Hemodynamics in the Cardiac Catheterization Laboratory of the 21st Century

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There has been a striking evolution in the role of the cardiac catheterization laboratory over the past decades.[1] In the 1950s and 1960s, hemodynamic assessment in the cardiac catheterization laboratory was essential for understanding the physiology and pathophysiology of patients with cardiovascular diseases. With the development of surgical interventions to treat patients with valvular and congenital heart disease, it became necessary for the cardiac catheterization laboratory to provide an accurate hemodynamic assessment, laying out a therapeutic road map. Nearly all patients who had open heart surgery underwent a complete hemodynamic catheterization before surgery.

In the 1980s and 1990s, the evolution of 2-dimensional echocardiography and Doppler echocardiography provided an alternative noninvasive approach for the assessment of both cardiac anatomy and hemodynamics in patients with structural heart disease.[2] By measuring blood flow velocities noninvasively, Doppler echocardiography was able to provide information on volumetric flow, intracardiac pressures, pressure gradients, and valve areas, as well as diastolic filling of the heart. Furthermore, noninvasive studies could be repeated easily, allowing the practitioner to follow the progress of his/her patient's condition longitudinally. At the same time, there was growing emphasis on coronary angiography for defining epicardial coronary disease with the subsequent development of interventional approaches for coronary disease with catheter-based therapies. As the major focus in the catheterization laboratory shifted to the diagnosis and treatment of the patient with acute and chronic coronary artery disease, the hemodynamic assessment of patients with structural heart disease was left to the noninvasive echocardiographic laboratory. As a consequence, many cardiac catheterization laboratories provided neither the training nor the expertise to assess hemodynamics properly.

However, the advent of procedures such as balloon valvotomy, percutaneous valve implantation, and septal ablation has revived interest in structural heart disease and provided the invasive cardiologist with an armamentarium to treat patients who previously had to undergo surgery or would have been considered inoperable.[3] For the invasive cardiologist to use these new tools appropriately, he/she must fully understand the advanced principles and nuances of complex hemodynamics. Invasive hemodynamic assessment still remains of great importance in the evaluation of the patient with congenital heart disease.[4] In addition, the noninvasive hemodynamic evaluation has inherent limitations, now recognized by clinicians who take care of the increasing number of patients who present with complex cardiovascular problems. The catheterization laboratory in the current era has become the place to solve the difficult diagnostic challenges that arise in patients with structural heart disease when answers are not apparent through the clinical examination and noninvasive testing.

Implications of the New Cardiac Catheterization Laboratory in the 21st Century

The changes that have occurred in patient evaluation throughout the last 2 decades have important implications for the new cardiac catheterization laboratory. Patients now coming for hemodynamic assessment have already had a thorough noninvasive evaluation. Thus, the remaining questions are complex and pose difficult diagnostic dilemmas. It is unacceptable for the patient to leave an invasive hemodynamic assessment without a definitive answer about his/her condition. Thus, hemodynamic assessment in the cardiac catheterization now requires meticulous attention to detail. There is no longer such a procedure as routine cardiac catheterization. The operator should be constantly evaluating the accrued data, ready to perform additional diagnostic interventions if necessary such as exercise or other provocative maneuvers.

Invasive cardiologists must understand the implications of the results of noninvasive testing and their correlation with the clinical examination. They need to determine the incremental information necessary for clinical decision making. Thus, a hemodynamically directed cardiac catheterization should be a goal-directed procedure, specifically individualized for each patient, based on the problem and the results of the noninvasive testing.

Principles of Cardiac Catheterization

The complex cardiac catheterization must be approached in a detailed systematic manner. First, the operator must be able to create a roadmap of what questions need to be answered. This includes assessment of the proper access and approach. For instance, in a patient who has unexplained dyspnea, a radial

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and internal jugular access might be appropriate instead of the standard femoral approach, so supine bicycle exercise could be implemented. Alternatively, there might be a need for direct left atrial pressure measurement, which would require a femoral approach for a potential transseptal catheterization.

The operator should be constantly obtaining and analyzing data throughout the study so that additional interventions can be performed on the basis of the initial data and the clinical question. These additional interventions may include vasodilator challenge in the presence of diastolic dysfunction, nitric oxide for unsuspected pulmonary hypertension, or oxygen supplementation for arterial desaturation. In patients who might be candidates for cardiac transplantation, full evaluation of the pulmonary arteriolar resistance and (if elevated) its reversibility should be undertaken. Exercise hemodynamic assessment or fluid loading should be considered for patients with severe symptoms in whom the resting hemodynamics are not markedly abnormal.

It is important to use the proper equipment for a catheterization aimed at a high-quality hemodynamic assessment. Coronary angiography has evolved to use the smallest-bore catheters, with many diagnostic angiograms using 5F or even 4F catheters to decrease vascular complications. However, proper evaluation of pressures during a complex hemodynamic catheterization is optimally performed with larger-bore catheters that yield high-quality hemodynamic data. To obtain proper hemodynamic tracings, 6F or even 7F catheters may be required if the smaller catheters do not produce high-quality pressure contours. Catheters with side holes should be used to measure ventricular pressures. Catheters with end holes should be used to measure wedge pressures. The use of high-fidelity manometer-tipped catheters might also need to be considered in those instances when intricate analysis of diastolic filling contours is required. If fluid-filled catheters are used, it is important to choose the shortest extension tubing possible to obtain optimal pressure contours. For this reason, the use of the coronary manifold with its long extenders that degrade pressure tracings should be avoided.

The invasive cardiologist must continually assess pressure contours throughout the study. Overdamped and underdamped pressure tracings and whip artifact should be anticipated and corrected. Formation of small thrombi in catheters can cause significant changes in pressure contour, especially in catheters with small internal diameters (Figure 1A). Thus, all catheters should undergo intermittent flushing with heparinized saline throughout their use, with constant monitoring of the pressure contour. Rebalancing the zero baseline should also be done while the pressures are being collected. Catheter entrapment will produce erroneous pressure measurements and can be identified by unusual pressure contours. Slight changes in position of a catheter may cause abnormal pressure contours, particularly if catheters with multiple side holes are placed straddling a valve (Figure 1B).

Valve Stenosis

General Principles

Assessment of valvular stenosis relies on measurement of the valve gradient and on calculation of valve area.[5] Wiggers[6] noted nearly a century ago that significant obstruction to flow occurred when a tube became limited to one third its normal area, and this principle is still in use today. Valve area is calculated in both the noninvasive and invasive laboratories with the same flow equation: $F=A\times V$ (where F is flow, A is area, and V is velocity), so $A=F/V$. Doppler interrogation of a valve measures flow velocity directly, whereas in the catheterization laboratory, velocity is imputed with the Torricelli law from the transvalvular pressure gradient: $V=\sqrt{2gh}$, where g is the velocity of acceleration resulting from gravity and h is the pressure gradient. The gravity acceleration term converts millimeters of mercury (the units of pressure) into the force that drives blood across the valve orifice. Thus, the invasive cardiologist has 3 basic tools to use to assess the severity of valvular stenosis: the transvalvular pressure gradient, the cardiac output, and the formula that relates the 2 variables (the Gorlin formula).

The Gorlin Formula

The Gorlins published their formula for calculating valve area in 1951. It stated that $A=F/(C_c\times C_v\times\sqrt{2gh})$, where C_c and C_v are the coefficients of orifice contraction and velocity loss, respectively.[6a] The coefficient of orifice contraction makes allowance for the fact that fluids moving through an orifice tend to stream through its middle so that the physiological orifice is smaller than the physical orifice. The velocity coefficient allows for the fact that not all of the pressure gradient is converted to flow because some of the velocity is lost to friction within the valve. These coefficients have never been determined. Instead, the Gorlins used an empirical constant to make their calculated mitral valve areas align better with actual valve areas obtained at autopsy or surgery. For the other 3 valves, not even an empirical constant has been developed. Thus, the coefficients for the aortic, pulmonic, and tricuspid valves have been assumed to be 1, a theoretical impossibility. These factors are important in understanding that calculated valve areas have clear limitations in the assessment of valvular stenosis. Valve area is one of the invasive cardiologist's tools of evaluation, but it is not the only one and must be used in conjunction with other parameters such as valve gradient, pressure contours, and the contractile state of the ventricle. In practical use, valve area is used to assess the severity of aortic and mitral stenosis. No valve area for defining severe tricuspid valve stenosis is agreed on, and pulmonic stenosis is usually assessed with gradient alone.

