Value of Dynamic Respiratory Changes in Left and Right Ventricular Pressures for the Diagnosis of Constrictive Pericarditis

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Abstract

Background Conventional cardiac catheterization criteria for the diagnosis of constrictive pericarditis (CP) rely on equalization of intracardiac pressures and have many recognized limitations. Recently, Doppler echocardiographic methods have been used to examine dynamic respiratory changes of increased ventricular interdependence and dissociation of intrathoracic and intracardiac pressures for the diagnosis of CP. These pathophysiological features may be best delineated by cardiac catheterization. Therefore, we studied the accuracy of these dynamic respiratory changes in left ventricular and right ventricular pressure for the diagnosis of CP at cardiac catheterization.

Methods and Results High-fidelity manometric catheters and respirometry were used to study 36 patients: 15 patients with surgically proven CP (group 1) and 21 patients with other causes of heart failure (group 2). Conventional cardiac catheterization variables used to establish the diagnosis of CP lacked sensitivity and specificity and failed to distinguish between these groups. However, the finding of discordance between right ventricular and left ventricular pressures during inspiration, a sign of increased ventricular interdependence, accurately distinguished patients in group 1 from those in group 2 (P<.05).

Conclusions Examination of dynamic respiratory changes indicating increased ventricular interdependence may be helpful in the diagnosis of CP in the cardiac catheterization laboratory.
**Key Words:** catheterization • diastole • pericardium

### Introduction

Patients with constrictive pericarditis present with symptoms due to severe elevation of right-sided pressures. Noninvasive modalities, such as two-dimensional and Doppler echocardiography and nuclear imaging techniques, have made it possible to accurately diagnose several causes of heart failure, such as myocardial systolic dysfunction, valvular heart disease, and pulmonary hypertension. However, in some patients with elevated right-sided pressures, it is still difficult to distinguish constrictive pericarditis from myocardial restrictive disease. Visualization of the pericardium by computed tomography or magnetic resonance imaging has been useful in some patients, because a thickened pericardium is usually present in constrictive pericarditis. However, these tests provide only anatomic information and do not necessarily indicate the physiological significance of the findings. Cardiac catheterization has been used to identify the hemodynamic consequence of right-sided heart failure, but the initial criteria that examined end-diastolic pressure relationships have been of limited predictive value. Recently, characteristic Doppler echocardiographic findings that show increased transvalvular flow velocity variation have been described in patients with constrictive pericarditis. These dynamic respiratory-driven changes in left and right ventricular filling were related to a dissociation of intracardiac and intrathoracic pressures and increased ventricular interdependence. Although these Doppler findings have been of diagnostic clinical utility in many patients presenting with the presumed diagnosis of constrictive pericarditis, a subset of patients remains whose diagnosis is still equivocal after this test. It has been hypothesized that these pathophysiological abnormalities may be accurately delineated by cardiac catheterization.

The purpose of this study was to critically evaluate the ability of cardiac catheterization to establish the diagnosis of constrictive pericarditis by examining the dynamic respiratory changes in left ventricular and right ventricular pressure relationships associated with this disorder. Right- and left-sided heart catheterizations with high-fidelity micromanometer-tipped pressure catheters were prospectively performed in all patients coming to the cardiac catheterization laboratory with the presumed diagnosis of constrictive pericarditis. To determine the specificity of these dynamic pressure relationships, these pressure measurements were compared with those from a group of patients who had other documented causes of heart failure.

### Methods

**Patient Population**

The cohort patient population (group 1) consisted of all patients referred for hemodynamic evaluation to the cardiac catheterization laboratory from July 1990 through October 1994 with the clinical diagnosis of constrictive pericarditis who subsequently had surgical confirmation. The research proposal was approved by the institutional review board for clinical research. There were 15 patients (14 men, 1 woman) with a mean age of 65 years (range, 43 to 77 years). Eleven were in normal sinus rhythm, 3 were in atrial fibrillation, and 1 was permanently paced. These patients all prospectively underwent a rigorously detailed hemodynamic cardiac catheterization, as described below. At operation, all had confirmed constrictive pericarditis by surgical and pathological description. Operative reports were reviewed in a blinded fashion by a cardiothoracic surgeon to confirm a surgical description consistent with...
pericardial constriction. All of the cases in the constrictive pericarditis cohort had an obliterated pericardial space and an adhesive pericarditis. Cardiac constriction was diagnosed by the surgeon when the heart bulged out of the pericardial incision as the pericardectomy was begun. The pericardial edges of the incision separated further as dissection of the ventricles progressed. The pericardium was usually but not always thicker than normal. In some patients, there was epicardial thickening and constriction as well; all abnormal epicardium was excised until the coronary arteries could be visualized, the heart had good contractions, and maximal hemodynamic improvement had been achieved. There were two perioperative deaths (13%) before hospital dismissal. However, all other patients experienced symptomatic improvement after the operation at a mean follow-up of 5 months.

