Advanced Functional Echocardiographic Views Including PDA Assessment and Hemodynamic Evaluation

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Echocardiographic Diagnosis and Hemodynamic Evaluation of the Patent Ductus Arteriosus

Echocardiography is the gold standard non invasive bedside imaging modality to evaluate a patent ductus arteriosus (PDA). In addition to make a confirmative diagnosis of PDA and exclude/diagnose any associated congenital heart defect (CHD), it can help in estimating the magnitude of shunt volume and assessing its hemodynamic significance—it can be used to assess the hemodynamic impact from pulmonary over-circulation and systemic hypoperfusion due to shunt volume [1–3]. This could be systematically achieved by assessing: (a) ductal characteristics, (b) parameters of pulmonary over-circulation, and (c) signs of systemic hypoperfusion (Fig. 1).

Various echocardiographic parameters have been described in the research setting as well as complex staging/scoring systems [3, 4]. In this chapter, we will focus on the parameters which can help clinicians in making a clinical decision at the bedside.

Echocardiographic Assessment of Ductal Ccharacteristics

Echocardiography can be used to assess the size of PDA by measuring transductal diameter. Interrogation of shunt direction, and velocity of blood flow across the ductus arteriosus can be measured by using Doppler technique.

Measuring Transductal Diameter

Although the PDA can be visualized from many windows, the high left-sided parasternal "ductal" view and suprasternal arch view are preferred to obtain a clear 2D image and accurately measure the size of the ductus arteriosus. PDA size is measured from the transductal diameter at the site of maximum constriction (narrowest dimension), which is usually at the pulmonary end. Many studies have described measuring the PDA size using color Doppler, although measuring its diameter in 2D is more accurate. However, to avoid an over or under-estimation, it is important to know the shape of the PDA [2, 5]. It will therefore be important to carry out a sweep starting at the level of the aortic arch up to the pulmonary artery.

If color Doppler is used to measure the ductal size, the gain setting should be adequately optimized to minimize the risk of over-estimation. Color comparison or simultaneous mode, which allows 2D and color Doppler images side by side, can be applied to measure ductal size in both modes using frame-by-frame technique [1] (Fig. 2).

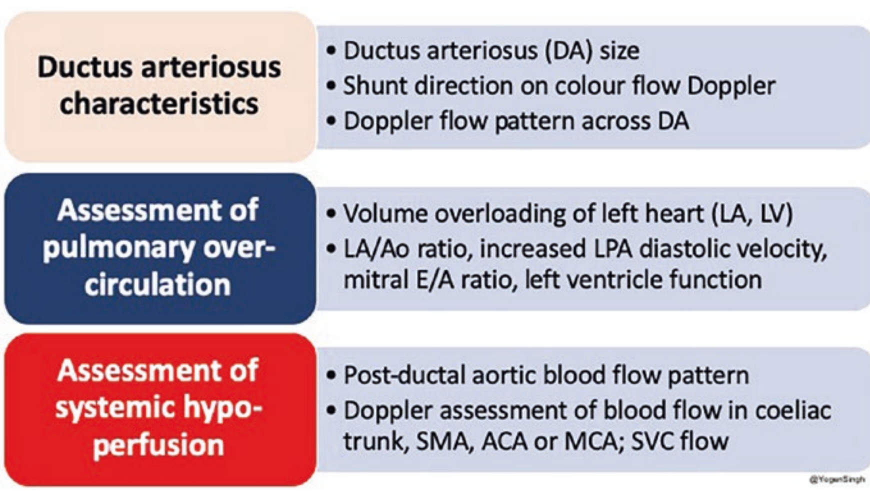


Fig. 1 Summary of an approach to the echocardiographic assessment of PDA and hemodynamic evaluation. *LA* left atrium, *LV* left ventricle, *DA* ductus arteriosus, *Ao* aorta, *SMA* superior mesenteric artery, *ACA* anterior cerebral artery, *MCA* middle cerebral artery, *SVC* superior vena cava, *LPA* left pulmonary artery (*copyright—Dr. Yogen Singh*)

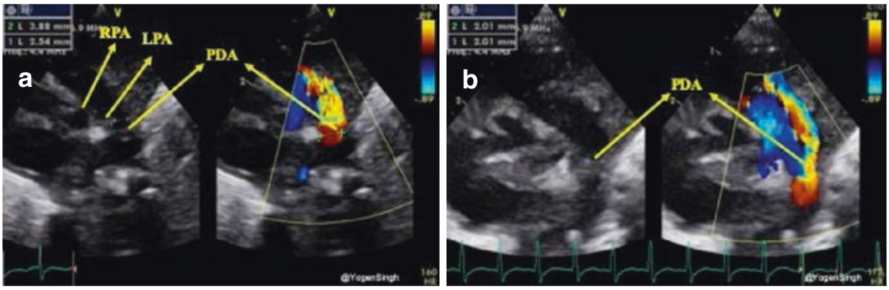


Fig. 2 Measurement of ductal size on 2D and color Doppler on high left parasternal "ductal view." (**a**) A significant discrepancy between ductal diameter measurement on 2D and color Doppler—over-estimation of ductal size on color Doppler due to gain setting; (**b**) no significant discrepancy between ductal diameter measurement on 2D and color Doppler after optimization of gain setting. *LPA* left pulmonary artery, *RPA* right pulmonary artery, *PDA* patent ductus arteriosus (*copyright—Dr. Yogen Singh*)