Cardiac Output

It is flow through the valve that generates the pressure gradient, so assessment of stenosis severity must take into account both flow and gradient together. Measurements of pressure gradients in patients with valve stenosis are discussed below and can usually be performed quite accurately. On the other hand, cardiac output measurement can be problematic. The gold standard for cardiac output determination is the Fick principle in which cardiac output is O_2 consumption divided by the difference between arterial and venous O_2. Although oxygen consumption can be measured quite accurately, that measurement is cumbersome, and many laboratories use standard tables for an assumed value instead of direct measurements. Such an estimation may cause an error of as much as 40% in the determination of cardiac

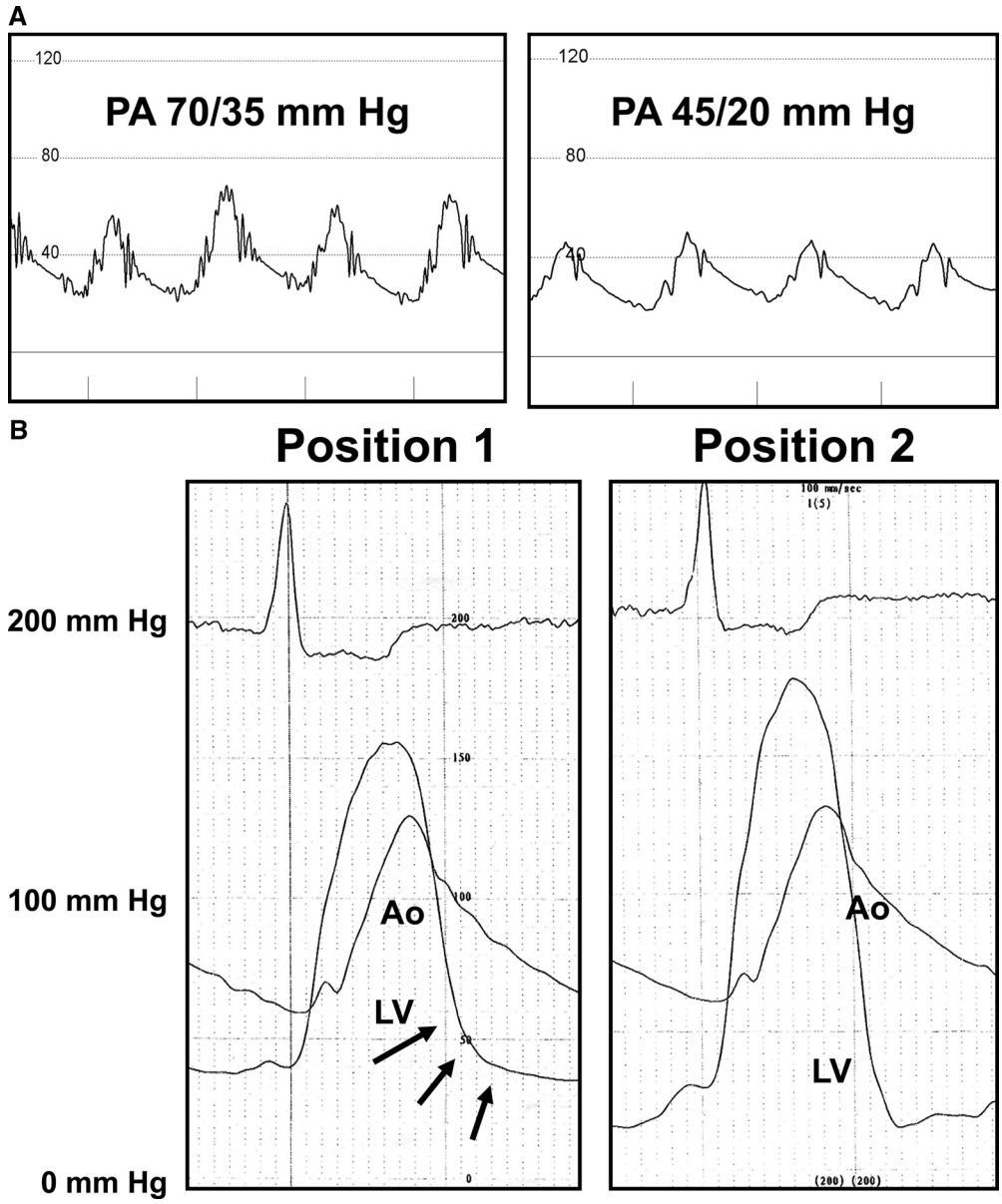

Figure 1. It is necessary to assess pressure contours continually throughout the catheterization procedure to identify pressure artifacts that may occur and lead to erroneous pressure measurements. **A**, The initial pulmonary artery (PA) pressure in this patient undergoing evaluation of pulmonary hypertension is 70/35 mm Hg (left). However, during the procedure, it was noted that the pulmonary artery pressure fell to 45/20 mm Hg in the absence of any other hemodynamic changes (right). This was due to the formation of a small thrombus in the small distal lumen of a thermodilution catheter. This pressure artifact should be avoided by meticulous technique, which includes constant monitoring of the pressure contour and intermittent frequent flushing of the lumen with heparinized saline. Using larger-bore catheters may be necessary to overcome this problem if damping of pressures continues despite the use of these techniques. **B**, In this patient with aortic stenosis, there is a pigtail catheter in the left ventricle (LV) and a separate catheter in the ascending aorta (Ao). In position 1, the contour of the left ventricular pressure is abnormal, with a marked delay in the fall of pressure during early diastole. This is due to some of the multiple side holes in the pigtail catheter straddling the aortic valve, resulting in a fusion of left ventricular and aortic pressure. Because the abnormal contour is recognized, the catheter is placed further distally so that all recording holes are in the left ventricle, as shown in position 2.

output.[5,7,8] Most laboratories now use thermodilution based on an indicator dilution methodology (a derivation of the Fick principle) to measure cardiac output. This technique is usually accurate in patients with a normal or high output who are in normal sinus rhythm. However, it becomes inaccurate in patients with intracardiac shunts, low-cardiac-output states, significant tricuspid regurgitation, or irregular rhythms, which frequently accompany advanced heart disease in severely ill patients. Calculation of the cardiac output by the Fick method can be done as an internal check to confirm the accuracy of the thermodilution method. It is critical to understand the limitations of these different methods of cardiac output measurement when assessing individual patients in the catheterization laboratory.

Aortic Stenosis

In evaluating the patient with aortic stenosis, the invasive cardiologist must understand the reliability of the data from

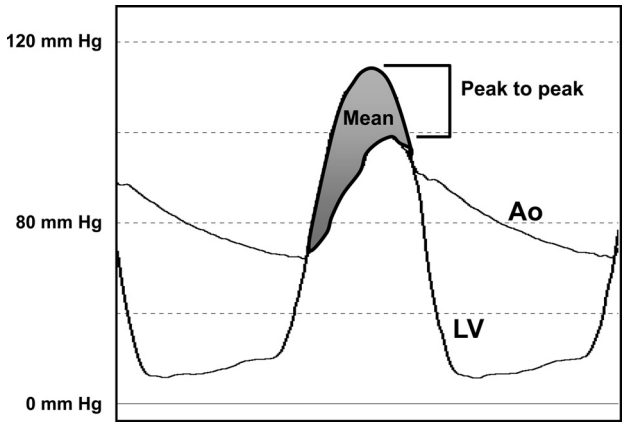

Figure 2. Simultaneous left ventricular (LV) and central aortic (Ao) pressures in a patient with aortic stenosis. The optimal way to measure the gradient in a patient with aortic stenosis is to use these simultaneous pressures. The peak-to-peak gradient is the difference between the peak left ventricular and peak aortic pressures, which is a nonphysiological measurement because the peak pressures occur at different points in time. The mean pressure gradient (the integrated gradient between the left ventricular and aortic pressure throughout the entire systolic ejection period) should be used to determine the severity of the aortic stenosis.

the noninvasive evaluation and the diagnostic issues that might remain despite a comprehensive 2-dimensional and Doppler echocardiographic evaluation. The caveat of a Doppler-derived aortic valve gradient is that the Doppler echocardiogram cannot overestimate an aortic valve gradient unless there is a problem with the assumptions incorporated into the modified Bernoulli equation (ie, seen in severe anemia or concomitant subvalvular stenosis when the proximal velocity cannot be assumed to be negligible). However, if the Doppler beam cannot be aligned parallel to the aortic jet, the Doppler velocity will underestimate the true aortic valve gradient. Calculation of valve area by Doppler echocardiography with the continuity equation may pose inaccuracies because it is the square of a measured left ventricular outflow tract diameter that is used to calculate outflow tract area. Overall, if the patient has clinical findings of severe aortic stenosis and the mean gradient is >40 mm Hg, no further hemodynamic information is required; the diagnosis of severe aortic stenosis is established except in the unusual instance when the cardiac output exceeds 6.5 L/min. However, in those cases when there is a discrepancy between the physical examination and the elements of the Doppler echocardiogram, a meticulous hemodynamically directed cardiac catheterization must resolve the issues.

