Chapter 28

Ductus Venosus

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The ductus venosus (venous duct, ductus Arantii) is one of the three physiological shunts responsible for the circulatory adaptation to intrauterine life. It is attributed to Giulio Cesare Aranzi (1530–1589), but the first written account dates back to his contemporary Vesalius in 1561 [1]. Its function was long recognized [2, 3] but of hardly any clinical importance until ultrasound techniques were introduced [4–6]. It is now widely used as an important part of the hemodynamic assessment of the fetus [7] and has been suggested for diagnostic use after birth as well [8].

Anatomy and Development

The ductus venosus is a thin, slightly trumpet-shaped vessel connecting the intra-abdominal umbilical vein with the inferior vena cava (IVC; Fig. 28.1). Its inlet, the isthmus, is on average 0.7 mm at 18 weeks and 1.7 mm at 40 weeks of gestation [9–11]. It leaves the umbilical vein (portal sinus) in a cranial and dorsal direction and reaches the IVC at the level of the hepatic venous confluence shortly below the atria. This section of the IVC is shaped as a funnel [12] but expands predominantly to the left side to receive blood from the ductus venosus and the left hepatic veins [13, 14]. Although variations in direction have been reported, the ductus venosus approaches the IVC at a fairly steep angle (on average 48°) [13]. In early pregnancy the ductus tends to be a straight continuation of the umbilical vein (Fig. 28.2). In late pregnancy a curvature after the isthmus is commonly observed. The relationship to the left and medial hepatic veins is close and sometimes their inlets into the IVC cannot be separated from that of the ductus venosus [15].

Topographically and functionally, the ductus venosus appears to be connected to the foramen ovale in the primate [16], fetal lamb [17, 18], and in the human fetus [2, 5, 19–21]. In the fetal sheep there is a valvular membrane that directs blood from the ductus venosus into the fairly long thoracic IVC to reach the foramen ovale [3]. Although this pattern is commonly presented in anatomical sketches of the human anatomy, it is quite different from the true human topography. The thoracic IVC is short or non-existent in the human fetus and there is no valve developed at the ductus venosus outlet, the effect being that the ductus venosus projects the blood flow directly towards the foramen ovale from a short distance and is less dependent on laminar flow arrangement to avoid extensive blending with low oxygenated blood from the abdominal IVC [13].

During early gestation, the ductus venosus is formed as a confluence of hepatic sinuses, then devel-

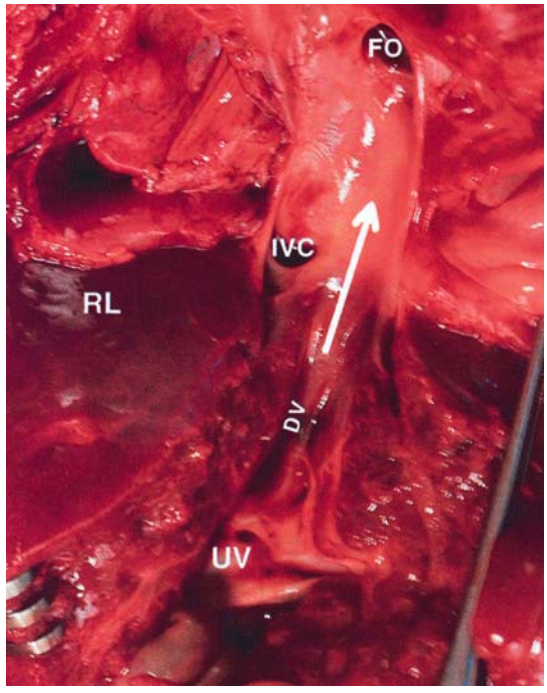

Fig. 28.1. Anterior anatomical view with the liver divided to expose the trumpet-shaped ductus venosus (*DV*) at 39 weeks of gestation. The DV leaves the abdominal portion of the umbilical vein (*UV*) in the direction of the foramen ovale (*FO*). The direction is slightly to the left of the abdominal inferior vena cava (*IVC*), which expands predominantly to the left side (*arrow*) as it reaches the liver confluence. This expansion represents also a continuation of the ductus venosus permitting umbilical blood to reach the FO without extensive blending with deoxygenated blood from the IVC. *RL* right lobe of the liver. (From [14])

ops into a separate channel [22–25], and is regularly recognized with ultrasound color Doppler in embryos of 8 weeks of gestation. Ultrasound visualization and volume flow calculations indicate that the ductus venosus has a more prominent role during early pregnancy than near term [11, 26].

