REVIEW

Spectral Doppler Interrogation of the Pulmonary Veins for the Diagnosis of Cardiac Disorders: A Comprehensive Review

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Data obtained from echocardiographic studies are used on a daily basis to guide clinical decision-making regarding patient management and the need for additional diagnostic investigations. Interrogation of blood flow in the pulmonary veins by spectral, most often pulsed-wave, Doppler is an important component of any comprehensive echocardiographic study. Whereas it is most often used to help assess left-sided filling pressure and quantify the severity of mitral regurgitation, the pulmonary vein Doppler profile provides added diagnostic insights into several disorders that affect heart function and allows assessment of their hemodynamic consequences on the heart. The aim of this review is to summarize current knowledge in the field of PV Doppler interrogation, highlight the physiological and pathological parameters that influence it, and delineate the manifestations of various cardiovascular disorders on the flow profile. (J Am Soc Echocardiogr 2021;34:223-36.)

Keywords: Doppler echocardiography, Pulmonary veins, Diastolic function, Mitral regurgitation

Noninvasive recording of pulmonary vein (PV) flow by pulsed-wave Doppler was first reported in the 1980s.[1] Since then, Doppler interrogation of PV flow has become a routine component of echocardiographic imaging.[2,3] Despite current emphasis on modern parameters such as tissue Doppler, strain, and volumetric analysis, the PV Doppler profile is useful for understanding the hemodynamic consequences of disorders that affect heart function.[4] Valvular, myocardial, pericardial, congenital, and rhythm and conduction disorders alter the PV Doppler profile, at times in a characteristic manner. Optimal recording of the PV flow signal and proper analysis of the direction, velocity, and duration of the Doppler waveforms distinguish normal from abnormal flow patterns and relate abnormal flow patterns to specific disorders that particularly involve the left heart.

The aim of this review is to provide a comprehensive review of the role of PV Doppler in the daily practice of echocardiography and highlight the manifestations of various cardiovascular disorders on the PV flow profile. Awareness of the consequences of disease states on the PV Doppler profile improves our diagnostic ability and promotes our understanding of the pathophysiology of several cardiac disorders.

In this report, we review the anatomy and imaging of the PVs by echocardiography, followed by an analysis of the normal flow profile and description of the physiology of PV flow, then discuss the alterations in Doppler signal that occur in various disease states, followed by a review of the differential diagnosis of different flow patterns, then elaborate on the prognostic value of the PV signal, and, finally, address the feasibility of flow recording and the use of ultrasound enhancing agents.

ANATOMY AND ECHOCARDIOGRAPHIC IMAGING OF THE PVS

Pulmonary Venous Anatomy

Typically, four distinct PVs with separate ostia drain into the left atrium, consisting of right and left upper and lower veins. However, this anatomy is present in only 70% of individuals.[5] The right upper and lower veins run posterior to the superior vena cava and right atrium and connect medially to the superior and posterior aspects of the left atrium, respectively, near the interatrial septum. The left upper and lower veins run anterior to the descending aorta and connect to the lateral wall of the left atrium. In the remaining 30% of individuals, PV anatomic variants are noted, including conjoined veins that join proximal to the left atrium, resulting in a single ostium.[5] Another variant is the presence of accessory PVs that drain either a pulmonary lobe or a segment of a lobe, thus representing supernumerary veins with separate ostia.[5]

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Abbreviations

LA = Left atrial

LLPV = Left lower pulmonary vein

LUPV = Left upper pulmonary vein

LV = Left ventricular

LVEDP = Left ventricular end-diastolic pressure

LVEF = Left ventricular ejection fraction

MR = Mitral regurgitation

PV = Pulmonary vein

RLPV = Right lower pulmonary vein

RUPV = Right upper pulmonary vein

RV = Right ventricular

SR = Systolic reversal

TEE = Transesophageal echocardiography

TTE = Transthoracic echocardiography

TVI = Time-velocity integral

Transthoracic Echocardiography

Various transthoracic windows allow visualization of different PVs. From the suprasternal window, all four PVs can be imaged (Figure 1A), but this window is usually accessible in the pediatric rather than the adult population.[2] Most often, the right upper PV (RUPV) and right lower PV (RLPV) offer the best alignment of flow with the Doppler beam from the apical four-chamber view.[6] The RLPV is imaged using a slight posterior tilt of the transducer (Figure 1B), whereas the RUPV is imaged with a slight anterior angulation toward the five-chamber view, partly visualizing the aortic valve (Figure 1C).[6]

The left upper PV (LUPV) can be visualized in the apical four-chamber and parasternal short-axis views, but flow is often not parallel with the Doppler beam to allow proper recording (Figure 1C). The left lower PV (LLPV) can be visualized using a modified parasternal short-axis view (Figure 1D).[6] Table 1 details the requirements for the optimal recording of PV flow by spectral Doppler from the apical window.

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) provides improved visualization of the PVs and allows sampling of flow from different veins. Additionally, TEE provides a higher quality recording of the Doppler signal than the transthoracic window because of the proximity of the transducer to the PVs and to near parallel interrogation of flow.[7] The PVs are imaged from the midesophageal window, and this can be facilitated by the use of color Doppler. Both upper veins and the LLPV run oblique or near vertical to the transesophageal imaging plane, whereas the RLPV runs more horizontal and is more posteriorly located. The upper veins are easier to visualize and, with the LLPV, are the most suitable to interrogate using pulsed-wave Doppler because of better alignment with the ultrasound beam. The orifices of the upper and lower veins are in close proximity to each other. When an upper PV is identified, a slight forward motion of the probe and/or minimal change in the transducer angle (10°) usually allows visualization of the corresponding lower vein. Therefore, it is possible to visualize the upper and lower PVs, right or left, in the same imaging plane. The sample volume should be positioned approximately 1 cm inside the vein from the ostium for pulsed-wave Doppler interrogation.

The LUPV is often well visualized adjacent to the left atrial (LA) appendage with some transducer angulation (30°–60°; Figure 1E).[8] More oblique angulation (90°–120°) with the image centered on the LUPV allows visualization of the LUPV and LLPV in an inverted "v" figure (Figure 1F).[8] The RUPV is easily identified by rotating the probe to the right from the LA appendage or the bicaval view. Advancing the probe by 1 to 2 cm and turning further to the right allows visualization of the RLPV (Figure 1G).[8]

NORMAL PULMONARY VENOUS FLOW PROFILE

The PVs are thin-walled, highly compliant conduits that allow maintenance of a constant left ventricular (LV) stroke volume despite beat-to-beat variation in right ventricular (RV) stroke volume.[1] Pulmonary venous blood flow is determined by the pressure gradient between the PVs and the left atrium. Consequently, Doppler waves in the PVs mirror the pressure waveforms in the left atrium.[9] The PV-LA pressure gradient and thus the PV flow profile are dependent mostly on the cardiac cycle and the function of the left heart.[9] Additionally, they are influenced by the respiratory cycle, albeit to a lesser degree than flow in the superior and inferior venae cavae. Therefore, PV flow is altered in disease states that either affect left heart function or disturb the cardiac rhythm.[2,3,9]

The normal flow profile in the PVs shows phasic and bidirectional waves, predominantly antegrade, that are temporally related to waveforms obtained on pressure recording of the left atrium (Figure 2A).[9,10] Fluctuations in flow direction and velocity indicate changes in LA pressure. PV flow reflects LA filling throughout the cardiac cycle and LV filling during diastole.

Four distinct Doppler waves can be identified in the PVs.[1,9,10] The first two antegrade waves are noted in early systole (S_1) and mid to late systole (S_2), respectively, and occur during the LA reservoir phase, corresponding to the "x" descent on LA pressure recording (Figures 2A and 2B). The S_1 and S_2 waves are fused on transthoracic echocardiography (TTE) in 70% to 85% of subjects, thus forming a single systolic wave (S wave; Figure 2C).[1,9,10] These two waves are discernable by TEE in most individuals. The third wave is antegrade and is noted in early to mid diastole (D wave), occurring during the LA conduit phase. The D wave is temporally related to the "y" descent on LA pressure recording and to the transmitral E wave on Doppler imaging (Figures 2A–2C).[1,9,10] The fourth wave is retrograde and is noted in late diastole (A wave), occurring during the LA pump phase. It is temporally related to the "a" wave on LA pressure and to the transmitral A wave on Doppler imaging (Figures 2A–2C).[1,9,10] Recording a measurable A wave has a lower success rate than recording the S and D waves by TTE.

