arm abduction until fatigue ensues. Others use a cycle ergometer, which provides a more controlled workload, but may pose risks for patients when catheterized via the femoral vein approach.

The minimum exercise load and target end point during exercise during catheterization has not been established. In addition, factors such as wider swings in intrathoracic pressure during rapid breathing with exercise, and the patient’s inability to maintain peak exercise during the entire hemodynamic registration, may render interpretation of the exercise procedure difficult. These issues are beyond the scope of this article.

Vasodilator Testing

Measurement of pulmonary vasoreactivity has an extremely important role in the diagnosis and management of patients with PAH, and it is prognostic although recent studies suggest that it be performed only in selected subgroups of PAH.

The presence of pulmonary vasoreactivity predicts the response to long-term calcium channel blocker (CCB) therapy. Patients who lack pulmonary vasoreactivity respond poorly to long-term CCB use and must be treated with specific pulmonary vasodilators. Patients with significant pulmonary vasoreactivity, by contrast, have been shown to respond well to CCB therapy. Moreover, cardiac catheterization is extremely useful in these patients, with graded dosing during catheterization helping to aid in choosing the appropriate effective dose of CCB. Finally, pulmonary vasoreactivity has been shown to correlate with survival in patients with idiopathic PAH (Figure 4).

A recent comprehensive retrospective review of the experience in Clamart, France, suggests that while 10% of patients with idiopathic and anorexigen-induced PAH have a good long-term response to calcium blockers that can be predicted by acute vasodilator testing, none of the other forms of PAH (related to connective tissue disease, congenital heart disease, or others) have good long-term responses. Thus, acute vasodilator testing should be reserved for patients with idiopathic or anorexigen-related PAH only.
Caution should be exercised when considering vasodilator testing and the use of a CCB for patients with PAH. Specifically, while about 25% of patients without significant heart failure symptoms exhibit pulmonary vasoreactivity, patients with New York Heart Association (NYHA) functional class III or IV symptoms exhibit pulmonary vasoreactivity at considerably lower rates. Furthermore, patients with overt signs and symptoms of right-heart failure do not tolerate the high doses of a CCB required to produce hemodynamic benefit. The use of a CCB in these patients carries significant risk of worsening right ventricular failure and death.

This illustrates the complexities associated with vasodilator testing and the importance of understanding how to use CCB therapy. These agents should not be prescribed empirically for patients with PAH and should be reserved for patients with pulmonary vascular vasoreactivity who do not have signs of right ventricular failure (see below).

**Vasodilator Testing: How Is It Done?**

The basics of pulmonary vasodilator testing in PAH include:

1. **Administration of appropriate pulmonary vasodilator.** The most commonly used pulmonary vasodilators for acute vasodilator testing are intravenous epoprostenol or adenosine and inhaled nitric oxide. These agents have been used by many PAH experts, and there is substantial documentation of their utility in PAH.

Initially, very low doses of the pulmonary vasodilator should be administered (Table 2). If at any time during uptitration of the vasodilator the systolic pressure falls below 85 mm Hg or the patient complains of dyspnea or dizziness, the vasodilator should be discontinued, and the patient watched carefully until hemodynamics return to baseline.

**Table 2. Common Pulmonary Vasodilator Agents and Their Dosages.**

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>Epoprostenol</th>
<th>Adenosine</th>
<th>Nitric oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion</td>
<td>Intravenous infliximab</td>
<td>Inhaled</td>
<td></td>
</tr>
<tr>
<td>Moderate decrease in systemic vascular resistance</td>
<td>No change in systemic vascular resistance</td>
<td>Short/long-term</td>
<td></td>
</tr>
<tr>
<td>Uses</td>
<td>Short/long-term only</td>
<td>Short/long-term</td>
<td></td>
</tr>
<tr>
<td>Done range</td>
<td>2-10 ng/kg/min</td>
<td>50-100 ng/kg/min</td>
<td>10 ppm</td>
</tr>
</tbody>
</table>

Pitfalls of Measurements

**Incorrect Recordings of Pulmonary Capillary Wedge (PCW) Pressure**

A common pitfall when measuring pulmonary capillary wedge pressure in patients with PAH involves incorrect interpretation. This occurs when the right-heart balloon flotation catheter is not in proper position, yielding an inaccurate pressure tracing (Figure 5). The most common cause of this error is the recording of a dampened pulmonary arterial pressure rather than a true occlusion pressure. This error results in a falsely elevated pressure measurement, often misleading the clinician into believing that the patient has pulmonary venous hypertension rather than PAH.

**Figure 5**

The authors frequently employ two techniques for avoiding this measurement error: 1) Partially inflating the balloon and gentle forward advancement of the catheter, in order to better seat and seal the catheter against the walls of the pulmonary artery branch. 2) Validating an abnormally elevated measurement by gently withdrawing a blood sample from the distal port of the right-heart catheter during balloon inflation and pulmonary capillary wedge pressure recording, to ensure that the saturation of the sample matches systemic arterial (left atrial) saturation, ie, if the catheter is correctly placed in the wedge position, the oxygen saturation of the blood distal to the catheter should be very high (see text, Figure 5).

Another problem with capillary wedge pressure measurements is overinflation or excessive advancement of the balloon, which results in “over-wedging.” Prolonged over-wedging will yield a falsely high pulmonary capillary wedge pressure and may result in pulmonary infarction. If an accurate pulmonary capillary wedge pressure cannot be obtained during right-heart catheterization, it is prudent to consider direct measurement of left ventricular end diastolic pressure via left-heart catheterization.

**Summary**

Cardiac catheterization is mandatory for definitive diagnosis in all patients suspected of PAH. It is the only reliable method for this purpose. It can be used for determining vasodilator responsiveness of the pulmonary vasculature in appropriate patients, and it is part of a standard diagnostic workup for patients with suspected congenital heart disease. It is also mandatory for the evaluation of patients with nonidiopathic PAH since it is especially important to be certain that the diagnosis is accurate, as many of these patients have concomitant left heart and lung disease that could confound the diagnosis.


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Related Resources

- 2012 Neonatal and Childhood Pulmonary Vascular Disease Conference Presentations
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- PAH 101: Introduction to PAH
- Pediatric PAH
- Oral PAH Medications