Direction of Shunt Across the Ductus Arteriosus

The direction of the ductal shunt depends upon the relationship between the pulmonary and systemic pressures. It is assessed using color Doppler. The direction of blood flow across the ductus arteriosus is normally left to right, from the aorta (high systemic pressure) to the pulmonary artery (low pulmonary pressure) but it can be right to left or bidirectional when there is high pulmonary vascular resistance or when there is an anatomical cause (due to certain CHDs). With the conventional setting of the Nyquist scale, left to right shunt is seen as a red jet while right to left shunt is seen as blue [1, 6]. A right to left shunt across the PDA is more difficult to see because the color Doppler will show it as a blue jet, blood going towards aorta from pulmonary end, similar to branch pulmonary arteries. Color comparison or simultaneous mode can be very helpful in this situation. Bidirectional flow is often seen during transitional circulation or when the pulmonary artery pressures are equal to the systemic pressures [2, 6]. Shunt direction can also be assessed using pulse or continuous wave Doppler, where left to right shunt is seen above the baseline (blood coming towards the probe) while right to left shunt is seen below the baseline (blood going away from the probe) [1, 6] (Fig. 3).

Velocity of Shunt Across PDA and Its Significance

The shunt velocity across the PDA during the cardiac cycle can be obtained by applying pulse or continuous wave Doppler in the ductus arteriosus. The maximum velocity during systole and diastole can be measured. Nonrestrictive shunts have a low peak systolic velocity with a high systolic to end-diastolic velocity gradient while restrictive shunts have a high peak systolic velocity and a low systolic to diastolic velocity gradient. A ratio of >2 between peak systolic and end-diastolic velocity is considered as a pulsatile flow pattern while a ratio of <2 is described as a restrictive shunt suggestive of a closing PDA [7, 8] (Fig. 4).

Echocardiographic Evaluation of Pulmonary Over-Circulation

The increased pulmonary blood flow from a significant left to right ductal shunt leads to pulmonary overcirculation and therefore, increased pulmonary venous return. This volume overload to the left atrium (LA) gradually dilates this chamber. If this significant left to right shunt persists over time then dilatation of the left ventricle from increased preload, especially in absence of a large intra-atrial shunt also occurs. As the aortic valve annulus (Ao) is a relatively fixed structure and it does not get dilated due to left heart overloading, the LA/Ao ratio can be used as a surrogate of increased pulmonary venous return [9, 10]. Similarly, the left ventricular end-diastolic diameter (LVEDD) can be used as a surrogate marker for pulmonary venous return. In clinical practice, the volume overload of the left heart can be subjectively assessed by "eyeballing" [11] (Fig. 5).