Useful PV Doppler measurements include the peak velocity of the S, D, and A waves, the S/D peak velocity ratio, the A-wave duration, and the deceleration time of the D wave. The systolic fraction represents the ratio of the time-velocity integral (TVI) of the S wave to the sum of the S and D waves (systolic fraction = $S_{TVI}/[S_{TVI} + D_{TVI}]$).

Effect of Age on PV Doppler Profile

Blood flow in the PVs varies with the state of LV myocardial relaxation, a parameter strongly influenced by age.[11] Normal adolescents and young adults with excellent elastic recoil manifest fast LV relaxation and thus rapid LV filling in early diastole, with only minor contribution to filling during atrial contraction. In synchrony with the transmitral Doppler that demonstrates a prominent E wave and a small A wave, the PV Doppler shows a prominent D wave with a diastolic dominant pattern (S/D ratio < 1) and a small A-wave reversal (Figure 2D). The normal decline in LV relaxation that occurs with aging leads to progressive decrease in LV filling in early diastole and an

HIGHLIGHTS

- PV Doppler interrogation should be performed as part of any comprehensive echocardiographic study.
- The PV Doppler provides added diagnostic insights into disorders that affect heart function.
- Certain findings on the PV Doppler are predictors of major adverse cardiac events.

increase in filling during atrial contraction. Normal individuals in their third and fourth decades demonstrate near equalization of the PV S and D waves. With aging, the transmitral Doppler shows progressive attenuation and prolonged deceleration of the E wave together with an increasingly prominent A wave in terms of velocity and duration. This transmitral pattern is mirrored by the PV Doppler profile that demonstrates a progressively prominent S wave, a smaller D wave, and more prominent A-wave reversal. Still, the velocity of the latter remains <35 cm/sec (Figures 2B and 2C).[11,12]

Influence of Various Physiologic Factors on Individual PV Doppler Waveforms

The physiologic hemodynamic parameters that influence the various PV Doppler waveforms are shown in Figure 3. S_1 occurs in response to the fall in LA pressure caused by the increase in atrial volume as a result of atrial relaxation with a "suction effect" on blood in the pulmonary vasculature. Thus, S_1 depends on the efficiency of LA relaxation, which is, in turn, dependent on atrial contractility. S_2 results from the propagation of the RV ejection wave across the pulmonary vasculature, causing a "pushing effect" on blood flow.[9,10] Additionally, S_2 is determined in part by LA compliance, itself dependent on the systolic displacement of the mitral annulus toward the apex. Therefore, S_2 depends on the RV stroke volume and on the LV longitudinal function, an important contributor to the increase in LA volume during systole.[9,10] The D wave results from the fall in LA pressure that follows mitral valve (MV) opening and emptying of the left atrium into the left ventricle. Thus, it is determined by the state of LV relaxation and compliance, and it is influenced by the same factors that affect early transmitral filling (E wave).[9,10] Finally, the A wave is caused by atrial contraction with subsequent rise in LA pressure that exceeds PV pressure, thus leading to flow reversal in the PVs. Therefore, the A wave is affected by LA contractile function and by LV stiffness.[9,10]

The timing of the S_2 and D waves is relatively fixed during the cardiac cycle because of their associations with RV systole and LV relaxation, respectively. In contrast, the timing of the A and S_1 waves may vary, as they are influenced by variable factors such as the cardiac rhythm, the duration of the PR interval, and the relationship between the P-wave and the QRS complex.

PV DOPPLER IN DISEASE STATES

Alterations of the PV flow profile occur in disease states that involve the LV myocardium, pericardium, MV, or conduction system. Additionally, PV stenosis and congenital anomalies that involve the left atrium cause alterations in PV Doppler. Some of these conditions lead to characteristic changes in the PV flow profile.

MV DISEASE

Mitral Regurgitation

The PV Doppler profile is a valuable tool for evaluating the hemodynamic consequences and aiding in the assessment of the severity of mitral regurgitation (MR). Worsening degree of MR is associated with a progressive reduction in the peak velocity of the S wave, due to a decrease of the S_2 component, together with an increase in the velocity of the D wave.[13] Some patients with severe MR demonstrate a characteristic systolic reversal (SR) that replaces the forward S wave (Figure 4A).[14,15] The SR results from the transmission of the LV systolic pressure to the left atrium and reflects a prominent "v" wave on LA or pulmonary capillary wedge pressure recording.[15] As the "v" wave is typically evident in the latter part of systole and SR replaces the forward S_2 component, SR is often noted in mid to late systole, with S_1 being either forward or absent, particularly in individuals with severe MR due to MV prolapse.[4] Holosystolic reversal is occasionally encountered with reversal of the S_1 and S_2 waves, especially when MR is very severe.

Whereas mild MR does not alter the PV flow profile in the absence of associated pathologies, it is tempting to speculate that moderate MR would lead to blunting of the S wave, leading to an S < D pattern, and severe MR would result in SR in the PVs. However, this simplistic scenario does not hold true in many patients with moderate or severe MR.[3] Even though the velocities of the S and D waves inversely correlate with the height of the "v" wave, the latter is neither sensitive nor specific for severe MR.[16]

Several hemodynamic parameters influence the height of the "v" wave in the left atrium and thus the peak velocity of the S wave and the presence or absence of SR.[9,17]

An important parameter is LA compliance, a major determinant of both LA filling pressure and the velocity of the S_2 component (Figure 3). Acute severe MR in the setting of a nondilated and poorly compliant left atrium leads to SR more often than chronic severe MR with similar regurgitant volume.[17] Still, in chronic severe MR, LA compliance gradually worsens over time, leading to a progressive increase in the height of the "v" wave, more blunting of the S wave, and, ultimately, possible development of SR.[17]

Beyond LA compliance, additional parameters influence the velocity of the S wave, including LV systolic function, the presence of atrial fibrillation, and mitral stenosis.[18,19] For instance, an asymptomatic patient with chronic severe MR, a dilated and compliant left atrium, and normal LV systolic function would likely have normal or near normal LA filling pressure and demonstrate a normal PV flow profile with S > D and no SR. This pattern is associated with trivial "v" waves on LA or pulmonary capillary wedge pressure recording.[20] Accordingly, 40% to 50% of individuals with severe MR exhibit either a normal PV flow profile or blunting of the S wave.[21] Conversely, a patient with chronic severe MR and one or more of the following conditions, including a noncompliant left atrium, LV systolic dysfunction, mitral stenosis, and/or atrial fibrillation, would have more likelihood of exhibiting large "v" waves on pressure recording and SR on the PV Doppler profile. Figure 4B illustrates the various PV flow patterns associated with MR.

A limitation to the assessment of MR severity by PV Doppler is that SR may be present in only one PV, depending on the direction and eccentricity of the MR jet.[22,23] As TTE most often permits sampling of a single PV, TEE provides added information to the assessment of MR severity by allowing sampling of additional PVs.[7,23] In one study, one third of patients with severe MR demonstrated discordant flow pattern between the RUPV and LUPV, with the former showing