A second group of patients presenting to the cardiac catheterization laboratory with symptoms of heart failure all prospectively underwent the same hemodynamic protocol but were subsequently shown to have causes of heart failure other than constrictive pericarditis (restrictive cardiomyopathy in 7, severe tricuspid regurgitation in 4, dilated cardiomyopathy in 3, ischemic cardiomyopathy in 4, aortic stenosis in 1, atrial septal defect in 1, and mitral prosthesis dysfunction in 1). This complete cohort of patients (n=21, group 2) consisted of 12 men and 9 women, with a mean age of 64 years (range, 36 to 72 years). Normal sinus rhythm was present in 12 patients, atrial fibrillation in 5, junctional rhythm in 1, and a paced rhythm in 2.

Seven patients had the diagnosis of restrictive cardiomyopathy. Amyloid heart disease was diagnosed in 3 patients, with typical echocardiographic features of increased left ventricular wall thickness with a scintillating appearance accompanied by low voltage on the ECG. Two patients were found to have a monoclonal gammopathy, and 1 had amyloid infiltration on endomyocardial biopsy. Three patients had an idiopathic restrictive cardiomyopathy with classic echocardiographic features, including small ventricular chambers and large atria. One of these patients had findings of marked interstitial fibrosis on endomyocardial biopsy. There were echocardiographic features of a restrictive cardiomyopathy with systemic findings of Fabry's disease in 1 patient.

**Cardiac Catheterization Technique**

Cardiac catheterization was performed with the patient in the fasting state. A femoral venous and arterial access site was used in all patients. Patients were sedated with midazolam, fentanyl, or both. All patients received 5000 U heparin IV at the start of the procedure.

High-fidelity micromanometer-tipped catheters (Millar Instruments) were used to obtain right- and left-sided heart pressure waveforms. One of two techniques was performed for measurement of the left-sided heart pressures. In the first technique, a 7F fluid-filled pigtail catheter was advanced retrogradely into the left ventricle. A 2F high-fidelity catheter was introduced through the lumen of the pigtail catheter and advanced to its distal orifice. The high-fidelity pressures were zeroed and balanced to the end-diastolic and peak systolic pressures of the fluid-filled system, as described previously in our laboratory. A second technique used a 7F pigtail catheter with both a fluid-filled end-hole lumen and a side-mounted high-fidelity sensor. The same calibration procedure for the high-fidelity pressures was performed as described above.

Right-sided heart catheterization was performed with either a 7F balloon-tipped, large-lumen pulmonary wedge catheter or a 7F endhole catheter. The catheter was advanced into the pulmonary tree until a pulmonary wedge contour was observed. Confirmation of the wedge position was obtained with an oxygen saturation >95%. A 2F high-fidelity micromanometer-tipped catheter was then inserted into the fluid-filled catheter, and the high-fidelity pressures were balanced against the fluid-filled pressures. For measurement of right-sided heart pressures in all chambers, the right-sided heart catheter was pulled back sequentially into the pulmonary artery, right ventricle, and mid right atrium. For each chamber, the high-fidelity pressures were rebalanced to the fluid-filled pressures.
For the eight patients in atrial fibrillation, a temporary pacemaker was placed to obtain a regular rhythm. For this, a second 7F sheath was introduced into the right femoral vein, and a 7F monophasic temporary pacing lead was advanced into the right ventricular apex. Adequate positioning was confirmed by fluoroscopic guidance as well as by obtaining a pacing threshold of <2 mA. The pacing rate was set 10 beats per minute higher than the resting heart rate to ensure continuous pacing.