The optimal technique to assess aortic valve gradient is to record simultaneously obtained left ventricular and ascending aortic pressures[9–11] (Figure 2). The peak-to-peak gradient has been the conventional measurement in the past. However, it is a nonphysiological parameter in that the peak left ventricular pressure does not occur simultaneously with the peak aortic pressure. Instead, it is recommended that the mean aortic valve gradient be used, which is the integrated gradient throughout the entire systolic ejection period and the optimal indicator of severity of obstruction.[12] Most catheterization laboratories now have the capability of computer analysis of the mean gradient, facilitating attainment of this measurement.

Pullback traces with a single catheter from the left ventricle to the aorta can be helpful, but only if the patient is in normal sinus rhythm with a regular rate. In patients with critical aortic stenosis, the Carabello sign may be present, in which the catheter across the valve itself will cause further obstruction to outflow.[13] This sign occurs in valve areas of <0.7 cm^2 when 7F or 8F catheters are used to cross the valve. Simultaneous left ventricular and femoral pressures should never be used because there can be both overestimation and underestimation of the true aortic valve gradient from either large-vessel stenosis or peripheral amplification of the distal pressures (Figure 3A). Some laboratories use dual-lumen pigtail catheters, but the operator must ensure that the small lumen in the ascending aorta is continually flushed and does not undergo "damping," causing a falsely high gradient to appear. A crucial part of the assessment is the perfect matching of the 2 pressures (from either 2 separate catheter lumens or both lumens of a dual-lumen catheter) in the proximal aorta before the left ventricle is entered. The 2 lumens are in fact subjected to 2 identical pressures so that 2 identical pressures should be recorded, confirming the accuracy for the 2 transducers and the recording systems. Failure to follow this step may lead to a false pressure gradient caused by errors in the recording system. Ideally, the pressures in the aorta should be measured with a side-hole catheter to avoid a damping artifact (Figure 3B).

A visual assessment of the contours of the aortic and left ventricular pressures during catheterization adds information regarding the type of obstruction present (Figure 4). In patients with fixed valvular obstruction, there is a delay (tardus) and reduction (parvus) in the upstroke of the central aortic pressure that begin at aortic valve opening. However, in the presence of a dynamic left ventricular outflow tract obstruction (as seen in hypertrophic cardiomyopathy), the aortic contour assumes a spike-and-dome pattern with an initial rapid upstroke. There is also a late peaking left ventricular pressure resulting from the mechanism of this dynamic obstruction. The response of the aortic pulse pressure after a long pause is often diagnostic in differentiating between a fixed and dynamic left ventricular outflow obstruction by demonstrating the Braunwald-Brockenborough sign (Figure 5). These observations not only confirm the site of obstruction as assessed by noninvasive imaging but also may identify latent dynamic outflow gradients that may not have been present at the time of the echocardiogram.

The aortic valve area should then be calculated from a meticulous measurement of the mean gradient and cardiac output, as described previously. Although current computer systems in the modern catheterization laboratories automatically perform this calculation, it is the responsibility of the operator to do a quick ballpark calculation offline to ensure that the input into the computer is accurate. The Hakki equation (valve area equals cardiac output divided by the square root of the gradient) can be used to ensure that the more complex Gorlin equation has been calculated with the proper data input.

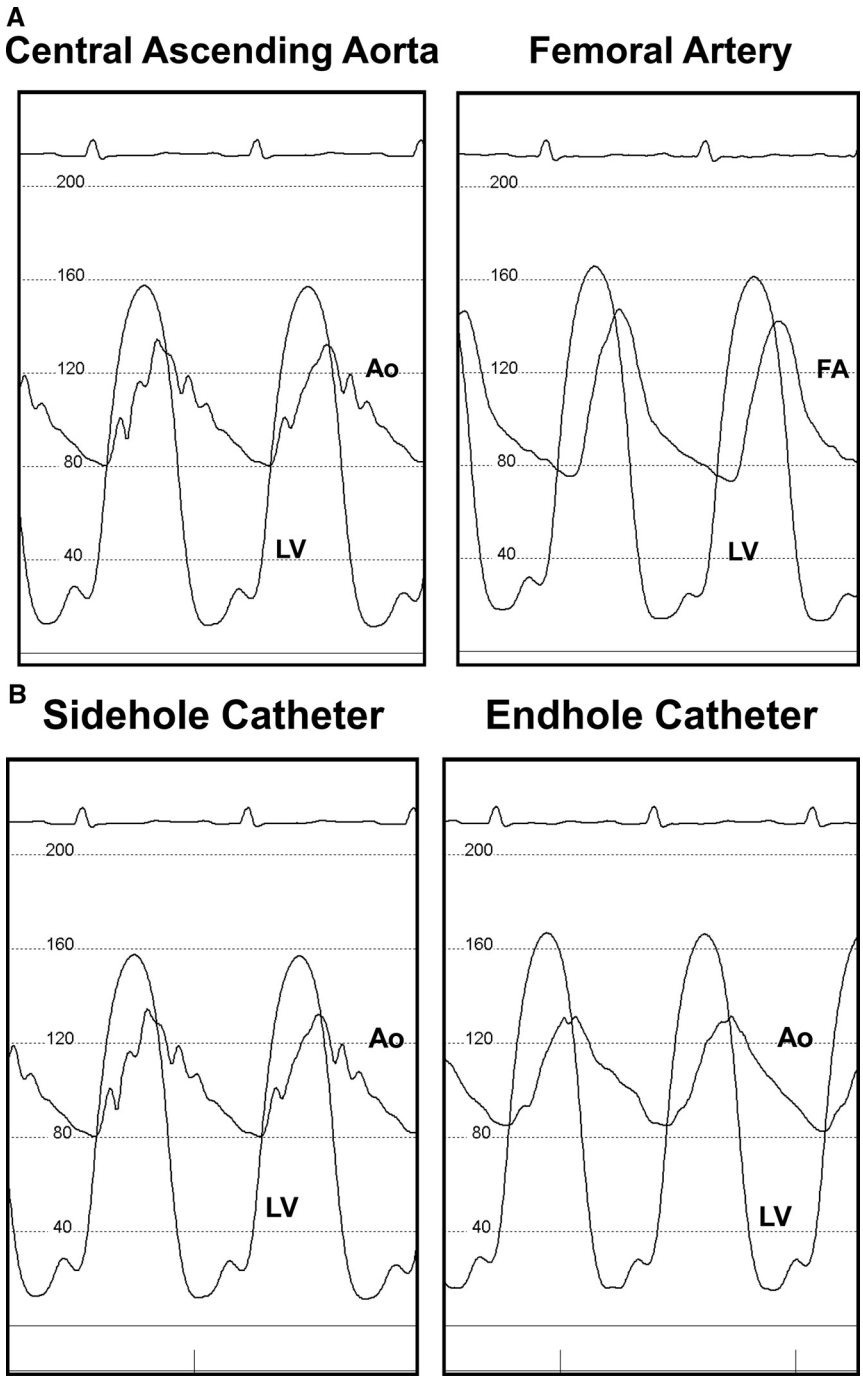

Figure 3. The optimal method to measure the transaortic gradient in a patient with aortic stenosis is a simultaneous left ventricular (LV) pressure and central aortic (Ao) pressure with side-hole catheters. Shown are examples in which alternative methods are used to obtain the pressures, which produce erroneous results. **A**, The simultaneous left ventricular and femoral artery (FA) pressures should not be used to measure the aortic valve gradient because peripheral amplification may cause a false decrease in gradient and peripheral artery stenosis may cause a false increase in gradient. There is also a temporal delay when a femoral artery pressure is used that will affect the calculation of the mean gradient. In this patient, the use of a femoral artery pressure would significantly underestimate the peak-to-peak gradient as a result of peripheral amplification of the pressure. **B**, In the measurement of left ventricular and aortic pressures, catheters with side holes should be used because damping can occur with an end-hole catheter (ie, coronary artery catheters). Shown is the typical damping that may occur in the aortic pressure when an end-hole catheter (right) is used compared with a side-hole catheter (left).