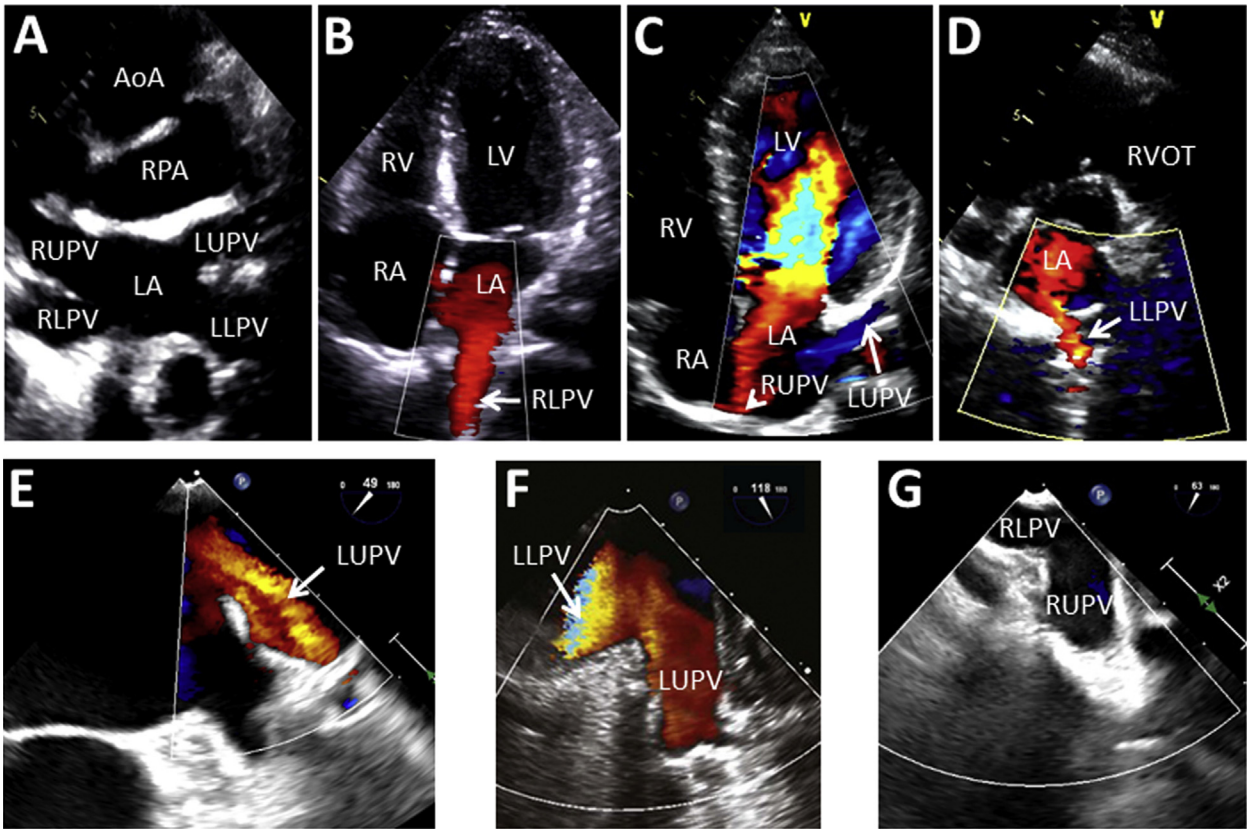

Figure 1 Transthoracic and transesophageal echocardiographic windows for visualization of the PVs. **(A)** Suprasternal short-axis view showing the left atrium (LA) and the four PVs. **(B)** Apical four-chamber view with color Doppler demonstrating blood flow in the RLPV *(arrow)*. (**C**) Modified apical four-chamber view with slight anterior angulation demonstrating blood flow in the LUPV *(arrow)*. Blood flow exiting the orifice of the RUPV is indicated by an *arrowhead*. **(D)** Modified parasternal short-axis view demonstrating flow in the LLPV *(arrow)*. **(E–G)** Transesophageal images showing the various PVs from the midesophageal window. Note the LUPV **(E)**, the LUPV and LLPV visualized simultaneously **(F)**, and the RUPV and RLPV visualized simultaneously **(G)**. *AoA*, Aortic arch; *LV*, left ventricle; *RA*, right atrium; *RPA*, right pulmonary artery; *RV*, right ventricle; *RVOT*, RV outflow tract.

Table 1 Requirements for the optimal recording of pulsed-wave Doppler interrogation of the RUPV or RLPV by TTE

- Ensure optimal ECG tracing showing "P" and "QRS" waves
- Position the ultrasound transducer in the apical four-chamber view
- Optimize 2D image quality
- Narrow the 2D sector
- Identify the orifice of the RUPV by slight anterior angulation or RLPV by slight posterior tilt
- If PV orifice is difficult to visualize, perform slight transducer rotation toward the apical three-chamber view
- Visualize blood flow within the RUPV or RLPV by color Doppler
- Narrow the color sector to maximize frame rate
- If flow is not well visualized, reduce the velocity scale (Nyquist limit) to improve visualization of the color signal
- Ensure alignment of the Doppler signal with flow
- Optimize pulsed-wave Doppler settings
  - Sample volume size: 2–3 mm
  - Sample volume location: 0.5–2 cm inside the PV
  - Gain
  - Relatively low filter (≤200 Hz) to visualize the onset and end of A wave
- Adjust recording speed
  - 25 mm/sec to assess the effect of respiration on PV flow
  - 50–100 mm/sec to measure the duration of the A-wave reversal
- Activate the respirometer, if needed, to determine the phase of the respiratory cycle (inspiration, expiration, apnea)
- In case excessive respiratory motion displaces the sample volume outside the PV, obtain recording during breath holding in end-expiration
- Obtain a transmitral Doppler at the same recording speed for comparison

2D, Two-dimensional; *ECG*, electrocardiographic.

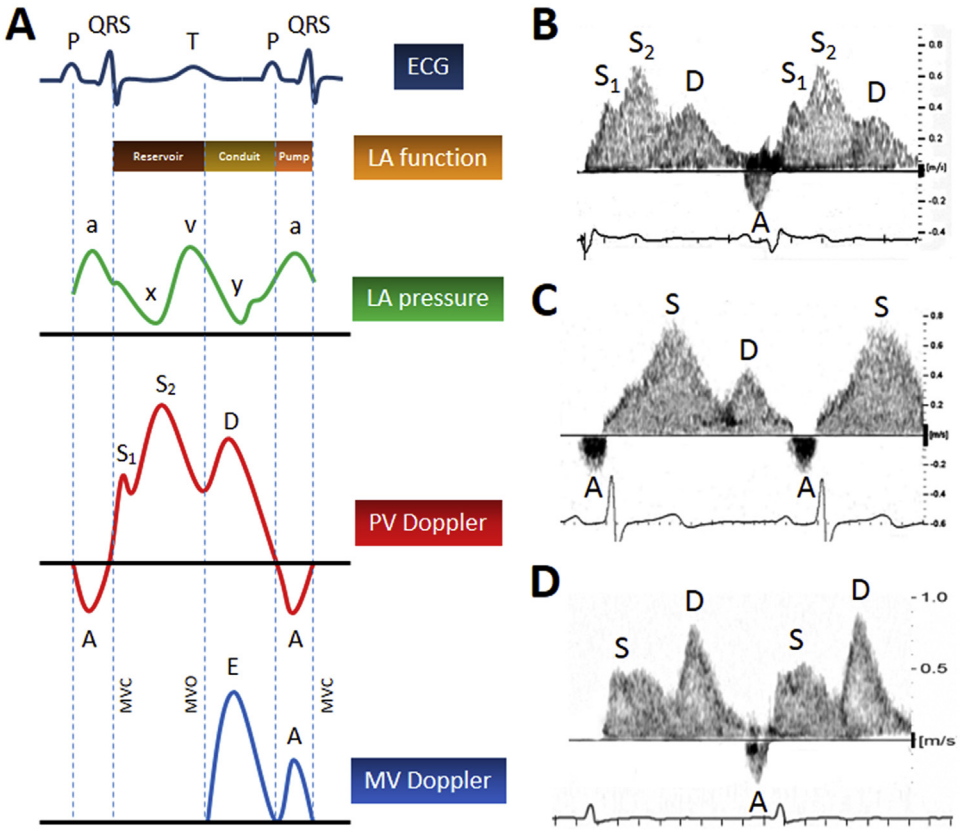

Figure 2 **(A)** Temporal relationship between the electrocardiogram (ECG), phases of LA function, LA pressure, PV Doppler, and MV Doppler. **(B–D)** Normal PV Doppler profiles. PV Doppler profile from the transthoracic window shows distinct S_1 and S_2 waves **(B)** versus a single S wave **(C)** in healthy individuals in their sixth decade. A dominant diastolic pattern (S < **D**) is evident in this 18-year-old healthy woman with no structural heart disease **(D)**. *MVC*, MV closure; *MVO*, MV opening.