A sphincter has been suggested to operate at the inlet [22, 27–30]. The scarcity of muscular and neuronal elements in the human ductus venosus have raised doubts as to whether such sphincter exists [21, 31–33]. Adrenergic nerves have been traced in the inlet area [34]. An α-adrenergic constriction and a β-adrenergic relaxation have been reported [33, 35, 36]. Both a prostaglandin and a peroxidase P-450 mechanism have been suggested to function in the ductus venosus in the same way as described for the ductus arteriosus [37–40]. The mechanisms could be responsible for the patency during fetal life and its closure in postnatal life; however, in contrast to the ductus arteriosus, oxygen does not seem to trigger the obliteration of the ductus venosus [41]. Recent studies indicate that it is the entire length of the ductus venosus that is active during regulation [33, 42, 43] and that the regulatory mechanism is less sensitive to adrenergic stimuli than the portal venous branches in the liver tissue [33].

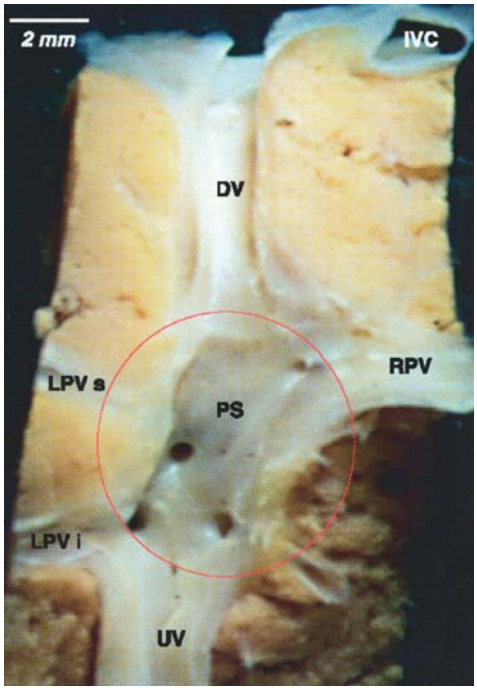

Fig. 28.2. Inferior and posterior view of the umbilical vein (*UV*), portal sinus (*PS*), and ductus venosus (*DV*) at 15 weeks' gestation. Note the considerable number of branches present in the area. Due to the preparation the main portal stem is not seen, but is expected to enter near the label for the right portal vein (*RPV*). *IVC* inferior vena cava, *LPV i* inferior left portal vein, *LPV s* superior left portal vein. (From [20])

Physiological Background

Via Sinistra

The ductus venosus is an important part of the via sinistra, a classical concept still valid at present (Fig. 28.3). As a direct connection between the umbilical vein and the central venous system, it has the capacity to shunt well-oxygenated blood directly into the central circulation and feed the left atrium

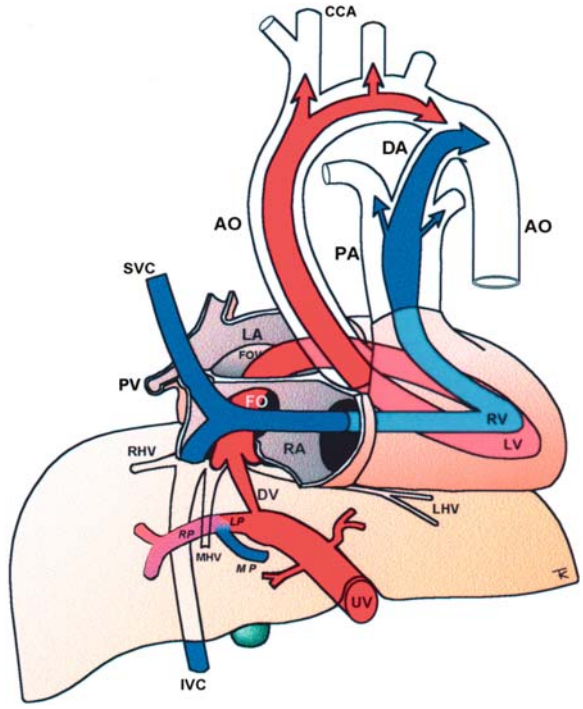

Fig. 28.3. Fetal circulatory pathways showing the three shunts, ductus arteriosus (*DA*), ductus venosus (*DV*), and the foramen ovale (*FO*). The via sinistra (*red*) directs blood from the umbilical vein (*UV*) through the DV and FO to reach the left atrium (*LA*), left ventricle (*LV*), and ascending aorta (*AO*) thus supplying the coronary and cerebral circuit with well-oxygenated blood before joining with the via dextra (*blue*) in the descending AO. The via dextra receives deoxygenated blood from the abdominal inferior vena cava (*IVC*) and superior vena cava (*SVC*) directed to the right atrium (*RA*), right ventricle (*RV*), and pulmonary trunk (*PA*) bypassing the pulmonary circuit through the DA. Splanchnic blood from the main portal stem (*MP*) is provided to the right liver lobe after blending with umbilical blood that reaches the right portal branch (*RP*) through the left branch (*LP*). *CCA* common carotid arteries, *FOV* foramen ovale valve, *LHV* left hepatic vein, *MHV* medial hepatic vein, *PV* pulmonary vein, *RHV* right hepatic vein. (Slightly redrawn from [11])