It is always necessary to reconcile the severity of disease indicated by mean gradient and that indicated by the valve area obtained by cardiac catheterization. There is a subset of patients in whom the magnitude of the gradient will not match the severity of valve stenosis predicted by valve area, and further evaluation of these patients is necessary. Some patients present with a low gradient (<30 mm Hg) and a low output, resulting in a small calculated valve area. If severe left ventricular dysfunction is present, dobutamine stimulation is warranted to determine whether the small valve area truly is due to critical aortic stenosis or might be due to pseudo–aortic stenosis, a condition in which there is not enough momentum from a ventricle with impaired myocardium to fully open a mildly or moderately stenotic valve[14,15] (Figure 6). Furthermore, the presence of inotropic reserve, defined as an increase in stroke volume >20% during dobutamine stimulation, is an important stratifier for operative risk.[14,15] Although dobutamine challenge may be performed in the echocardiography laboratory, performance in the catheterization laboratory where coronary anatomy is assessed can also be quite useful in determining whether ischemia might be a cause of failed inotropic reserve. In patients at high risk for critical coronary disease, coronary angiography should be performed before dobutamine infusion. There is also a growing recognition of a population of patients who have low-output/low-gradient aortic stenosis with a preserved ejection fraction. Further

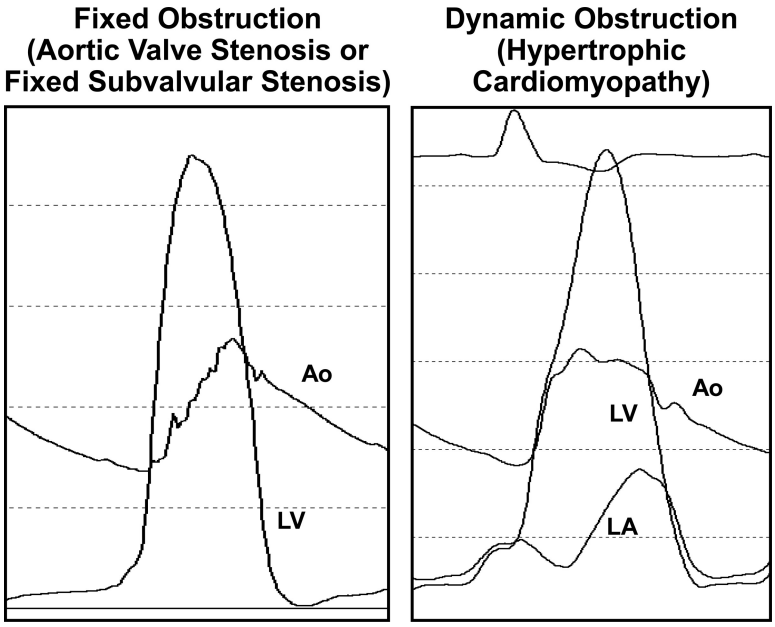

Figure 4. A visual assessment of the contour of the aortic (Ao) and left ventricular (LV) pressures is important during cardiac catheterization. **Left**, Patients with fixed obstruction (either valvular stenosis or fixed subvalvular stenosis) will demonstrate a parvus and a tardus in the upstroke of the aortic pressure, beginning at the time of aortic valve opening. **Right**, In patients with a dynamic obstruction (such as that found in hypertrophic cardiomyopathy), the aortic pressure will rise rapidly at the onset of aortic valve opening and then develop a spike-and-dome contour as the obstruction occurs in late systole. The left ventricular pressure also has a late peak because of the mechanism of this dynamic obstruction. LA indicates left atrium.

evaluation of these patients may be indicated, perhaps with vasodilators to lower the high peripheral resistance seen in these patients[16,17] (Figure 7).

Mitral Stenosis

Patients with mitral stenosis frequently come to the cardiac catheterization laboratory for further hemodynamic evaluation when the noninvasive estimations of valve gradient and valve area are inconsistent with one another or when there are symptoms of pulmonary hypertension out of proportion to the apparent severity of the mitral valve disease. The transmitral gradient measured by continuous-wave Doppler echocardiography is highly accurate.[18] As opposed to aortic stenosis, it is much easier to align the Doppler beam with the mitral inflow jet, providing a very reproducible method for determining mean gradient. In those rare patients in whom a transmitral gradient cannot be obtained by transthoracic echocardiography, transesophageal echocardiography should be performed. In the echocardiography laboratory, the mitral valve area may be measured by direct planimetry or by the pressure–half-time method. Poor images on transthoracic echocardiography may preclude accurate measurement of the valve area by planimetry. The valve area by half-time techniques used by Doppler echocardiography have potential limitations in that the half-time is dependent not only on the severity of stenosis but also on the compliance of the left atrium and left ventricle and concomitant mitral regurgitation.[19]

In the cardiac catheterization laboratory, evaluation of the transmitral gradient is frequently made with a simultaneous pulmonary artery wedge pressure and left ventricular pressure (Figure 8). Although the mean pulmonary artery wedge pressure will usually reflect the mean left atrial pressure, the pulmonary artery wedge pressure/left ventricular pressure gradient frequently overestimates the true severity of mitral stenosis owing to a phase shift in the pulmonary artery wedge pressure and a delay in transmission of the change in pressure contour through the pulmonary circulation. Thus, there may be a 30% to 50% overestimation of the true gradient when conventional catheters are used, even with correction for the phase shift.[18] Overestimation of the true left atrial pressure by wedge pressure can be reduced by scrupulous oximetric confirmation that the catheter is truly wedged.[20,21] If necessary, a transseptal approach to obtain true left atrial pressures should be performed in patients with mitral stenosis if therapeutic decisions depend on the accuracy of these data.

An important indication for cardiac catheterization in the patient with mitral stenosis is a discrepancy between symptoms, transmitral gradient, and pulmonary pressure. Cardiac catheterization is able to provide accurate measurements of absolute pressures that are not possible by Doppler echocardiography. Thus, if a patient has symptoms or pulmonary hypertension out of proportion to the noninvasive measurements, cardiac catheterization is important to determine whether pulmonary hypertension is secondary to the mitral stenosis, left ventricular diastolic dysfunction, pulmonary veno-occlusive disease, or intrinsic pulmonary vascular disease. Exercise hemodynamics can be performed noninvasively with Doppler echocardiography or can be performed in the catheterization laboratory. These hemodynamic responses to exercise are most useful in determining the cause of severe symptoms when only a mild to moderate degree of mitral stenosis is apparent at rest (Figure 9A).

Valve Regurgitation

Most patients with valve regurgitation are able to be fully evaluated by clinical and noninvasive testing, coming to the catheterization laboratory only for definition of the coronary anatomy before operation. However, there is a subset of patients in whom further information is required for proper clinical decision making, usually when there is a discrepancy between the clinical presentation and the results of the echocardiogram. Hemodynamic catheterization is also indicated when the noninvasively obtained parameters are not