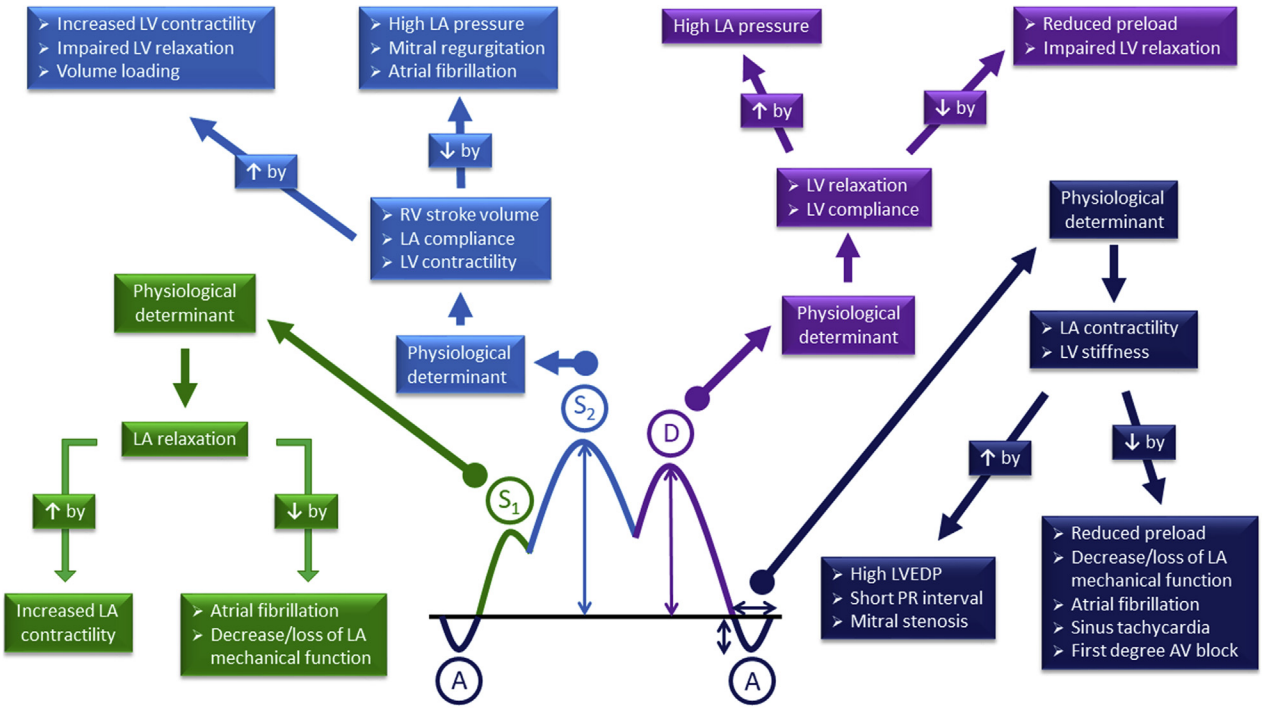

Figure 3 Influence of various physiologic factors on individual pulmonary venous waveforms. *AV*, Atrioventricular; ↑, increased; ↓, decreased.

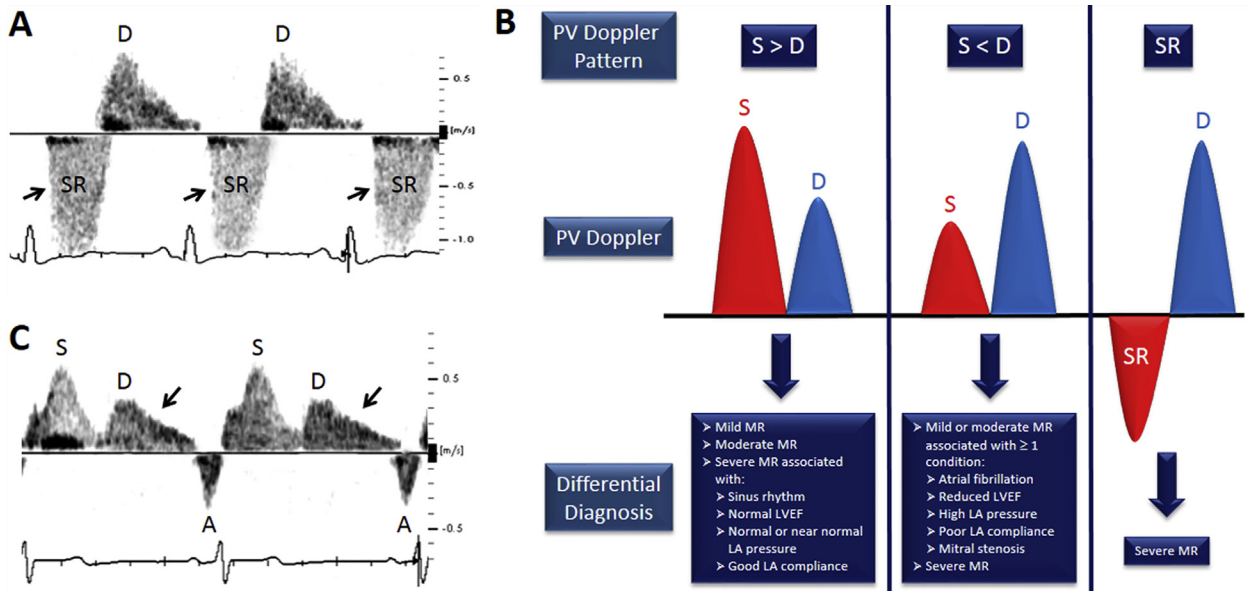

Figure 4 MV disease. **(A)** Severe MR in a 55-year-old man with ischemic heart disease. The PV Doppler profile demonstrates characteristic SRs *(arrows)*, occurring in the last two thirds of systole and replacing the forward S wave. **(B)** Various pulmonary venous flow patterns associated with MR. **(C)** Severe mitral stenosis in a 44-year-old woman with rheumatic heart disease. There is prolongation of the D-wave pressure halftime at 160 msec *(arrows)*, which is comparable with the transmitral E-wave pressure halftime of 165 msec, reflecting the obstruction to flow across the MV. *PCW*, Pulmonary capillary wedge.

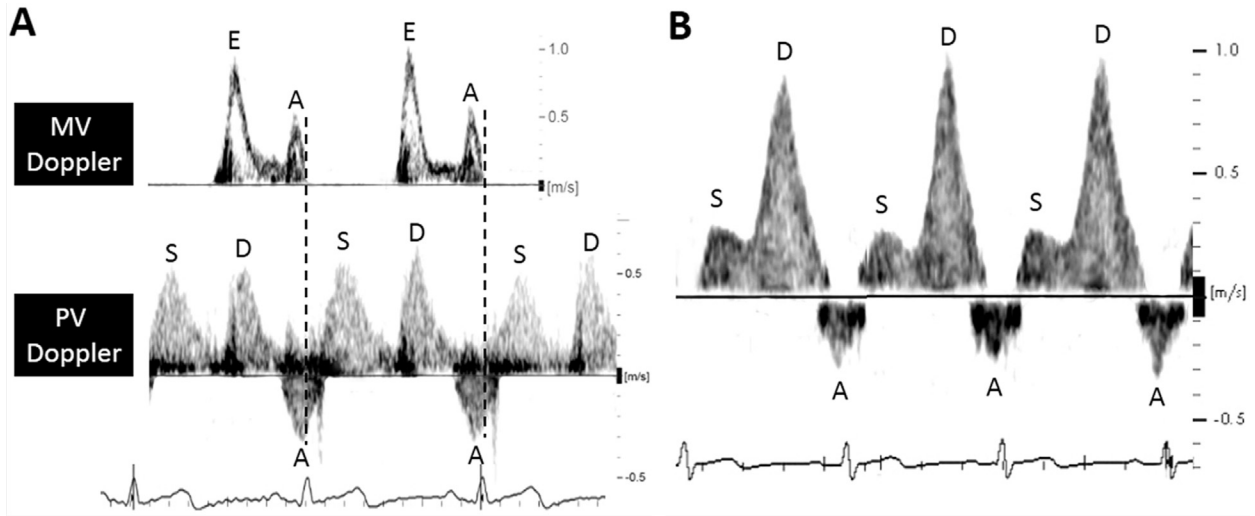

Figure 5 Abnormalities of LV diastolic function. **(A)** Elevated LVEDP in a 65-year-old man with hypertensive heart disease. The temporally aligned MV and PV Doppler show a shortened transmitral A_{MV} with a prominent A_{PV} reversal that ends 50 msec after A_{MV}. **(B)** Elevated LA filling pressure in a 72-year-old man with ischemic cardiomyopathy and an LVEF of 35%. The PV Doppler profile demonstrates an attenuated S wave with an S < D pattern indicative of elevated LA pressure. The widened A-wave reversal is likely due to elevated LVEDP.

more commonly SR and the latter more often blunting of the S wave or a normal flow profile.[23]

As discussed below, atrial fibrillation and elevated LA pressure of any etiology independently lead to blunting of the S-wave in the absence of MR. Therefore, caution must be exercised not to use systolic blunting as the sole marker of MR severity, particularly in the setting of LV systolic dysfunction. Additionally, systolic blunting as a marker of MR severity is more valuable in the setting of primary rather than secondary MR.[24]

On the basis of the aforementioned information, the PV Doppler should not be used alone but in conjunction with other parameters to help assess the severity of MR.[4] The presence of SR carries high specificity but low sensitivity for severe MR, and specificity is further increased if SR is evident in two separate PVs by TEE.[4,14,21] Importantly, SR should be evident on every cardiac cycle, and care should be taken to distinguish it from intermittent SR due to atrioventricular dissociation and from early SR due to junctional or idioventricular rhythm (see section under "Rhythm and Conduction

Disorders").[4] Therefore the absence of SR does not exclude severe MR, whereas its presence makes severe MR highly likely.