A thermistor respirometer was placed in the nostril of all patients to document the phase of respiration. Patients were instructed to inspire deeply during dynamic respiratory measurements. All pressure recordings and the respirometer tracings were recorded on paper at 25, 50, and 100 mm/s for at least 1 minute at each speed during normal respirations. The pressure tracings were also recorded in digital format by a computer for further off-line analysis.

**Analysis of Pressures: Conventional Criteria**
Baseline pressure waveforms from high-fidelity catheters were measured simultaneously in the right and left sides of the heart at end expiration from the digitized signals, incorporating an average of five consecutive beats. These measurements included the LVSP, RVSP, LVEDP, RVEDP, mean PCWP, mean pulmonary artery pressure, PASP, MRAP, and mean aortic pressure. Systolic measurements were taken from the peak of the pressure waveform, whereas end-diastolic pressures were measured just before the onset of the ventricular contraction. The height of the RFW was measured from the left ventricular pressure minimum in early diastole to the mid-diastolic pressure plateau. The height of the ventricular A wave was measured from the P wave of the corresponding QRS complex to its maximum positive deflection on the ventricular pressure tracing.

Previously described "classic" hemodynamic criteria used for the diagnosis of constrictive pericarditis were defined as LVEDP-RVEDP ≤5 mm Hg; PASP <55 mm Hg; RVEDP/RVSP >1/3; dip-and-plateau filling, as reflected in the height of the left ventricular RFW; and lack of respiratory variation in the MRAP.25 26 27 28 29 30

**Analysis of Pressures: Dynamic Respiratory Changes**
Analysis of the dynamic respiratory changes in hemodynamics was made from the paper recordings. To assess whether an abnormal dissociation of intrathoracic and intracardiac pressures was present, the PCWP minus the minimum early LVDP gradient was measured during the inspiratory and expiratory phases of respiration. Inspiration was defined as the first ejection beat that followed the first inspiratory diastolic filling period, and the first expiratory ejection beat was the beat after the first expiratory diastolic filling period.36 The maximal increase and decrease of the PCWP were also measured during the same respiratory cycle.

Evidence for abnormal ventricular interdependence was assessed by analyzing the simultaneous left ventricular and right ventricular waveforms during respiration. The onset of inspiration (beat number one) was defined as the first ejection beat after a decline in early LVDP. Maximum inspiration was defined as the ejection phase of the beat after the diastolic filling phase with the lowest early LVDP. The peak LVSP and RVSP were measured for beat number one as well as the following beats throughout one respiratory cycle. The maximum LVSP and RVSP were then assigned a value of 100% and the lowest systolic pressure, a value of 0% for each respective ventricle, with the remaining beats assigned a percentage of the maximum difference as described previously.36 The right ventricular index was defined as this percentage calculated at peak inspiration.

**Statistical Analysis**
Data are expressed as mean±SD. Unpaired Student's t test was used to compare continuous variables between the two groups. Statistical significance was defined as $P<.05$.  

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**Note:** The original content included a URL to a specific article, which is not provided here. The text focuses on the methods and criteria used for analyzing hemodynamic changes in patients with constrictive pericarditis. The analysis includes both conventional and dynamic respiratory criteria, along with statistical methods for comparison between groups.
Results

Constrictive Pericarditis (Group 1): Presenting Features
For patients in group 1, the mean duration of symptoms was 13 months (median, 6 months; range, 3 to 48 months). All group 1 patients presented with dyspnea, and 8 presented with edema. On physical examination, 13 of 15 patients had an increased jugular venous pressure and 4 had a pericardial knock. Of those patients who had an ejection fraction measured by echocardiography, the mean was 51% (range, 30% to 70%). Table 1 provides the number of patients in group 1 who underwent other diagnostic tests as well as their associated sensitivities: chest radiography for the identification of pericardial calcification (20%), computed tomography for the presence of pericardial thickening (58%), and echocardiography for Doppler indexes consistent with constrictive pericarditis (50%).