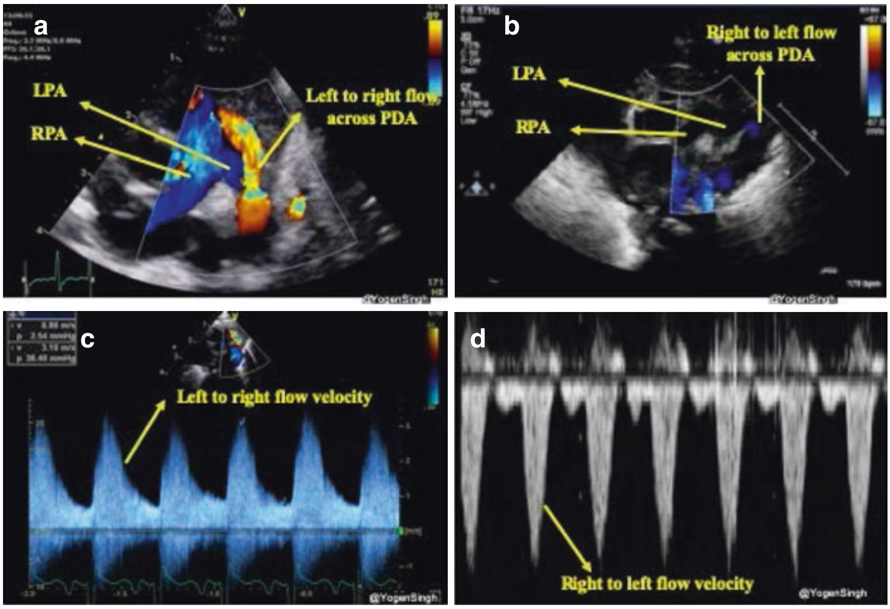


Fig. 3 Assessment of PDA shunt direction on color flow and spectral Doppler. (**a**) Left to right shunt seen as red (blood coming towards probe) while blood in branch pulmonary arteries is seen as blue (blood going away from the probe); (**b**) right to left shunt seen as blue color—similar to branch pulmonary arteries in a view "three legged trouser"; (**c**) Pulsed Wave Doppler assessment showing left to right shunt (above the baseline as blood coming towards the probe) and (**d**) Doppler assessment showing right to left shunt (below the baseline as blood going away from the probe). *LPA* left pulmonary artery, *RPA* right pulmonary artery, *PDA* patent ductus arteriosus (*copyright—Dr. Yogen Singh*)

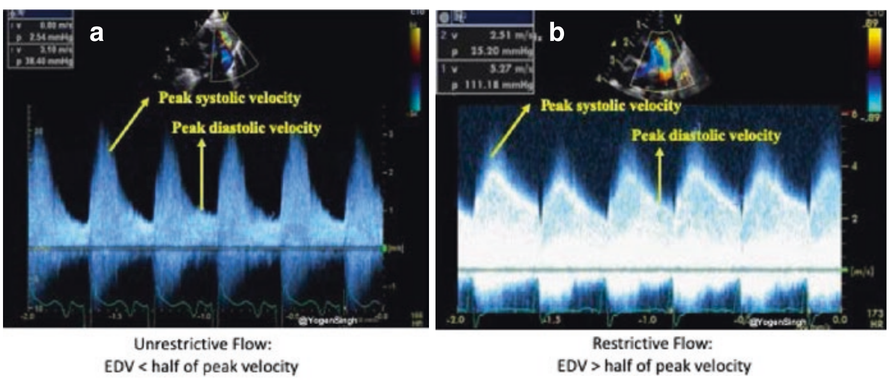


Fig. 4 Assessment of restrictive and unrestrictive flow pattern on Doppler assessment of PDA. (**a**) Unrestrictive flow pattern with end-diastolic velocity (EDV) less than half of the peak systolic velocity and (**b**) A restrictive flow pattern with end-diastolic velocity (EDV) more than half of the peak systolic velocity. (*copyright—Dr. Yogen Singh*)

Both LA/Ao ratio and LVEDD can be measured from the parasternal long axis view using M-mode with the cursor perpendicular to the aorta at the level of the aortic valve or at the tip of the mitral valve leaflets, respectively (Fig. 6). LA/Ao ratio of >1.4 is considered significant and has been used as a cut-off value in many clinical trials [11]. The normal reference ranges for LVEDD in preterm infants in relation to body weight and postnatal age have been published and z-scores should be used for LVEDD [12].

Variable degree of mitral valve insufficiency is often seen in infants with a persistently large

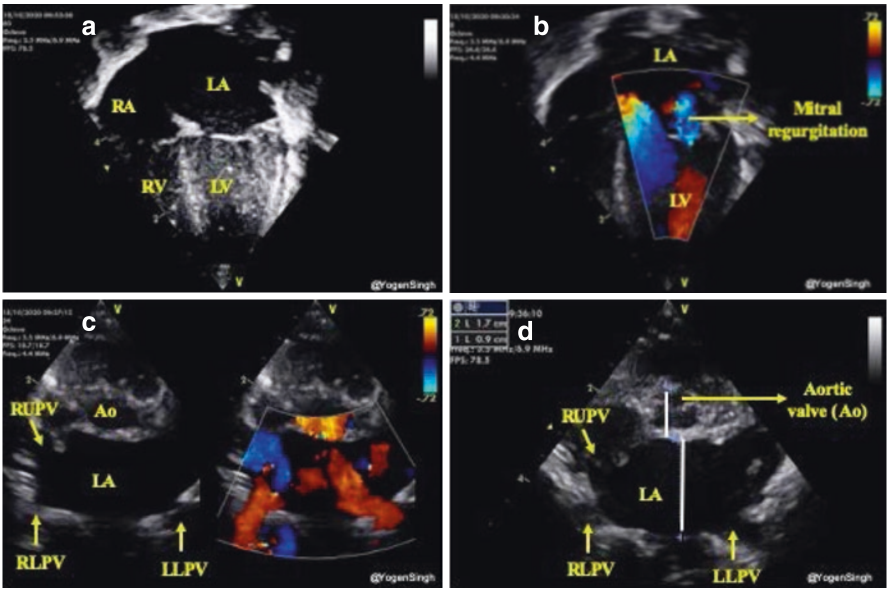
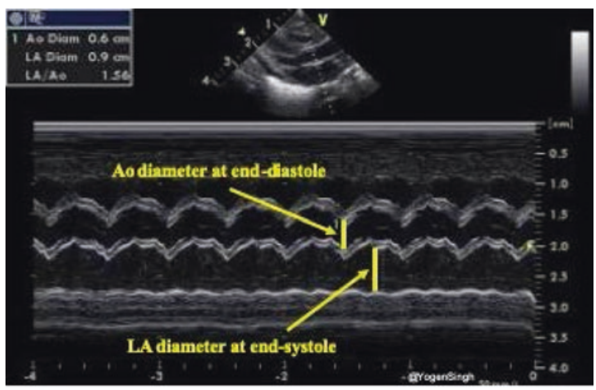