An important technical factor during interrogation of the PV flow is to ensure correct positioning of the pulsed-wave Doppler sample volume (Table 1). If the latter is inadvertently placed in the posterior aspect of the left atrium rather than inside the PV, contamination by the MR jet may lead to a false diagnosis of SR and overestimation of MR severity.[4]

MV Repair

Recent data demonstrate a value for the intraprocedural assessment of the PV Doppler profile at the time of percutaneous MV repair for severe MR. TEE-derived PV flow data obtained in the catheterization laboratory and demonstrating a low S/D TVI ratio (<0.72) after transcatheter edge-to-edge MV clip implantation predict recurrent MR and worse long-term outcome.[25] Conversely, postrepair improvement in the PV flow profile from SR to blunted signal (S < D) and from blunted signal to a normal pattern (S > D) is a better predictor of outcome than MR grade and is associated with survival benefit and lower rehospitalization rate.[26]

Mitral Stenosis

Significant obstruction to flow across the MV is associated with a decrease in the velocity of all PV waveforms (S, D, and A waves).[19] A prolonged pressure halftime of the D wave is usually evident (Figure 4C), a reflection of the abnormally slow pressure decay across the MV in early diastole. This pattern is mirrored by an abnormally prolonged pressure halftime of the transmitral E wave. Additionally, a prominent A wave is occasionally noted during sinus rhythm, indicative of forceful LA contraction against the stenotic MV.[27] A similar PV pattern showing a prolonged deceleration of the D wave can be encountered in the setting of impaired LV relaxation.

ABNORMALITIES OF LV DIASTOLIC FUNCTION

Elevated LV End-Diastolic Pressure

Elevated LV end-diastolic pressure (LVEDP) is one of the earliest measurable markers of diastolic dysfunction that usually precedes the increase in mean LA pressure. The MV A wave (A_{MV}) and PV A wave (A_{PV}) normally begin simultaneously, and in healthy subjects, their durations are either similar or A_{MV} is slightly longer (Figure 2A).[11] In the setting of elevated LVEDP, the rise in LV diastolic pressure causes the MV to close before atrial relaxation has begun and thus before LA pressure has decreased. This phenomenon results in a more pronounced backflow of blood into the PVs and leads to a wider A_{PV} than A_{MV}. An A_{PV}-A_{MV} duration > 30 msec predicts high LVEDP with high accuracy and in an age-independent manner (Figure 5A).[28,29] A simpler approach to measuring the duration of

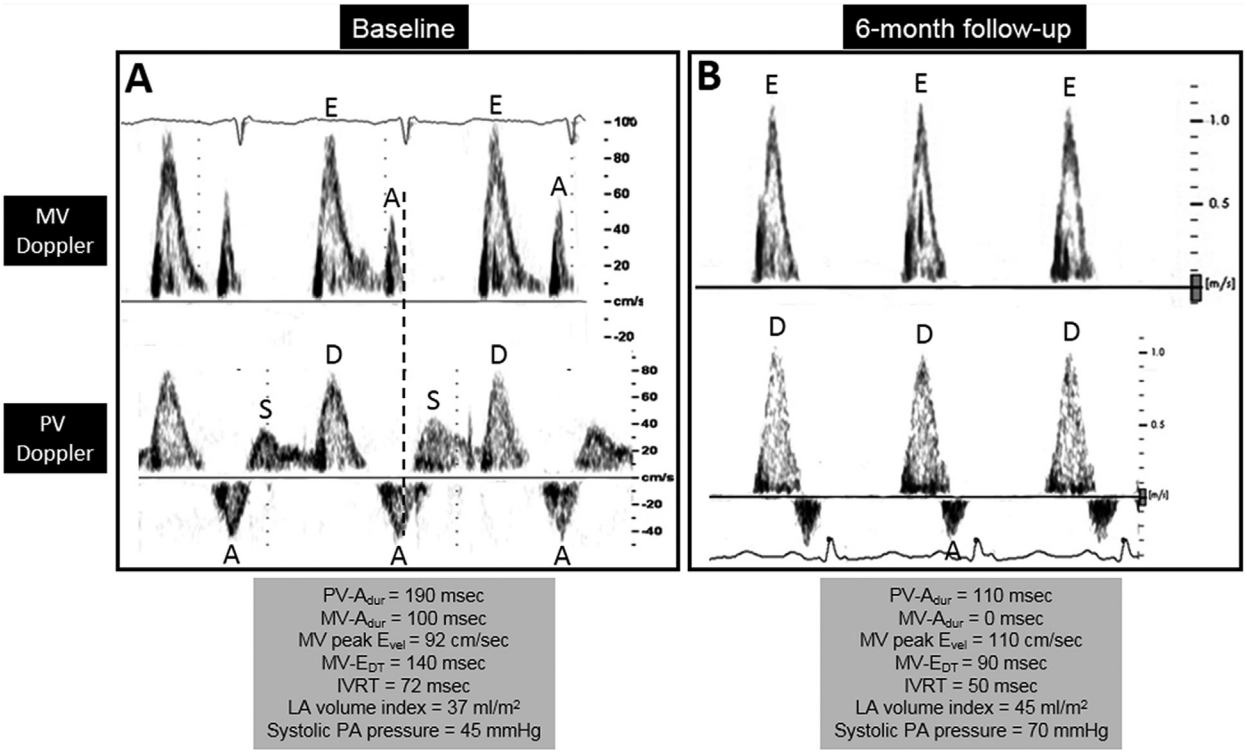

Figure 6 LA mechanical failure in a 72-year-old man with ischemic cardiomyopathy and severe LV systolic dysfunction. Baseline evaluation with temporally aligned MV and PV Doppler shows evidence of elevated LA pressure with E/A velocity ratio of 2, shortened E-wave deceleration time and isovolumic relaxation time (IVRT), and A_{PV}-A_{MV} difference = 90 msec, suggestive of elevated LVEDP. Six months later, he presented with worsening heart failure. A follow-up study showed further increase in LA pressure as evidenced by an increase in peak E-wave velocity, shortening of the deceleration time and IVRT, disappearance of the PV S wave despite sinus rhythm, and increase in D-wave velocity. The transmitral A wave has vanished and the PV A wave has decreased in velocity and duration despite higher filling pressure. These findings are suggestive of LA mechanical dysfunction. *A_{dur}*, A-wave duration; *EDT*, E-wave deceleration time; *E_{vel}*, E-wave peak velocity; *PA*, pulmonary artery.

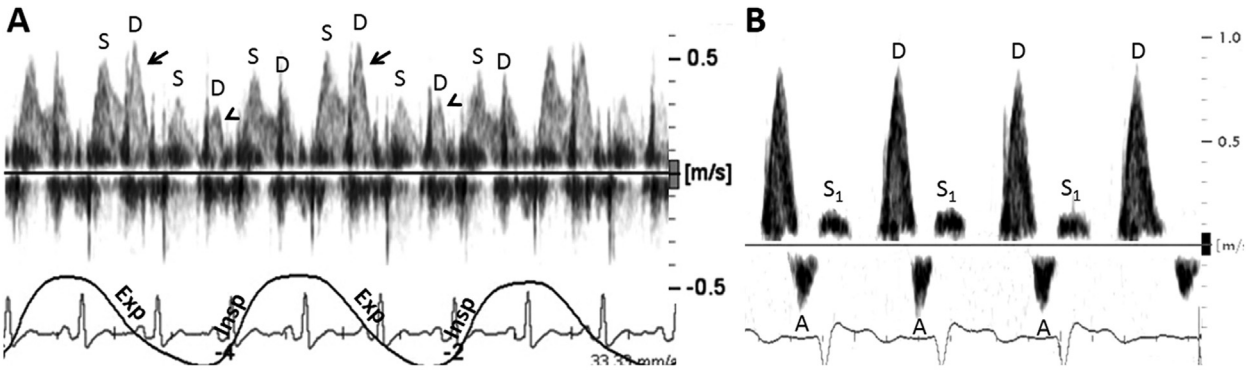

Figure 7 Pericardial and myocardial disease. **(A)** Constrictive pericarditis. In this 60-year-old man with idiopathic constrictive pericarditis, the D-wave velocity decreases by 60% from expiration (Exp; *arrows*) to the first beat of inspiration (Insp; *arrowheads*). **(B)** Restrictive cardiomyopathy. In this 72-year-old man with cardiac amyloidosis, the atrial relaxation wave (S_1) is evident, whereas S_2 is absent. The marked attenuation of S_2 is due to significant impairment of LV longitudinal function and elevated filling pressure. The D wave is prominent and exhibits minimal respiratory variability.