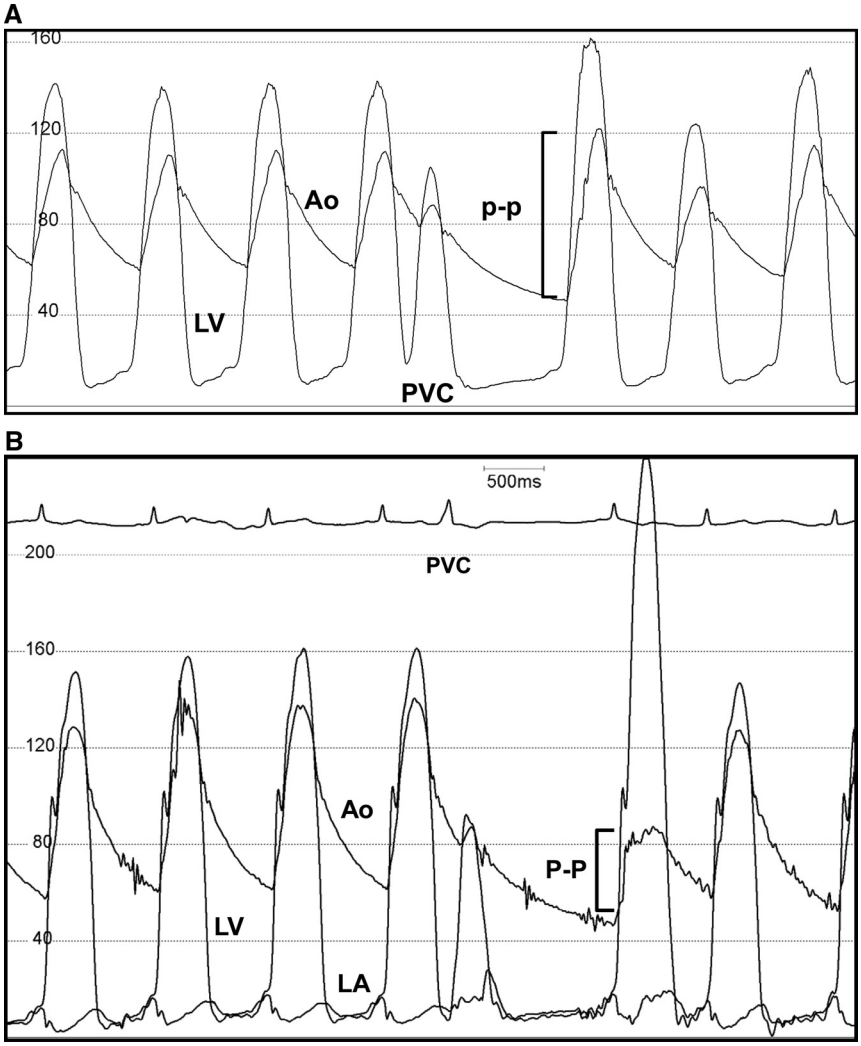

Figure 5. Response of the aortic pressure after a long pause is useful in differentiating between the fixed obstruction of valvular aortic (Ao) stenosis and the dynamic obstruction of hypertrophic cardiomyopathy. **A**, In this patient with valvular aortic stenosis, the beat after the premature ventricular contraction (PVC) has an increase in pulse pressure (P-P). **B**, In this patient with hypertrophic cardiomyopathy, there is a reduction in the pulse pressure on the beat after the premature ventricular contraction. LV indicates left ventricle; LA, left atrium.

compatible with each other, eg, severe pulmonary hypertension out of proportion to the degree of mitral regurgitation.

Two-dimensional and Doppler echocardiography can provide indirect clues to the severity of valve regurgitation and quantitative measurements of valve severity. In the era of early operation for severe valve regurgitation in the absence of symptoms, it is essential that the clinician be confident of the severity of valve regurgitation.[12,22] There are major problems with assessing valve regurgitation using only the extent of color flow jets into the proximal chamber. The methodology for quantitative measurement of valve regurgitation uses the proximal isovelocity surface area, which in many instances can provide an accurate measurement of regurgitant volume and effective orifice area. However, there are limitations and caveats to these Doppler measurements even when transesophageal echocardiography is used. Therefore, when the clinical presentation and physical examination do not fit with the Doppler assessment of valve regurgitation severity, cardiac catheterization is required.

Although quantitative analysis of valve regurgitation can also be performed in the catheterization laboratory by subtracting forward flow (cardiac output) from total left ventricular output (angiographic volumes), this is a tedious technique with limitations. Thus, left ventriculography and aortic angiography are the modalities most often used to assess the severity of valve regurgitation. The time and density of contrast going back into a proximal chamber are used to grade valve regurgitation on a scale of 1 to 4 scale the Sellar criteria. Although only semiquantitative, the contrast injections are better than conventional color-flow imaging for valve regurgitation because they reflect the volume of blood going retrograde through the valves rather than changes in blood velocity.

All contrast injections must be made with large-bore catheters and a large amount of contrast to completely opacify the cardiac chambers; using too little contrast results in underestimation of lesion severity. Avoidance of ventricular ectopy and entrapment of the mitral valve apparatus by the catheter are especially important in left ventriculography. One should not be hesitant to repeat a left ventriculogram if ectopy occurs because even 1 or 2 premature ventricular contractions may result in an underestimation or overestimation of the severity of valve regurgitation. High right anterior oblique views for left ventriculograms may be necessary to avoid the retrograde contrast from being superimposed on the spine or descending aorta.

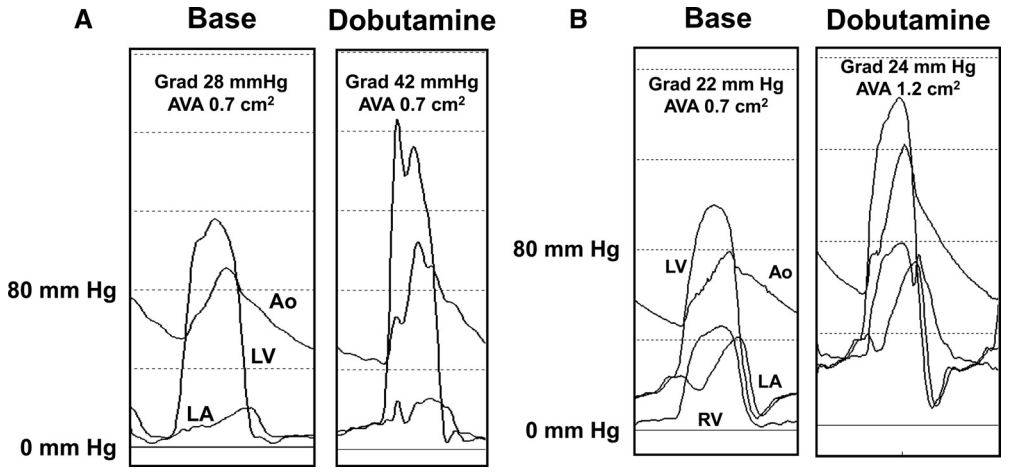

Figure 6. In patients in whom there is a low-output, low-gradient (Grad) state, it may be necessary to perform dobutamine stimulation to normalize cardiac output. This can be used to differentiate between patients with true aortic (Ao) stenosis and those with pseudo–aortic stenosis. **A**, With dobutamine stimulation, the gradient increases from 28 to 42 mm Hg and the valve area remains small at 0.7 cm^2. This indicates that there is severe fixed valvular stenosis in this patient. **B**, In this patient with similar resting hemodynamics, dobutamine infusion does not change the gradient remaining at 24 mm Hg. The valve area increases to 1.2 cm^2. This is an example of pseudo–aortic stenosis in which the valve area is small at baseline owing to the lack of momentum from a ventricle to fully open a mildly stenotic aortic valve. AVA indicates aortic valve area; LV, left ventricle; RV, right ventricle; and LA, left atrium.

Evaluation of Unexplained Dyspnea

There are significant limitations to noninvasive methods in determining the cause of dyspnea. This is particularly pertinent to patients with normal left ventricular systolic function and the absence of severe valvular heart disease who have dyspnea out of proportion to the noninvasive parameters. In these instances, direct measurements of intracardiac and pulmonary pressures are required to determine the cause of the dyspnea.

In cases of unexplained dyspnea, the invasive cardiologist must be prepared to perform additional interventions if the results of resting hemodynamics are inconclusive or if such interventions can help guide management. If there is a high left ventricular diastolic or pulmonary artery wedge pressure, afterload reduction in the cardiac catheterization laboratory is useful to determine whether the elevation of diastolic pressures is reversible with lowering of systemic pressure. Most patients presenting with diastolic dysfunction have enhanced