Fig. 5 Assessment of left heart volume overload on visual inspection "eyeballing." (**a**) Apical 4-chamber view in 2D showing dilated left side of the heart (dilated left atrium and left ventricle); (**b**) Mitral regurgitation on color flow mapping as blue jet going back to the left atrium (see explanation in text); (**c**) "Crab view" showing dilated pulmonary veins reflecting increased pulmonary venous return and (**d**) Dilated left atrium in parasternal short axis view—on visual inspection LA looks double the size of the aortic valve (Ao). *LA* left atrium, *LV* left ventricle, *RA* right atrium, *RV* right ventricle, *Ao* aortic valve, *RUPV* right upper pulmonary vein, *RLPV* right lower pulmonary vein, *LLPV* left lower upper pulmonary vein (*copyright—Dr. Yogen Singh*)

Fig. 6 Assessment of left atrium (LA) to aorta (Ao) ratio in parasternal long axis view. LA and Ao diameter measurement shown using M-mode. (*copyright—Dr. Yogen Singh*)



Left atrium (LA) / Aorta (Ao) ratio measurement

PDA and significant left heart dilatation. It occurs due to left atrial dilatation resulting in stretching of mitral valve and left ventricular volume overload. The mitral valve regurgitation usually improves significantly with normalization of left atrial size and resolves completely within weeks after PDA closure [13].

While assessing left heart volume overload one should be mindful of intra-atrial shunts. A large left to right shunt through the foramen ovale or atrial septal defect can "offload" the left side of the heart even in the presence of a significant ductal shunt leading to an artificially low/normal LA/Ao ratio or low LVEDD.

The presence of forward pulmonary flow in diastole in the left pulmonary artery (LPA) has been described as a sign of significant left to right shunt through the PDA. Using pulsed wave Doppler in the LPA, mean and end-diastolic velocity can be measured and cut-off points of

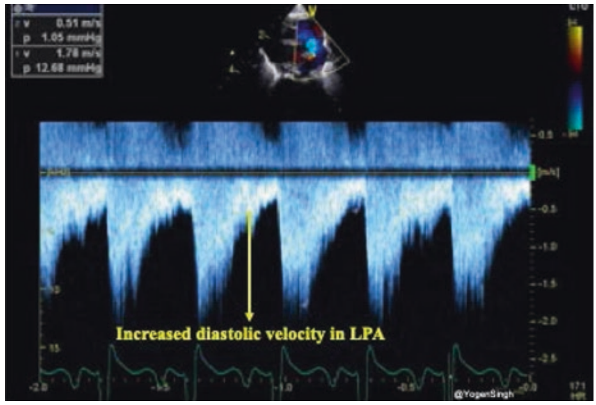


Fig. 7 Doppler assessment of blood flow in left pulmonary artery (LPA) showing increased diastolic velocity indicative of significant ductal shunt in diastole leading to turbulence and increased velocity. (*copyright—Dr. Yogen Singh*)

0.42 m/s and 0.20 m/s, respectively have been described as indicative of significant ductal shunt [14] (Fig. 7).

The mitral valve E/A ratio refers to the ratio of the velocity of the early (E) diastolic phase of ventricular filling versus the late atrial (A) contraction component. Mitral valve E/A ratio can be obtained from apical 4-chamber view with the pulse Doppler range gate set slightly below the mitral valve annulus. In preterm infants, mitral valve E/A ratio is usually <1 due to poor compliance of the myocardium leading to moderate impairment of diastolic performance and low early diastolic filling velocity. In the presence of a hemodynamically significant PDA (hsPDA), atrial pressure increases because of high pulmonary venous return and this leads to a reversal of the E/A ratio >1 [2].

Various other echocardiographic parameters have been studied and described to assess pulmonary circulation such as left ventricular output (LVO) to superior vena cava flow (SVC) ratio and decreased isovolumic relaxation time (IVRT) using tissue Doppler Imaging (TDI) [14]. However, echocardiographic assessments (such as SVC flow and LVO estimation) that need multiple measurements are not only time-consuming but also has the potential to make errors in measurements and they have significant intra- and inter-observer variability [15–17]. Hence, the common echocardiographic parameters often used in clinical decision-making at the bedside remain qualitative assessment on visual inspection "eyeballing," LA/Ao ratio, LPA diastolic velocity and LVEDD measurement. Mitral E/A ratio is easy to measure but one should be mindful that even in preterm infants with no hsPDA E/A ratio gradually become >1 with time as myocardium compliance improves.