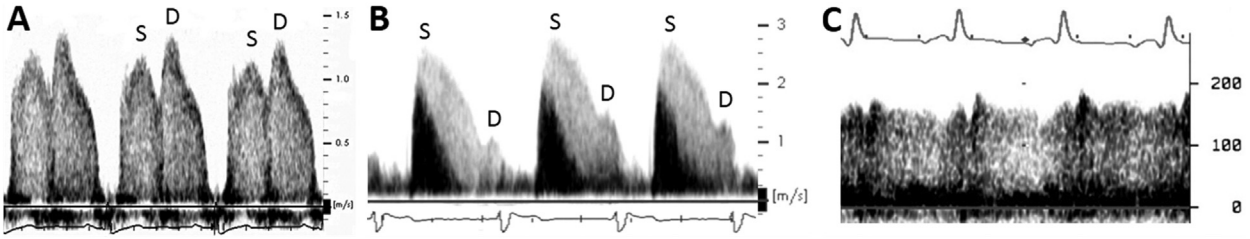

Figure 8 PV stenosis. **(A)** PV stenosis in a 50-year-old man following catheter ablation of atrial fibrillation. Continuous-wave Doppler of the RLPV shows increased peak velocity of the S and D waves at 1.3 m/sec. **(B)** High-grade PV stenosis. The S wave demonstrates markedly elevated peak velocity at 2.8 m/sec. **(C)** High-grade PV stenosis in a 25-year-old woman following lung transplantation complicated by thrombosis of the RLPV anastomosis. A monophasic and high-velocity flow is evident with loss of distinct S and D waves.

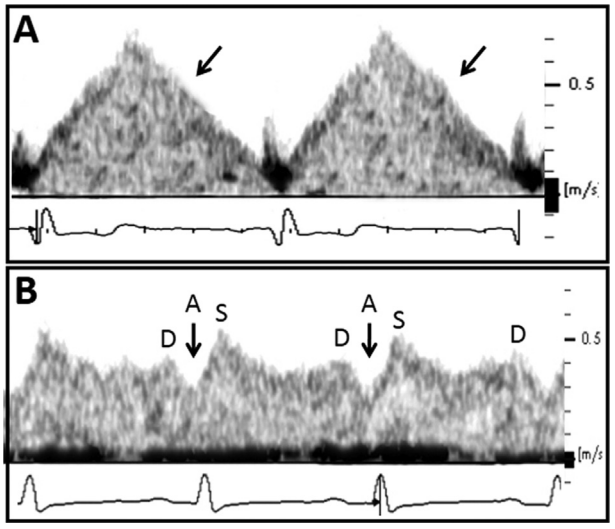

Figure 9 Congenital heart disease. **(A)** Atrial septal defect. The PV Doppler profile of a 32-year-old woman with large secundum defect demonstrates a single continuous antegrade wave *(arrows)* that replaces the S and D wave. Additionally, no A-wave reversal is evident. **(B)** Cor triatriatum. The PV Doppler profile of this 16-year-old boy shows dampening of the forward S and D wave with no A-wave reversal. The effect of the A-wave is evident on the forward velocities *(arrows)*.

A_{MV} and A_{PV} is to compare the ends of both waves using the R wave on the electrocardiogram as a reference.

The A_{PV}-A_{MV} difference helps separate patients with impaired relaxation pattern into those with normal filling pressure and those with elevated LVEDP and normal mean LA pressure. In contrast to the S/D ratio (see below), an A_{PV}-A_{MV} difference $>$ 30 msec is indicative of elevated LVEDP regardless of LV ejection fraction (LVEF) and remains useful in patients with hypertrophic cardiomyopathy.[30,31] An abnormal A_{PV}-A_{MV} difference is associated with a higher readmission rate in patients with heart failure.[32]

A less robust indicator of elevated LVEDP is an increased A_{PV} velocity $>$ 35 cm/sec. Importantly, assessment of A_{PV} is not feasible during atrial fibrillation, because of the loss of atrial contraction.

Elevated LA Pressure

In normal adults older than 40 years of age, the S/D ratio is $>$1 and exhibits an inverse relationship to LA pressure. As the latter increases, the velocity of the S wave decreases, and the PV Doppler profile typically demonstrates a diastolic-dominant (S $<$ D) pattern. The prominent D wave reflects a high-velocity transmitral E wave, itself a manifestation of the high LA-LV pressure gradient (Figure 5B).[33] Shortening of the D-wave deceleration time is often noted, and occasionally, an A_{PV}-A_{MV} difference $>$ 30 msec is evident, indicating high LVEDP.[34] As the S_2 wave is influenced by LV contractility and stroke volume, an S/D ratio $<$ 1 is a marker of elevated LA pressure in

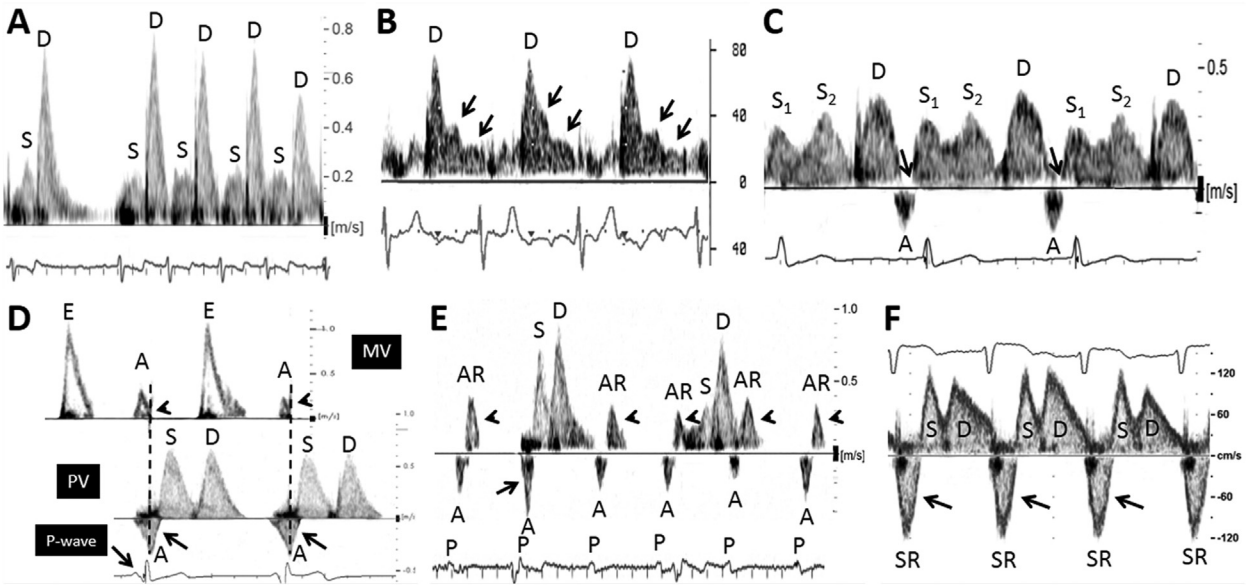

Figure 10 Rhythm and conduction disorders. **(A)** Atrial fibrillation in a 56-year-old man. The PV Doppler profile demonstrates an attenuated S wave with prominent D wave and no A-wave reversal. **(B)** Atrial flutter in a 60-year-old man. The PV Doppler profile shows abrupt changes in the velocity of the D wave *(arrows)*. **(C)** First-degree atrioventricular block in a 75-year-old woman with a PR interval of 260 msec. The PV Doppler profile demonstrates one forward systolic velocity (S_2 wave) and two forward diastolic velocities that correspond to the D wave and the atrial relaxation (S_1) wave, respectively. Note the wide separation of the peaks of S_1 and S_2 and the onset of S_1 well before the QRS complex *(arrows)*. **(D)** Short PR interval of 90 msec in an 18-year-old woman with no structural heart disease. The temporally aligned MV and PV Doppler demonstrate a large PV A-wave reversal *(arrows)* with high velocity (45 cm/sec) and a long duration (150 msec) that ends 70 msec after the small and shortened transmitral A-wave *(arrowheads)*. This finding can be mistaken for elevated LVEDP if the short PR interval is not recognized on the electrocardiogram. **(E)** Atrioventricular dissociation in a 74-year-old man with third-degree atrioventricular block. Note the unrelated P and QRS waves on the electrocardiogram. The PV Doppler profile demonstrates dissociation between the A and atrial relaxation (AR) waves *(arrowheads)* that follow the electrocardiographic P wave and the S and D waves that are dependent on the QRS complex. Additionally, a prominent SR wave *(arrow)* is noted, resulting from LA contraction occurring against a closed MV, thus leading to more prominent backflow into the PVs. **(F)** Junctional rhythm in a 35-year-old man with retrograde atrial activation. The simultaneous occurrence of atrial and ventricular systole leads to large early systolic flow reversals (cannon A-waves; *arrows*) in the PV, noted with every beat. This phenomenon results from atrial contraction occurring against a closed MV.