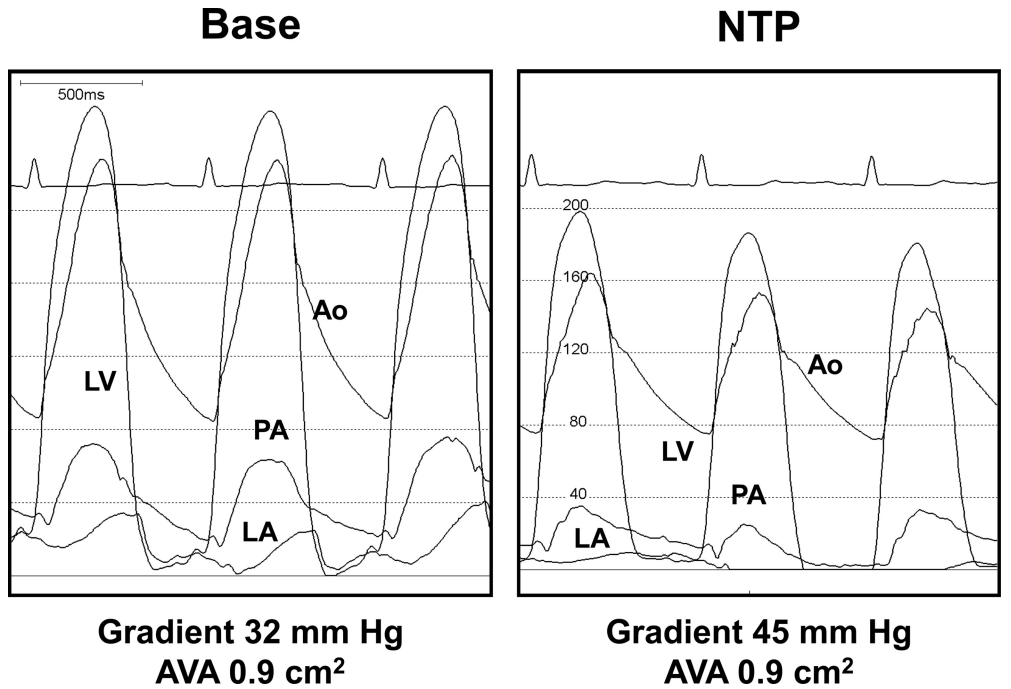

Figure 7. Low-output, low-gradient state may also be seen in patients with preserved ejection fraction. In these patients, a high additional afterload resulting from a noncompliant aortic system further contributes to the low cardiac output. Through lowering of the peripheral resistance with a vasodilator such as nitroprusside (NTP), patients with true aortic stenosis may be able to be identified by demonstrating an increase in aortic valve gradient and a fixed valve area. LV indicates left ventricular; AO, central aortic; PA, pulmonary artery; LA, left atrium; and AVA, aortic valve area.

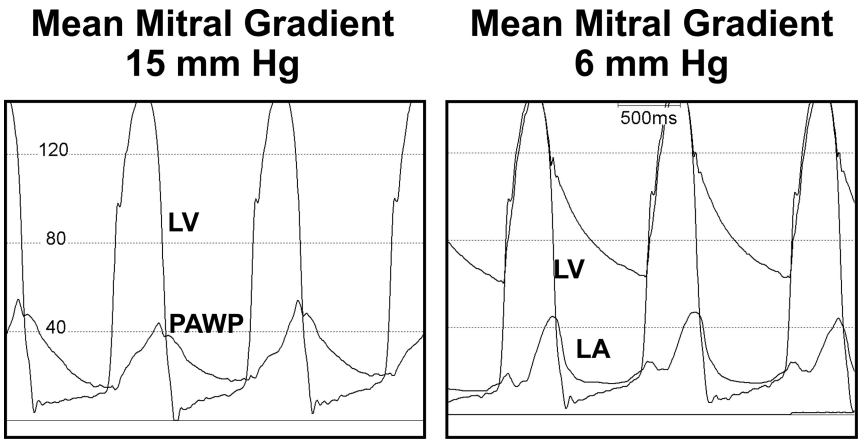

Figure 8. Measurement of the transmitral gradient by cardiac catheterization is frequently made with a simultaneous pulmonary artery wedge pressure (PAWP) and left ventricular (LV) pressure. However, as a result of the delay in transmission of the change in pressure contour and a phase shift, the gradient using a pulmonary artery wedge pressure will frequently overestimate the true transmitral gradient. **Left**, Simultaneous left ventricular and pulmonary artery wedge pressure in a patient with mitral stenosis. The measured mean gradient is 15 mm Hg. **Right**, In the same patient, the transmitral gradient is measured with a left ventricular and direct left atrial (LA) pressure. The true mean transmitral gradient is only 6 mm Hg.

ventriculovascular coupling; in these patients, lowering afterload with vasodilators will normalize high filling pressures, in turn guiding outpatient medical management.[23,24] High left ventricular diastolic pressures that do not decrease with a lowering of afterload indicate a severe irreversible restrictive myocardial process, and endomyocardial biopsy might be indicated. For those patients who have high pulmonary pressures, nitric oxide inhalation or other vasodilators can establish reversibility of pulmonary hypertension and are useful to determine optimal treatment.

In patients who have symptoms of heart failure and normal filling pressures, either fluid challenge or exercise should be implemented. Exercise hemodynamics are extremely useful in the evaluation of patients with unexplained dyspnea who do not have a significant elevation of filling pressures in the resting state.[25] With evaluation of the pulmonary artery pressure, wedge pressure, and cardiac output at rest and exercise, a differentiation can be made between a pulmonary cause, a cardiac cause, or even a noncardiac cause of dyspnea. In some laboratories, supine bicycle exercise is now being used to assess hemodynamics in patients with unexplained dyspnea because this type of intervention best simulates the physiological responses to exercise (Figure 9B).

Pulmonary Hypertension

A cardiac catheterization should be performed in the initial evaluation of patients with pulmonary hypertension. The cause of the pulmonary hypertension can be diagnosed by cardiac catheterization by determining whether the pulmonary hypertension is secondary to left-sided disease (and elevated left ventricular filling pressure), secondary to intrinsic pulmonary vascular disease, or a combination of both. Although noninvasive methodology is useful for initially identifying patients with pulmonary hypertension, absolute assessment of the severity of pulmonary hypertension needs to be done at catheterization, especially if tricuspid regurgitation is either absent or difficult to interrogate. Current assessment of diastolic filling by noninvasive Doppler is not accurate enough to determine the absolute left ventricular filling pressure in an individual patient. Sorting out the origin rests largely on assessing the transpulmonary pressure gradient (mean pulmonary artery pressure minus pulmonary artery wedge pressure [PA−PAWP]), the numerator in the equation for pulmonary vascular resistance (PVR): PVR=(PA−PAWP)/CO, where CO is cardiac output.

Thus, a meticulous cardiac catheterization must be performed in patients presenting with pulmonary hypertension to directly measure pulmonary pressure and either the pulmonary artery wedge pressure or the left atrial pressure. The pulmonary artery wedge pressure in this instance is best achieved with a large-bore end-hole catheter, usually balloon tipped. Confirmation of the wedge by looking at the pressure contour and obtaining saturation >95% should ideally be done to ensure that true pulmonary artery wedge pressure is measured instead of a damped pulmonary pressure (Figure 10). In the cardiac catheterization laboratory, careful measurements of cardiac output are necessary to calculate the pulmonary arterial resistance with either the Fick or the thermodilution technique. The response of pulmonary hypertension to nitric oxide, adenosine, or a vasodilator is helpful for the clinician to determine optimal therapy. Nitric oxide should be given only to patients with pulmonary hypertension and a normal pulmonary artery wedge pressure because the nitric oxide may dilate the postcapillary bed and result in a further elevation of left-sided filling pressures in patients with baseline left atrial pressure elevation; a similar deleterious response may be possible with administration of adenosine. Pulmonary artery capacitance has been shown to have additional prognostic value and should be measured at the time of cardiac catheterization.[26]

Constrictive Pericarditis Versus Restrictive Cardiomyopathy

The differential diagnosis of the cause of severe right-sided heart failure in a patient with normal systolic function remains a major diagnostic challenge in 2012.[27] The major elements in the differential diagnosis are constrictive pericarditis versus restrictive cardiomyopathy, although left-to-right shunt, high-output states, and tricuspid regurgitation must also be considered. An increasing number of patients who come with this differential diagnosis have had previous radiation to the chest for malignancy or previous open heart surgery. These patients frequently may have a combination of both myocardial and pericardial disease.