View this table:  Table 1. Diagnostic Studies Other Than Cardiac Catheterization Performed on Patients in Group 1

Conventional Catheterization Criteria
Pressure recordings during end expiration are reported in Table 2 for groups 1 and 2. Only the MRAP, left ventricular RFW, RVEDP, and LVEDP are significantly different. Fig 1 displays the raw data for the conventional criteria used for the diagnosis of constrictive pericarditis. Neither PASP nor respiratory variation of MRAP differed significantly between groups. The height of the RFWs during early diastole in the left and right ventricles was also not appreciably different.

View this table:  Table 2. Pressure Recordings During End Expiration

Figure 1. Conventional hemodynamic criteria used in an attempt to differentiate constrictive pericarditis from restrictive cardiomyopathy. Individual patient data for group 1, constrictive pericarditis, and group 2, other causes of heart failure. Open circles are from those patients in group 2 identified as having a restrictive cardiomyopathy. The overlap between individuals in each group is apparent. Values are mean±SD. LV indicates left ventricle; MRA, mean right atrial pressure; and PA, pulmonary artery. *P<.05. n=19.
The LVEDP and RVEDP were not significantly different for group 1 (31±7 and 26±8 mm Hg) but were for group 2 (24±9 and 18±7 mm Hg; P<.05). LVEDP minus RVEDP was significantly different between groups 1 and 2 (4±4 and 6±7 mm Hg, respectively; P<.001). The ratio of RVEDP to RVSP was also significantly different between groups 1 and 2 (0.57±0.14 and 0.38±0.12, respectively; P<.001). However, as shown in Fig 1#, there was noticeable overlap between the two groups for all conventional criteria, including the patients from group 2 who had been sent to the laboratory to rule out constrictive pericarditis. When the classic criterion of LVEDP-RVEDP ≤5 mm Hg was used, there was a sensitivity of 60% and a specificity of 38%. Similarly, when the criterion of RVEDP/RVSP >1/3 was used, there was a sensitivity of 93% and a specificity of 38%.

A separate analysis of these conventional catheterization criteria was performed comparing group 1 patients with the seven patients with restrictive cardiomyopathy. The sensitivity and specificity of an LVEDP-RVEDP ≤5 mm Hg for the diagnosis of constrictive pericarditis were 60% and 71%, respectively. The sensitivity and specificity of an RVEDP/RVSP >1/3 for the diagnosis of constrictive pericarditis were 93% and 57%, respectively.

**Analysis of Dynamic Respiratory Changes**

Dissociation of intrathoracic and intracardiac pressures has been assessed with Doppler echocardiography by examination of respiratory fluctuations in mitral inflow velocities. In the cardiac catheterization laboratory, this is equivalent to examining the respiratory variation of the gradient of left ventricular pressure to PCWP during the rapid filling phase of diastole. Fig 2 displays a tracing from a representative patient in group 1 and provides the raw data of this analysis for both patient groups. Although there is no difference in the gradient during the respiratory cycle of patients in group 2, patients in group 1 demonstrated a significant respiratory change consistent with dissociation of intrathoracic and intracardiac pressures. A difference of 5 mm Hg in this gradient between inspiration and expiration was 93% sensitive and 81% specific for constrictive pericarditis. As with the conventional criteria, there was overlap between groups. When group 1 patients were compared with the seven patients with restrictive cardiomyopathy, the sensitivity and specificity of this finding for the diagnosis of constrictive pericarditis were 93% and 86%, respectively.

**Figure 2.** Respiratory changes in the early diastolic transmitral pressure gradient as estimated by PCWP and left ventricular (LV) minimum pressure. Left, Sample tracings of PCWP and LV pressure with respirometry in a patient with constrictive pericarditis (group 1). Right, Individual patient data for groups 1 and 2 depicting the difference between the PCWP-LV early diastolic pressure gradient during expiration (Exp) minus inspiration (Insp). Open circles are from those patients in group 2 identified as having a restrictive cardiomyopathy. As in Fig 1#, the overlap in individuals between groups is seen. *P<.05.