patients with reduced LVEFs and/or low cardiac output.[35] In individuals with normal LVEFs, the S/D ratio is not a sensitive marker of elevated filling pressure, because of preserved mitral annular motion that opposes blunting of S_2.[35] Thus, an S/D ratio >1 does not exclude elevated LA pressure in the setting of preserved LVEF. When present, a low S/D ratio is an independent predictor of survival and future cardiovascular events in individuals with preserved LVEF and provides prognostic information beyond the traditional grading of diastolic function.[32] Another parameter, the systolic fraction (S_{TVI}/[S_{TVI} + D_{TVI}]), predicts normal filling pressure with high accuracy when it is >55%.[33]

Healthy individuals <40 years of age normally exhibit S/D ratios <1 (Figure 2D), and this pattern should not be considered to reflect elevated LA pressure. Furthermore, the S/D ratio is not predictive of LA pressure in the setting of atrial fibrillation, severe MR, and hypertrophic cardiomyopathy.

LA Mechanical Dysfunction

Stretching of the left atrium or infiltration of the LA wall with amyloid fibrils may lead to atrial mechanical failure.[36] Despite sinus rhythm, the PV A wave can be small or absent despite elevated LVEDP (Figure 6).

DISEASES OF THE PERICARDIUM AND MYOCARDIUM

Constrictive Pericarditis and Cardiac Tamponade

Constrictive pericarditis leads to hemodynamic disturbances, including exaggerated ventricular interdependence and limited transmission of the intrathoracic pressure to the cardiac cavities.[37] Inspiration results in augmented RV filling with leftward shift of the interventricular septum and subsequent decrease in LV filling. The resulting PV Doppler profile demonstrates a significant decrease in the forward flow velocities with inspiration, particularly the D wave.[38] Expiration is associated with opposite changes (Figure 7). These respirophasic alterations are usually most evident on the first inspiratory and expiratory beats. The inspiratory decrease and expiratory increase in D-wave velocity parallel those for the transmitral E wave, but the percentage change in velocity is often more marked in the PVs. The combination of an S/D ratio ≥ 0.65 coupled with a decrease in D-wave velocity of $\geq$40% from expiration to inspiration helps distinguish patients with constrictive pericarditis from those with restrictive cardiomyopathy.[38] Similar findings of respirophasic variation on the PV Doppler are noted with cardiac tamponade.

Respiratory variation in flow is neither sensitive nor specific for pericardial diseases. Studies have shown the absence of respirophasic variation in at least one third of patients with constrictive

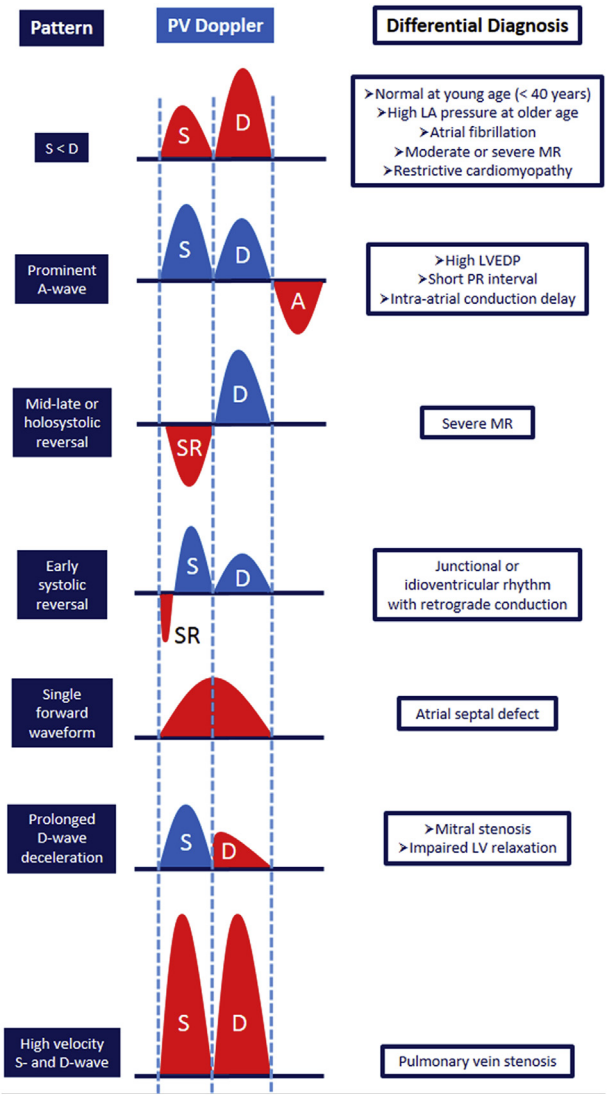

Figure 11 Common or characteristic PV Doppler patterns with diagnostic correlation. Abnormal waveforms are shown in *red*.

pericarditis.[39,40] Additionally, variation does occur in individuals with exaggerated fluctuation in intrathoracic pressure, often in the setting of increased respiratory effort due to obesity or airway obstruction associated with chronic obstructive lung disease. Therefore, the presence of respirophasic variation on PV Doppler is supportive of constrictive pericarditis or cardiac tamponade within the echocardiographic context. However, its absence should not be used to exclude the diagnosis.

Restrictive Cardiomyopathy

The main hemodynamic abnormality is an increase in LV chamber stiffness leading to a rise in LA filling pressure. The PV Doppler profile typically demonstrates blunting of the S wave with a prominent D wave showing minimal respiratory variation and rapid deceleration time, all indicative of elevated LA pressure (Figure 7B).[38] Blunting of the S wave is often pronounced because of the elevated filling pressure, the impairment of LV longitudinal function, and occasional atrial fibrillation.

PV STENOSIS

This condition most often results from an injury during catheter-based PV isolation for atrial fibrillation.[41] Even though TTE does not allow optimal visualization of all four PVs, the color Doppler identification of a turbulent flow originating from the direction of a PV should raise the suspicion of PV stenosis.[41] PV Doppler demonstrating an abnormally high peak velocity of the forward waveforms ≥1.1 m/sec is suggestive of this diagnosis (Figure 8A).[42,43] The identification of a peak waveform velocity > 1.6 m/sec (Figure 8B) or a high-velocity monophasic flow with loss of distinct S and D waves (Figure 8C) indicates high-grade PV stenosis.[43] TEE allows improved assessment of the presence and severity of PV stenosis compared with TTE.

CONGENITAL HEART DISEASE

Atrial Septal Defect

In the setting of an atrial septal defect with a large left-to-right shunt, flow in the PVs becomes more dependent on interatrial shunting than on left cardiac hemodynamics. This uncoupling phenomenon between the PVs and left heart parameters confers characteristic changes to the PV Doppler profile, resulting in the loss of distinct S and D waves. Instead, many patients demonstrate a single continuous antegrade wave from the onset of systole to atrial contraction, reflecting the run-off of blood from the left atrium into the right atrium across the defect (Figure 9A).[44,45] Additionally, the A wave is often attenuated because atrial contraction pushes the blood not only into the PV and left ventricle but also into the right atrium, thus reducing backflow into the PVs (Figure 9A).[44,45] The specificity and positive predictive value of a single antegrade wave to indicate the presence of an underlying atrial septal defect is not known. The PV Doppler profile returns to a normal pattern following closure of the defect.[44,45]

Cor Triatriatum

This condition is characterized by obstruction to flow within the LA cavity and leads to partial uncoupling between PV flow and left heart hemodynamics. The resulting PV Doppler profile demonstrates dampening of the waveforms with partial fusion of the S and D waves and no A-wave reversal (Figure 9B).[46] The effect of the A wave remains evident on the forward flow velocities (Figure 9B).