Echocardiographic Evaluation of Systemic Hypoperfusion

In the presence of a large PDA, blood shunts away from the systemic circulation throughout the cardiac cycle; however, this becomes more apparent during diastole and it can be studied using pulsed wave Doppler on echocardiography [11, 16]. Retrograde or absent blood flow during diastole in descending aorta below the ductal ampulla, in the coeliac axis or sin the uperior mesenteric artery have been described as indicators of significant PDA shunt leading to systemic blood steal (systemic hypoperfusion) [9, 17]. Doppler flow patterns from the descending aorta can be obtained from a suprasternal or high parasternal view with the pulsed wave Doppler sample gate placed distal to the origin of ductus arteriosus (ductal ampulla) (Fig. 8).

Similarly, celiac trunk or superior mesenteric artery can be interrogated using pulsed wave

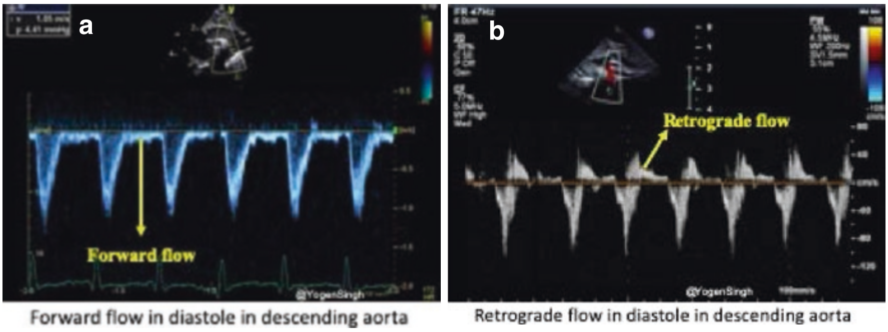


Fig. 8 Pulsed Wave Doppler assessment of blood flow in descending aorta (Post-ductal flow). (**a**) Forward blood flow during disatole and (**b**) Retrograde blood flow during diastole indicating "ductal steal" in the presence of a large PDA. (copyright—Dr. Yogen Singh)

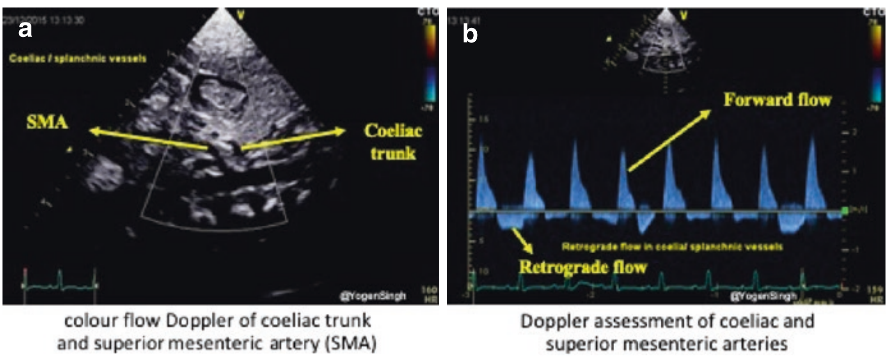


Fig. 9 Color flow mapping and pulsed wave Doppler assessment of blood flow in the coeliac trunk and superior mesenteric artery in sub-costal sagittal view. (**a**) Color flow mapping of the coeliac and superior mesenteric artery and (**b**) Retrograde blood flow during diastole in the coeliac and superior mesenteric artery indicating "ductal steal" in the presence of a large PDA. (*copyright—Dr. Yogen Singh*)

Doppler in the sagittal abdominal view (Fig. 9). Doppler assessment of the anterior cerebral artery in the mid-sagittal view of brain ultrasound can be performed and retrograde flow during diastole would suggest significant ductal shunt—similar to coeliac or superior mesentery artery Doppler assessment. However, to date, the clinical relevance and long-term outcomes of the deranged cerebral Doppler flow patterns remain unknown [1, 18] (Fig. 9).

Based upon the clinical and echocardiographic criteria various staging systems have been described and have been shown to help in decision-making for intervention [3, 19]. Recently, van Laere et al. (2018) suggested essential various echocardiographic parameters including measuring left ventricular output in all infants needing assessment of PDA [4]. However, these staging systems that require extensive echocardiographic measurements have not been widely adopted in pediatric cardiology clinical practice. We have summarized the most commonly used measurements which help clinicians in assessing the PDA and its hemodynamic significance on echocardiography (Table 1).