Increased ventricular interdependence was assessed by comparing LVSP and RVSP during respiration. Fig 3# (top) displays a representative pressure tracing from a patient in group 1 along with a left ventricular/right ventricular graph representing the four beats of the respiratory cycle for this patient. During peak inspiration (beat 2), there is an increase in RVSP and a decrease in LVSP. Fig 3# (bottom) displays a representative pressure tracing and analysis from a patient in group 2. There is a concordant decrease in both RVSP and LVSP during peak inspiration. Fig 4# depicts the raw data for the percentage assigned to the RVSP at peak inspiration, the right ventricular index. RVSP was at its maximum in all patients in group 1, whereas all but one patient in group 2 had RVSP concordant with LVSP and did not reach maximum systolic pressure until peak expiration.
Discussion

It is important to make the diagnosis of constrictive pericarditis because untreated patients have progressive hemodynamic and physical deterioration and a limited life span. Conversely, complete resection of all constrictive pericardium and myocardium can result in marked improvement in symptoms as well as prolongation of life. The advent of
noninvasive imaging modalities has been helpful in identifying patients more likely to have constrictive pericarditis by eliminating other causes that can mimic this disorder clinically, such as myocardial systolic dysfunction, valvular heart disease, and pulmonary hypertension. However, a subset of patients with elevated right-sided pressures remains in whom it is unclear whether myocardial or pericardial disease is responsible. This group of patients presents even more of a diagnostic dilemma than several decades ago because tuberculosis pericarditis, which could be diagnosed by diffuse calcification of the pericardium on chest radiography, is no longer the most common cause of constrictive pericarditis.44 Instead, prior cardiac surgery or radiation therapy is a more common cause, which may result in combined myocardial and pericardial disease or patchy areas of pericardial restraint.45 46 47 48 49 50 51 52 53 54 55

Computed tomography and magnetic resonance imaging can now examine the thickness of the pericardium noninvasively.2 3 4 5 6 7 8 However, pericardial thickening can be present in patients without physiological constriction, particularly after open-heart surgery. As demonstrated in the patients in this study, there can still be pericardial constriction with normal-appearing pericardium on these imaging modalities.51 52 53 54 55 Epicardial constriction can occur with a normal-thickness pericardium. Thus, the presence or absence of pericardial thickening cannot reliably be used for the diagnosis of constrictive pericarditis in individual cases.

Previously, the hemodynamic diagnosis of constrictive pericarditis has focused on pressure variables measured during held respiration. "Classic criteria" have included equalization of end-diastolic pressures (≤5 mm Hg), PASP <55 mm Hg, RVEDP >1/3 RVSP, lack of respiratory variation in MRAP, and dip-and-plateau diastolic filling (eg, the square root sign).27 28 29 30 31 32 33 34 35 36 37 However, suboptimal specificity and sensitivity of these criteria, as shown in this study and by others,9 10 11 12 13 14 15 16 have limited the clinical applicability of these criteria in individual patients.

Hatle et al17 provided insight into the dynamic respiratory changes in ventricular filling and pressures that occur in patients with constrictive pericarditis. These changes include a dissociation of intrathoracic and intracardiac pressures and increased ventricular interaction. In normal individuals and cardiac patients without constrictive pericarditis, there is an inspiratory decrease in intrathoracic pressures that is transmitted to the cardiac chambers. Thus, transmitral filling pressure during early diastole is essentially unchanged throughout the respiratory cycle, and there is minimal change in left ventricular filling. In the presence of a constricting pericardium around the heart, the inspiratory decrease in pulmonary venous and intrathoracic pressure is not transmitted into the cardiac chambers, resulting in a reduced transmitral pressure gradient and less ventricular filling. The constricting pericardium also results in an increase in ventricular interaction, so that as the left ventricular volume decreases, there is a corresponding increase in right ventricular volume.