In patients with constrictive pericarditis, there is the finding of early rapid filling and elevation with end equal-

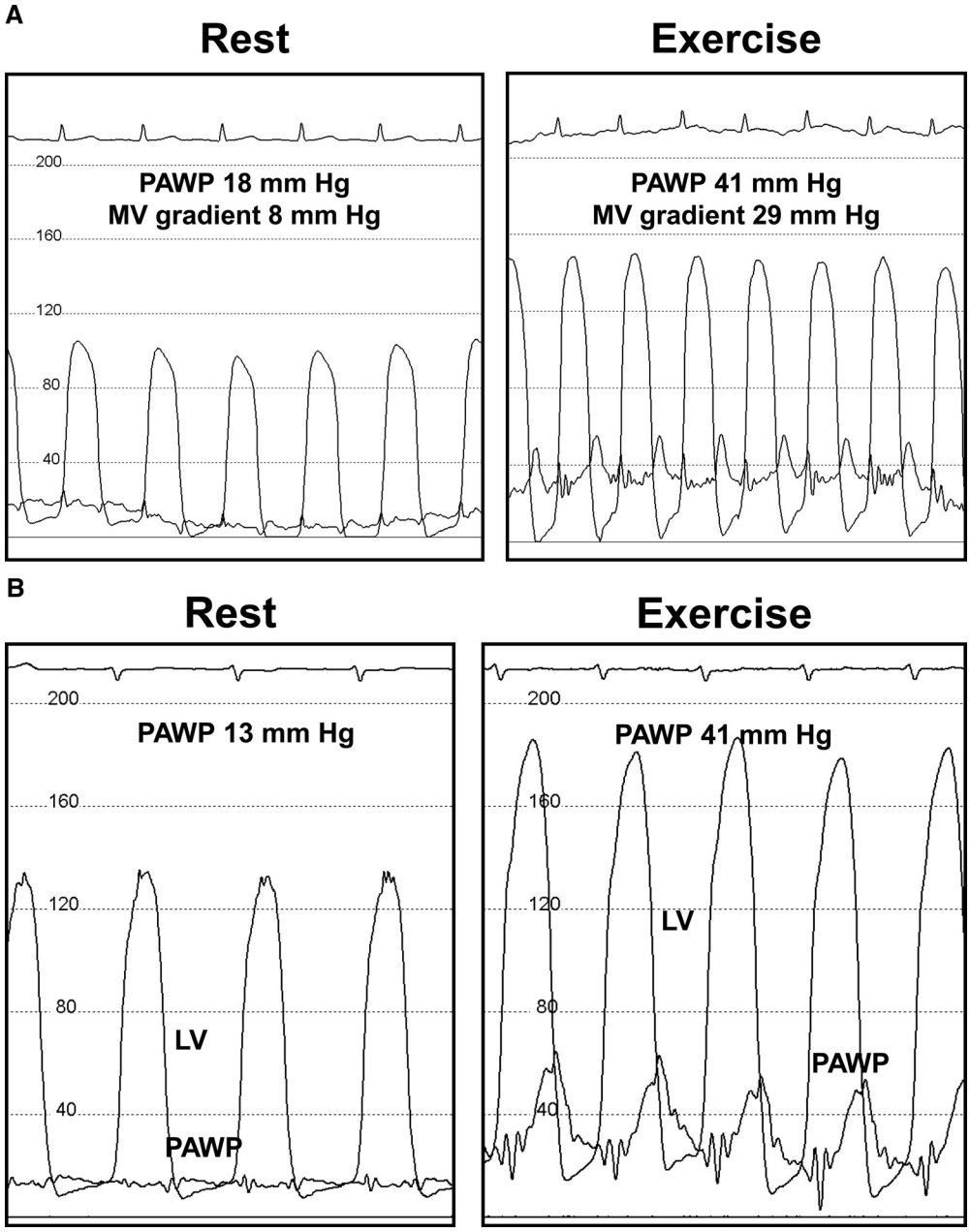

Figure 9. Exercise is frequently helpful in the cardiac catheterization laboratory to determine the cause of dyspnea in patients who do not have marked abnormalities of pressures in the resting state. **A**, In this patient with mitral stenosis, the mean resting gradient was only 8 mm Hg and the pulmonary artery wedge pressure (PAWP) was only 18 mm Hg. This patient had significant symptoms out of proportion to the resting hemodynamics. With supine bicycle exercise, the mean gradient rose to 29 mm Hg and the pulmonary artery wedge pressure rose to 41 mm Hg, indicating that the mitral stenosis was hemodynamically significant and causing the severe symptoms. **B**, This patient had no significant valve disease, normal left ventricular (LV) systolic function, but significant dyspnea on exertion. In the resting state, the pulmonary artery wedge pressure was only 13 mm Hg. However, at a low level of supine bicycle exercise, there was a marked increase in pulmonary artery wedge pressure to 41 mm Hg with a large V wave. There was not significant mitral regurgitation by simultaneous echocardiography, indicating that these symptoms were due to noncompliance of the left atrium and left ventricle. MV indicates mitral valve.

ization of diastolic pressures in all cardiac chambers. In patients who are on diuretics and have relatively normal diastolic filling pressures, volume loading may be required to bring out these classic findings. Because patients with restrictive cardiomyopathy may also have similar hemodynamic findings, criteria to differentiate constrictive pericarditis from restrictive cardiomyopathy have been proposed. The absolute pulmonary pressure, the ratio of right ventricular end-diastolic pressure to right ventricular systolic pressure, and the difference between the left ventricular end-diastolic pressure and right ventricular end-diastolic pressure were all used in attempts to make this differentiation. However, these criteria have been shown to have a relatively low specificity and are rarely useful in an individual patient.

The current evaluation of these patients with severe right heart failure uses criteria based on respiratory changes that

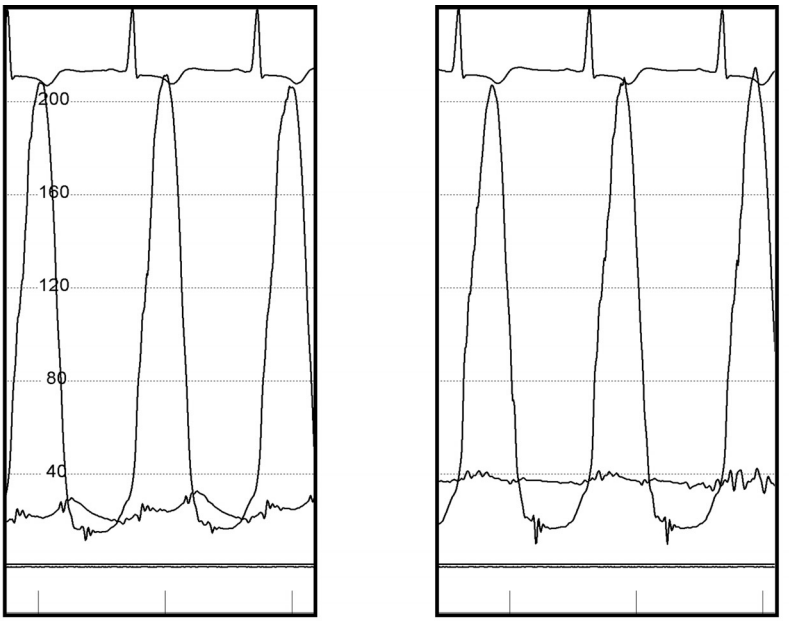

Figure 10. The pulmonary artery wedge pressure (PAWP) must be obtained meticulously during cardiac catheterization, optimally performed with a large-bore end-hole catheter. Confirmation of the pulmonary artery wedge pressure examining the pressure contour for respiratory variation and a >95% saturation is recommended to ensure an accurate pressure measurement. **Left**, Pulmonary artery wedge pressure was taken with a large-bore 7F balloon wedge catheter with a 98% saturation confirmation. There is appropriate respiratory variation and a proper contour of the pulmonary artery wedge pressure. **Right**, The attempt at pulmonary artery wedge pressure was done with a small-lumen thermodilution catheter. This most likely represents a damped pulmonary artery pressure. Confirmation by saturation was not performed.

show the presence or absence of enhancement of ventricular interaction.[28] In assessments of the cause of right heart failure, evaluation of the respiratory changes that occur in both the pulmonary artery wedge/left ventricular pressures and the right ventricular/left ventricular pressures is crucial. In patients with constrictive pericarditis, there is a dissociation of intrathoracic and intracardiac pressures; thus, the initial driving pressure between the pulmonary veins and left ventricle is decreased during inspiration and increased during expiration. This results in a decrease in left ventricular preload during inspiration. Because of the rigid pericardium surrounding the heart, the ventricular interaction is enhanced so that diminution in left heart filling during inspiration causes simultaneous enhancement of right ventricular preload. This results in a discordance of left ventricular and right ventricular pressures during respiration in patients with pericardial disease compared with a concordance in these pressures with myocardial disease (Figure 11). In patients with severe abnormalities of right ventricular systolic and diastolic dysfunction and/or severe tricuspid regurgitation, there can be elevation and end equalization of diastolic pressures and mild discordance of left and right ventricular pressures during respiration. Examination of the left and right ventricular diastolic pressures during respiration is helpful in differentiating constrictive pericarditis from these abnormalities of right ventricular filling.[29]

There are patients who will present with elevated right-sided diastolic pressures and low forward output resulting from cardiac tamponade. As opposed to patients with constrictive pericarditis, early diastolic rapid filling will be blunted in patients with tamponade. Although the treatment of tamponade is to remove the pericardial fluid, a subset of patients will continue to have elevated diastolic pressures after pericardiocentesis, with the emergence of early rapid filling that is seen in constrictive pericarditis. These patients have effusive-constrictive pericarditis and should be treated with pericardiectomy.

Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy is a unique disease in which there is hypertrophy of the myocardium in the absence of the hemodynamic factors that cause hypertrophy that is associated with genetic mutations of the sarcomere.[30–32] There is frequently a dynamic left ventricular outflow tract obstruction that is highly dependent on loading conditions and the contractile state of the ventricle.[33] This obstruction can be associated with severe symptoms, and treatment of the obstruction may result in relief of symptoms. Although many patients respond to medical therapy with β-blockers, calcium channel blockers, or disopyramide, there is a subset of patients whose symptoms are unresponsive to medical therapy. These patients benefit greatly from septal reduction therapy with either septal myectomy or, more recently, septal ablation.[34] The indications for septal reduction therapy are a suitable anatomy, severe symptoms unresponsive to medical management, and a documented left ventricular outflow gradient of >50 mm Hg either at rest or during provocation. Because the gradient is labile, cardiac catheterization may be required to document the severity of the gradient during provocative maneuvers.[35]

Cardiac catheterization in these patients requires meticulous attention to detail, given the number of problems that may occur as a result of the measurement of pressures in small hypertrophied hyperdynamic ventricles. Catheters frequently become entrapped in these ventricles, resulting in erroneous pressure measurements. The optimal approach is transseptal catheterization for the measurement of left ventricular inflow pressures, which avoids catheter entrapment.[32] If a retrograde catheter is used for left ventricular pressure measurements, pigtail catheters with multiple side holes

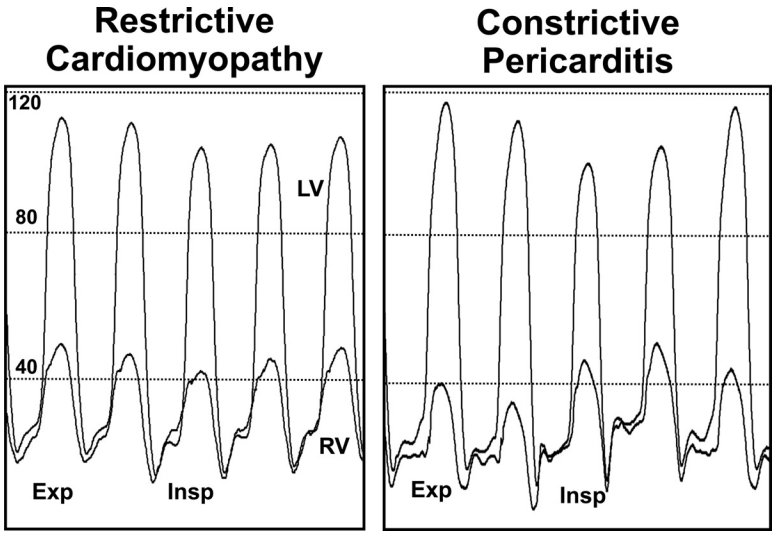

Figure 11. High-fidelity manometer-tipped catheters in the left ventricle (LV) and right ventricle (RV) during the respiratory cycle. **Left**, In this patient with restrictive cardiomyopathy, there is a drop in left ventricular pressure and a drop in right ventricular pressure during inspiration (Insp). This indicates that the elevation of ventricular filling pressures is due to a myocardial restrictive disease. **Right**, In this patient with constrictive pericarditis, there is ventricular discordance, with an increase in right ventricular pressure and a decrease in left ventricular pressure during inspiration. This is due to the enhancement of ventricular interaction and dissociation of intrathoracic and intracardiac pressures. Exp indicates expiration.

extending several centimeters along the shaft should be avoided. It is recommended that catheters such as a multipurpose or Rodriquez catheter with side holes at the distal portion of the catheter should be used to determine the exact location of obstruction. If a single end-hole catheter is used, constant analysis of the pressure contour and small hand injections of contrast should be performed to ensure that the catheter is not entrapped but free within the ventricular cavity.

The left ventricular outflow tract gradient is dynamic and can change significantly during a single diagnostic catheterization. If there is a gradient $<$50 mm Hg at rest, provocative maneuvers such as the Valsalva maneuver or induction of a premature ventricular contraction should be performed (Figure 5B). However, if a gradient is not provoked with these maneuvers, infusion of isoproterenol is helpful because direct stimulation of the β1 and β2 receptors simulates exercise and may uncover a labile outflow tract gradient[36] (Figure 12). In patients undergoing septal ablation, it is important to evaluate the outcome of the ablation not only with resting gradients but also with provoked gradients (if there is no resting gradient).

Conclusion

In the new era of cardiac catheterization, there is no longer a routine cardiac catheterization. Patients enter the laboratory after a battery of noninvasive tests have failed to yield the diagnosis on structural heart disease, and there is every expectation that the patient will leave the catheterization laboratory with a firm diagnosis. To accomplish this, a

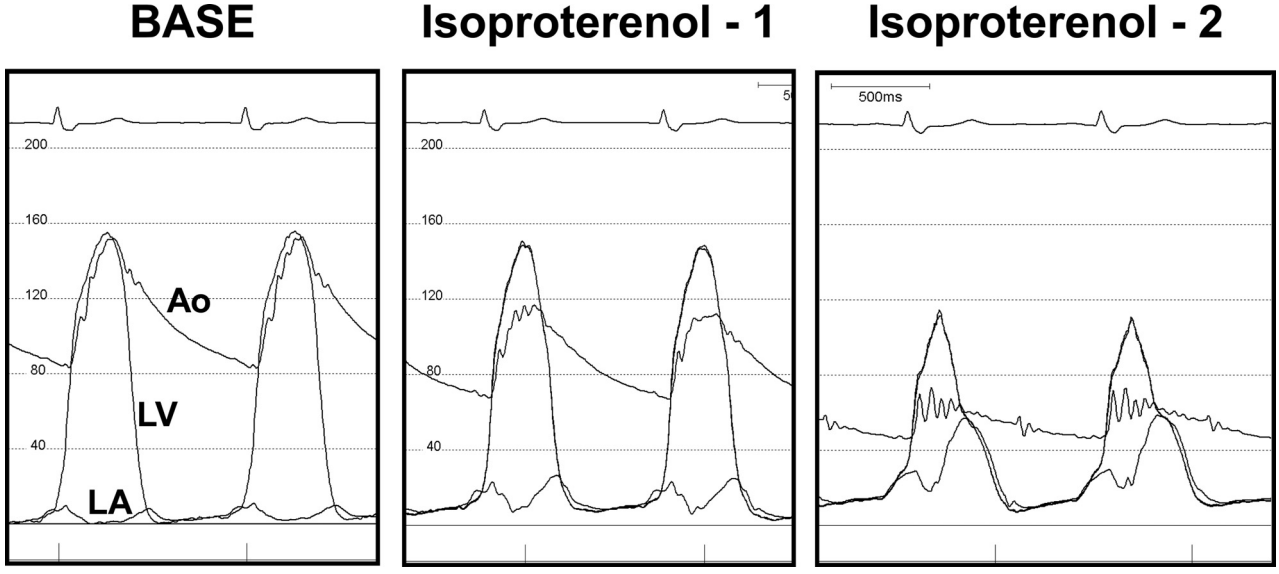

Figure 12. Patients with hypertrophic cardiomyopathy may have labile left ventricular (LV) outflow tract gradients. If septal reduction therapy is to be considered, there must a gradient of $>$50 mm Hg either at rest or during provocation. Exercise would be the optimal physiological mechanism to provoke a labile obstruction but is difficult in the catheterization laboratory. Isoproterenol infusion is an excellent method to simulate exercise by stimulating both B1 and B2 receptors. **Left**, There is no left ventricular outflow gradient at rest. **Middle**, With initial infusion of isoproterenol, there is a 40-mm Hg gradient across the left ventricular outflow tract. **Right**, With a greater infusion of isoproterenol, there is a 65-mm Hg left ventricular outflow gradient. Ao indicates central aortic; LA, left atrial.

goal-oriented approach must be undertaken with meticulous attention to detailed skills that may not have been developed during fellowship. In many cases, it will be necessary to retrain cardiologists in the art of cardiac catheterization, emphasizing pitfalls in pressure recording and in maneuvers performed in the catheterization laboratory to sort out difficult hemodynamic problems. In this way, we can ensure that our patients will receive the full benefits of an invasive evaluation.

Disclosures

None.

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