Table 1 Summary of the most common echocardiographic parameters used for assessment and hemodynamic evaluation of PDA

PDA evaluation criteria	Essential echocardiographic parameters for assessment of PDA and hemodynamic evaluation
Ductal characteristics	• PDA size (small <1.5 mm, moderate 1.51–2 mm, large >2 mm) and • Flow direction (Left to right, right to left, or bidirectional), and • Doppler assessment with maximum velocity (Vmax) in systole and end diastole
Assessment of pulmonary over-circulation	• Dilated left side of the heart on visual inspection "eyeballing" and • LA/Ao ratio (mild <1.4, moderate 1.41–1.6, severe >1.6) OR • LVEDD (correlate with z-scores) OR • LPA diastolic velocity—mean velocity >0.42 m/s, end diastolic velocity >0.2 m/s OR • Reversal of mitral E/A ratio
Assessment of systemic hypoperfusion	• Retrograde or absent blood flow during diastole in: – descending aorta OR – coeliac trunk or superior mesenteric artery (SMA) OR – anterior or middle cerebral artery

A comprehensive echocardiographic assessment should be performed to rule out any underlying congenital heart defect or pulmonary hypertension and delineate orientation of the arch (left or right sidedness) before any intervention to close the PDA

Advanced Hemodynamic Evaluation—Measurement of Blood Flow and Cardiac Output

Echocardiography can help in the advanced hemodynamic evaluation including measurement of cardiac output, superior vena cava flow, and fluid responsiveness. Evaluation of fluid responsiveness has been discussed in the chapter on assessment of neonatal shock (chapter "POCUS in Shock and Hypotension") and a detailed assessment of pulmonary hypertension has been described in chapter "Focused Ultrasound in Right Ventricular Function and Pulmonary Hypertension" on pulmonary hypertension. We have discussed the estimation of left ventricular output, right ventricular output, and superior vena cava flow, which have not been discussed elsewhere in this book. However, advanced hemodynamic evaluation and these measurements are out of the scope of POCUS applications.

Assessment of Cardiac Output and Blood Flow on Echocardiography

The echocardiographic assessment of blood flow across any "vessel or outflow tract" can be estimated by multiplying the cross-sectional area (CSA) of the vessel with the velocity time integral (VTI) of the blood flow across a specific point where CSA is calculated and the heart rate (HR), applying these values in the following equation below [20, 21].

$$\text{Blood flow}\left(\text{mL}/\text{kg}/\text{min}\right)=\frac{\text{CSA}\times\text{VTI}\ \left(\text{in cm}\right)\times\text{HR}}{\text{Body weight}\ \left(\text{in kg}\right)}$$

It is applied in clinical practice to estimate left ventricular cardiac output (LVO), right ventricular output (RVO), and superior vena flow in children.

Estimation of Left Ventricular Output

The CSA for LVO is calculated by measuring the diameter at the level of aortic valve (AV) annulus at end systole in the parasternal long axis view (PLAX) and the VTI is measured just distal to the AV valve by using pulsed wave Doppler in the apical 5-chamber view. HR is calculated automatically by the ultrasound machine from the ECG recording (Fig. 10).

$$\text{Left ventricular output}\ (\text{mL / kg / min}) = \frac{\text{CSA}\ (\text{at AV annulus}) \times \text{VTI} \times \text{LVOT}\ (\text{in cm}) \times \text{HR}}{\text{Body weight}\ (\text{in kg})}$$

Despite various assumptions and limitations (discussed below), the assessment of LVO on echocardiography correlates strongly to the measurements acquired by other well-established techniques such as pressure measurement by cardiac catheter and Fick's dye dilution method. The published studies showed a bias under 10%. A recently published study on the estimation of left ventricular cardiac output on echocardiography correlated strongly with the assessment by phase contrast MRI, which is very reassuring [22, 23].