These pathophysiological abnormalities have been applied to Doppler echocardiographic studies in which the dissociation of intrathoracic and intracardiac pressures is manifested by an inspiratory increase in the peak tricuspid flow velocity and a simultaneous decrease in mitral flow velocity, with opposite changes occurring in expiration.17 18 19 20 Although these Doppler findings are usually diagnostic in the presence of other clinical and noninvasive findings consistent with constrictive pericarditis, both false-positive and false-negative results exist, as shown in this study. Severe lung disease with marked respiratory changes in intrathoracic pressures and movement of the sample volume relative to the heart can cause changes in the mitral flow velocity curves mimicking those of constrictive pericarditis.20 Marked increases in left atrial pressures may mask these Doppler respiratory changes. In addition, in the presence of irregular rhythms, such as atrial fibrillation, it is difficult to determine the significance of changes in the initial mitral velocities.20 Thus, there are instances when additional diagnostic methods for evaluating possible constrictive pericarditis are helpful.
In this study, the dynamic respiratory changes in cardiac hemodynamics in patients with constrictive pericarditis were assessed by cardiac catheterization. The dissociation of intrathoracic and intracardiac pressures was analyzed in terms of the respiratory changes in the early diastolic transmural pressure gradient as estimated by the PCWP/left ventricular pressure gradient. Although increased respiratory variation was present in most patients with constrictive pericarditis, this finding alone was nonspecific and was seen in patients with other causes of heart failure.

The finding of increased ventricular interaction, as assessed by respiratory discordance of left ventricular and right ventricular pressures, was the most reliable hemodynamic factor for distinguishing patients with constrictive pericarditis from those with other disease entities. In patients with constrictive pericarditis, there was a consistent increase in right ventricular pressure during peak inspiration, a time when left ventricular pressure is lowest. These findings are concordant with prior studies in dogs with experimental cardiac tamponade36 and confirm the earlier observations of Hatle et al.17

Of interest were the patients who presented to the laboratory with atrial fibrillation. For each of these patients, the Doppler echocardiographic diagnosis of constrictive pericarditis was equivocal because of the changes that occur in early filling with varying RR intervals. Overdrive ventricular pacing was instituted in each of these patients to achieve a regular heart rate and greatly aided in the overall analysis of the dynamic respiratory changes.

The population of patients in this study represents a select subgroup of patients who presented with constrictive pericarditis at our institution. As a result of prior experience,20 patients with clinically suspected constrictive pericarditis who have classic findings on Doppler echocardiography now undergo pericardiectomy without the need for cardiac catheterization at our institution. Only the patients in whom there have been equivocal findings either on clinical presentation or on noninvasive testing then undergo further hemodynamic assessment.

**Limitations**

The population of patients with constrictive pericarditis in this study was relatively small. This is because constrictive pericarditis is a relatively uncommon entity, and only patients in whom the diagnosis could not be made from clinical and noninvasive testing underwent cardiac catheterization. It would have been ideal to compare the cardiac catheterization results in patients with constrictive pericarditis only with results in those rare patients with a true restrictive cardiomyopathy. Despite these number limitations, the results of this study confirm that the diagnosis of constrictive pericarditis can be made with a much higher degree of certainty if dynamic respiratory changes in left ventricular and right ventricular hemodynamics are assessed at cardiac catheterization as opposed to the conventional analysis of pressure waveforms obtained during apnea. The dynamic respiratory changes were observed by use of high-fidelity micromanometer-tipped catheters in this study. A fluid-filled system should afford similar diagnostic capabilities if the fidelity of the fluid-filled system is good, but further investigation is necessary to confirm this.

**Clinical Implications**

Constrictive pericarditis remains an elusive diagnostic challenge for the clinician. Noninvasive technologies are helpful in establishing the diagnosis of constrictive pericarditis in the majority of patients. However, a subset of patients remains in whom there is still an equivocal diagnosis after the noninvasive evaluation. In this subset of patients, cardiac catheterization is recommended. From the cardiac catheterization laboratory, the conventional diagnostic criteria are insensitive and nonspecific. However, the dynamic respiratory changes in left ventricular and right ventricular pressures appear to provide a sensitive and specific means of diagnosis and should be incorporated into the hemodynamic assessment of constrictive pericarditis.
Selected Abbreviations and Acronyms

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<th>Abbreviation</th>
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<tr>
<td>LVDP</td>
<td>left ventricular diastolic pressure</td>
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<tr>
<td>LVEDP</td>
<td>left ventricular end-diastolic pressure</td>
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<td>LVSP</td>
<td>left ventricular systolic pressure</td>
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<td>MRAP</td>
<td>mean right atrial pressure</td>
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<td>PASP</td>
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<td>PCWP</td>
<td>pulmonary capillary wedge pressure</td>
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<td>rapid filling wave</td>
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<td>right ventricular end-diastolic pressure</td>
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<td>RVSP</td>
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Footnotes

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