RHYTHM AND CONDUCTION DISORDERS

Atrial Fibrillation

An important hemodynamic consequence of atrial fibrillation is the loss of effective atrial contraction and relaxation. As the A wave is generated by LA contraction, atrial fibrillation leads to the loss of the A wave on the PV Doppler profile. Additionally, the absence of atrial relaxation results in the vanishing of the S_1 wave. Therefore, the forward systolic waveform results from the sole contribution of S_2. As S_2 normally arises before S_1 has ended, this phenomenon causes S_2 to start at a low velocity, thus leading to blunting of the S wave and a diastolic-dominant (S < D) pattern (Figure 10A).[18] This pattern resembles the flow profile seen in older individuals in sinus rhythm with elevated LA pressure. Thus, a false diagnosis of high filing pressure can be made if this phenomenon is not recognized. Following conversion to sinus rhythm, the resulting atrial stunning is

Table 2 Prognostic value of PV flow patterns

Finding on PV Doppler	Cardiac condition	*n*	Mean age, y	Follow-up duration	Outcome	Study
A_{PV}-A_{MV} difference ≥ 30 msec	HFrEF	145	70	15 mo	Higher cardiac mortality and hospitalization	Dini *et al.*[51]
Peak S < D	LVEF < 45%	115	69	1 y	Higher rate of HF hospitalization and death	Dini *et al.*[52]
S < D TVI ratio	IHD	102	66.9	4.1 y	Higher rate of HF hospitalization or death	Ren *et al.*[53]
Lower peak S/D Higher A_{PV}-A_{MV}	LVEF > 50%	365	64.9	7.9 mo	Higher rate of HF readmissions	Buffle *et al.*[32]
Improved PV Doppler*	Post-PMVr	93	76	1 y	Improved survival and reduced hospitalization	Corrigan *et al.*[26]
S/D TVI ≤ 0.72†	Post-PMVr	300	76	1 y	Higher mortality, recurrent MR, MV surgery, redo PMVR	Ikenaga *et al.*[25]

HF, Heart failure; *HFrEF*, heart failure with reduced ejection fraction; *IHD*, ischemic heart disease; *PMVr*, percutaneous MV repair.
*Improved PV Doppler is defined as a positive change in S-wave morphology from reversed to blunted or from blunted to normal pattern on intraprocedural TEE done in the immediate postrepair period.
†S/D TVI ratio ≤ 0.72 on intraprocedural TEE done in the immediate postrepair period.

Table 3 Feasibility of obtaining optimal pulmonary venous velocity recording by TTE from the apical window

Authors	Year of publication	Feasibility of assessing S and D waves	Feasibility of assessing A wave
Jensen *et al.*[54]	1997	190/200 (95%)	180/200 (90%)
Gentile *et al.*[12]	1997	143/174 (82%)	101/174 (58%)
Dini *et al.*[51]	2000	110/145 (76%)	90/145 (62%)
Buffle *et al.*[32]	2015	284/393 (73%)	255/393 (65%)

associated with low velocity of all waveforms, particularly the S_1 and A waves. Within 10 days after cardioversion, increases in the velocities of all waveforms are usually noted.[47]

Atrial Flutter

The most characteristic pattern is an abrupt change in the forward flow velocities with indentations on the contour of the waveforms, particularly the D wave (Figure 10B). This pattern reflects the rapid change in the PV-LA pressure gradient due to the fast sequence of atrial contraction and relaxation.

First-Degree Atrioventricular Block

With an abnormally long PR interval, atrial contraction occurs before the rapid filling phase has ended. The atrial relaxation (S_1) wave that follows starts before the delayed QRS complex and gives a "double diastolic peak" pattern to the PV signal (Figure 10C). Additionally, the systolic wave becomes clearly biphasic, with wide separation between the peaks of S_1 and S_2.[48]

Short PR Interval

Because of the short atrioventricular delay, the rapid rise in LV pressure in early systole causes premature closure of the MV and thus abrupt termination of the transmitral flow with shortening of the MV A-wave duration (Figure 10D). As LA relaxation has not fully developed, the relatively high LA pressure at the time of MV closure causes backflow into the PVs and leads to a prominent PV A wave with longer duration than the transmitral A wave (Figure 10D).[49] The same flow pattern occurs in individuals with intra-atrial conduction delay due to late activation of the left atrium. This finding on PV Doppler mimics an elevation in LVEDP (Figure 5A). Therefore, before a diagnosis of elevated LVEDP is considered, one must ensure that the PR interval is not abnormally short.

Atrioventricular Dissociation

The electrical dissociation between the P and QRS waves leads to mechanical dissociation between the left atrium and left ventricle. The resulting PV Doppler profile demonstrates a dissociation between both the A wave and atrial relaxation wave that follow the electrocardiographic P wave and the S and D waves that are dependent on the QRS complex (Figure 10E).[9] Additionally, intermittent and prominent SR waves are noted. These waves result from LA contraction occurring during ventricular systole, thus against a closed MV, causing further rise in LA pressure and backflow into the PVs (Figure 10E).[50]

Junctional and Idioventricular Rhythm

In patients with retrograde electrical conduction to the atria, atrial activation and contraction occur during ventricular systole and thus against a closed MV. This phenomenon leads to a rise in LA pressure, resulting in prominent and early systolic flow reversals (cannon A waves) in the PVs (Figure 10F).[49] This pattern of early SR should be distinguished from the holosystolic or mid to late SR encountered in severe MR.

In summary, the PV Doppler profile is altered in various rhythm and conduction disorders. Recognition of these alterations prevents the misinterpretation of the Doppler signal as to represent a structural of hemodynamic abnormality of the left heart.

DIAGNOSTIC CORRELATION OF PULMONARY VENOUS FLOW PATTERNS

Figure 11 illustrates common or characteristic PV Doppler flow patterns with correlation to specific diagnosis.

PROGNOSTIC VALUE OF PULMONARY VENOUS FLOW PARAMETERS

PV Doppler parameters including the S/D ratio and A_{PV}-A_{MV} have prognostic value and are predictors of major adverse cardiac events, including hospitalization for heart failure, readmission, and higher mortality rates in specific patient populations.[32,51-53] Additionally, various findings on PV Doppler following percutaneous MV repair are associated with either survival benefit or with worse patient outcomes.[25,26] These studies are detailed in Table 2.

FEASIBILITY OF PULMONARY VENOUS FLOW RECORDING AND USE OF ULTRASOUND ENHANCING AGENTS

An interpretable PV flow profile can be acquired from the transthoracic apical window in up to 90% of adults. The S and D waves are optimally recorded in 73% to 95% of individuals, whereas the lower velocity A wave is more difficult to visualize and is recordable in 58% to 90% of individuals (Table 3).[12,32,52,54]

In individuals with suboptimal flow profile, the use of ultrasound enhancing agents during TTE improves the quality and facilitates interpretation of the PV Doppler signal.[55] Ultrasound enhancing agents allow improved visualization of biphasic systolic waves and recording of higher peak velocity of the forward waves, thus increasing the accuracy of interpretation of the Doppler data.[55] Technically, PV flow is best evaluated in the later part of the contrast injection.[51,52,55]

LIMITATIONS AND PITFALLS

The major challenge to the use of the PV Doppler in everyday practice is the ability to obtain a good-quality and interpretable flow signal by TTE. Several conditions, such as chronic lung disease, shadowing from mitral calcifications, reverberations from prosthetic valves, mechanical ventilation, and inability to properly position patients, such as in the intensive care setting, increase the difficulty in obtaining an optimal PV Doppler signal. Additionally, obesity and severe LA and/or LV enlargement make an optimal signal difficult to record because of the far-field sector and distortion of cardiac anatomy.

The A wave is often more difficult to record than the S and D waves because of its lower velocity and timing. The most common and problematic artifact encountered on the PV Doppler profile occurs during atrial contraction and results in a low-velocity wall motion signal in late diastole that obscures the A wave. Table 1 summarizes the appropriate steps that help improve the quality of the PV Doppler signal.

CONCLUSION

Spectral Doppler interrogation of the PVs should be routinely performed as part of any comprehensive echocardiographic study. Even though findings on the PV Doppler profile should not be used as the sole parameters for diagnostic purposes, their use in combination with two-dimensional, spectral, color, and tissue Doppler parameters provides added hemodynamic information regarding a wide variety of diseases that involve the left heart. A good-quality recording of the PV flow signal and proper interpretation of the waveforms are important requirements to improve diagnostic accuracy and optimize medical care.

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