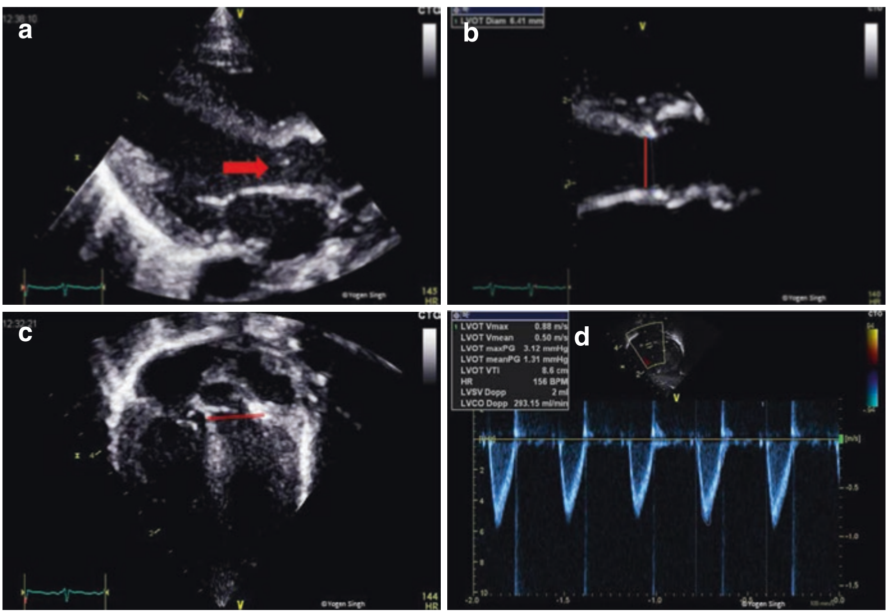


Fig. 10 Assessment of left ventricular output (LVO) on echocardiography. (**a**) LV outflow tract (red arrow) and AV annulus (red line), which has been zoomed in (**b**) to measure diameter at the hinge point of AV valve. (**c**) LV outflow tract and the site for pulsed wave Doppler to measure VTI (red line showing pulsed wave sample gate). (**d**) LVO in mL/min. *AV* aortic valve, *LV* left ventricle (*copyright @Yogen Singh, adopted from Singh, Y. Echocardiographic evaluation of hemodynamic in neonates and children. Front Pediatr 2017*)

Estimation of Right Ventricular Output

The RV output equals systemic venous return in the absence of cardiac shunts. RV output can be easily assessed on echocardiography. The CSA is calculated by measuring the diameter at the hinge point of pulmonary valve (PV) annulus at end-systole in the parasternal long axis sweep view (PLAX) or parasternal short axis view (PSAX), and VTI is measured just proximal to the pulmonary valve by using PW Doppler in the same views. HR is calculated automatically by the ultrasound machine from the ECG recording (Fig. 11).

$$\text{Right ventricular output}\ (\text{mL/kg/min}) = \frac{\text{CSA}\ (\text{at PV annulus}) \times \text{VTI} \times \text{RVOT}\ (\text{in cm}) \times \text{HR}}{\text{Body weight}\ (\text{in kg})}$$

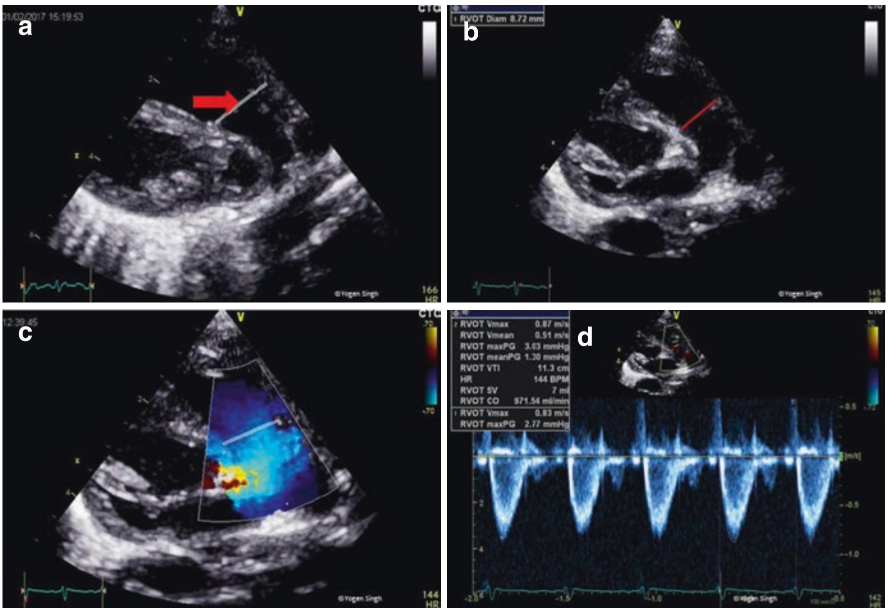


Fig. 11 Assessment of right ventricular output (RVO) on echocardiography. (**a**) RV outflow tract (red arrow) and (**b**) measurement of PV annulus (red line) at the hinge point of AV valve. (**c**) RV outflow tract and the site for PW Doppler to measure VTI (red line showing PW sample gate). (**d**) RVO in mL/min. *PV* aortic valve, *PW* pulse wave, *RV* right ventricle (*copyright @Yogen Singh, adopted from Singh, Y. Echocardiographic evaluation of hemodynamic in neonates and children. Front Pediatr 2017*)

Limitations of LVO and RVO Measurement Using Echocardiography

The measurement of LVO and RVO using echocardiography has various limitations including [1]:

1. LVO and RVO assessment may be contaminated by trans-atrial and ductus arteriosus shunts, which are quite common in neonates during transitional circulation and those with congenital heart defects. In the presence of a PDA, LVO reflects systemic blood flow plus the amount of ductal shunt. Similarly, in the presence of trans-atrial shunt (via persistent foramen ovale (PFO) or atrial septal defect), RVO reflects the systemic blood flow plus atrial shunt volume.
2. Measurement of AV diameter is prone to mistake and CSA is calculated by squaring the diameter, any error in measurement is multiplied.
3. Measurement of VTI (stroke distance) is also prone to errors. The angle of insonation, angle between the ultrasound waves and the blood flow, during Doppler assessment, should be minimal. If the angle of insonation is >10% it would underestimate the cardiac output.

The echocardiographer should be aware of these limitations and precautions should be taken to minimize such errors. In clinical practice, considering the trend of measurement values by serial echocardiography may be more useful than the absolute values.

Superior Vena Cava (SVC) Blood Flow

SVC flow has been proposed as a surrogate measure of cerebral blood flow, and it has been associated with short-term and long-term outcomes in neonates [24, 25]. Several studies have reported an association between low SVC flow in the first 24 h and intraventricular hemorrhage (IVH) and/or neonatal death in preterm infants [24, 25]. However, other studies could not demonstrate such association [26].

CSA is calculated by measuring SVC diameter in a modified PSAX view, and VTI is measured just proximal to its connection to RA by using PW Doppler in the sub-costal view. The SVC is a venous structure that is D-shaped and collapsible. Hence, measuring CSA of superior vena cava is prone to increased error as compared to a relatively noncollapsible AV or PV annulus. It is recommended that SVC diameter should be averaged over 5–10 heart cycles and best measured in M-mode. Similarly, VTI is also averaged over 5–10 cardiac cycles. HR is calculated automatically by the ultrasound machine from the ECG recording (Fig. 12).

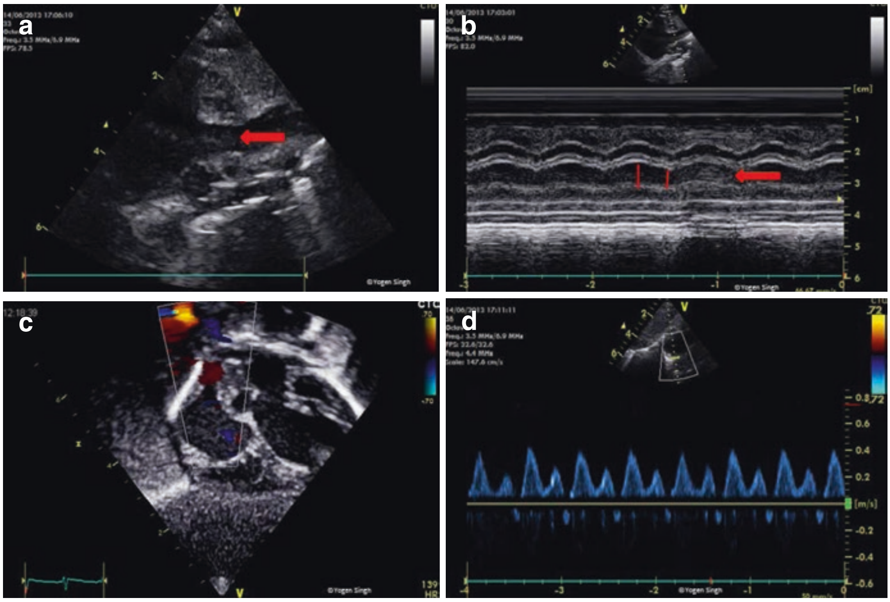


Fig. 12 Measurement of superior vena cava (SVC) flow on echocardiography. (**a**) SVC in modified parasternal short axis view (PSAX) on 2D and (**b**) measurement of SVC diameter in M-mode. (**c**) Acquisition of color flow Doppler in sub-costal view and (**d**) SVC flow in mL/min calculated after measuring velocity time integral. (*copyright @Yogen Singh, adopted from Singh, Y. Echocardiographic evaluation of hemodynamic in neonates and children. Front Pediatr 2017*)

$$\text{SVC blood flow}\ (\text{mL/kg/min}) = \frac{\text{CSA}\ (\text{SVC in M} \times \text{mode}) \times \text{VTI}\ (\text{in cm}) \times \text{HR}}{\text{Body weight}\ (\text{in kg})}$$

The reference values for SVC flow in term and preterm infants have been published with considerable variations [15, 27, 28]. However, given the risk of errors in measuring SVC diameter accurately, there is no surprise that the validation studies on estimating SVC blood flow by using echocardiography in neonates showed poor correlation when compared to MRI [22]. The studies have reported high intra- and inter-observer variability, a significant bias, and an error percentage of up to 55% [15, 22, 27, 28]. With the current published evidence, it is hard to recommend using SVC flow in clinical decision-making; however, a trend in SVC flow can be useful in clinical practice to assess the impact of any intervention.

Advanced echocardiographic techniques and views can be applied for detailed hemodynamic evaluation in neonates and children including evaluation of cardiac output, preload, afterload, cardiac contractility/function, fluid responsiveness, diagnosis, and hemodynamic evaluation of patent ductus arteriosus and pulmonary hypertension. This advanced evaluation needs a depth of knowledge and high-quality echocardiography skills, and they are out of the scope of POCUS practice. This protocol-based evaluation using advanced echocardiographic parameters is often used by clinicians formally trained in neonatologist-performed echocardiography.

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