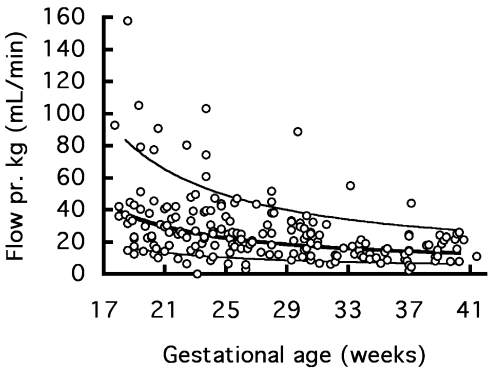

Fig. 28.4. Ductus venosus blood flow (ml/min per kg) in 193 low-risk fetuses presented with 10th, 50th, and 90th percentiles. The relative flow appears more prominent at mid-gestation than during the third trimester. (From [11])

Table 28.1. The fraction of umbilical blood shunted through the ductus venosus during the second half of the human pregnancy [11]

Gestational age (weeks)	Number	Degree of ductus venosus shunting (%)	
		50th percentile	(10th; 90th percentiles)
18–19	34	28	(14; 65)
20–24	45	25	(10; 44)
25–28	34	22	(10; 44)
29–32	32	19	(9; 46)
33–36	21	20	(10; 31)
37–41	27	23	(7; 38)

through the foramen ovale, thus ensuring oxygenated blood to the coronary and cerebral circuit. Animal studies have shown that around 50% of the umbilical blood bypassed the liver through the ductus venosus [16, 17, 44, 45]. In human fetuses it is around 30% at 20 weeks and 20% at 30–40 weeks of gestation when measured by Doppler ultrasound techniques [11, 26]; thus, the shunting through the ductus venosus seems more prominent at mid-gestation than at term (Fig. 28.4; Table 28.1).

During experimental hypoxemia and hypovolemia, the ductus venosus flow is maintained [16, 44, 46–49]; however, since the flow to the liver is reduced, it implies that the fraction of umbilical blood directed through the ductus venosus increases to 70% [16, 44, 46–50]. A similar effect seems to be present in growth-restricted human fetuses [50].

The size of the foramen ovale, the position, and the direction of the ductus venosus, and its high kinetic energy, are suggested to play a role to reduce degree of blending with de-oxygenated blood in the IVC and to force open the foramen ovale valve [13, 14]. Since the oxygen extraction in the liver tissue is low, causing a reduction in saturation of 10–15% [51, 52], the hepatic venous blood flow from the left liver constitutes another important source of oxygenated blood directed towards the foramen ovale. In total, it is an abundant volume of oxygenated blood that predominantly fills the foramen ovale but additionally spills over to the right side. The result is a notably small difference in oxygen saturation between the left and the right ventricle, 10% under experimental conditions increasing to 12% during hypoxemic insults [3, 53].

Umbilical Liver Perfusion

Another aspect of the ductus venosus function is its role in the fetal liver circulation. Since 20%–30% of the umbilical blood is shunted through the ductus, it implies that 70%–80% of the umbilical blood perfuses the liver as the first organ in the fetus [11]. The pattern indicates the importance of the fetal liver during intrauterine development. Recent studies indicate that blood flow in the fetal liver regulates fetal growth (Fig. 28.5) [54, 55], and that this blood flow depends on external factors such as maternal nutritional state and dietary habits, at least during late pregnancy [56]. In addition to an active regulation of the ductus venosus influencing the distribution of umbilical blood to the liver, both passive regulation (blood pressure and viscosity) [17, 57, 58] and active regulation (vessel constriction) [33, 59, 60] tune the portal liver blood flow. This makes the liver a very delicate watershed area regulated at low pressures. In the long run, umbilical liver flow has a high priority in maintaining growth and development. During acute challenges (i.e., hypoxemia or hypovolemia) short-term responses with increased shunting through the ductus venosus ensures survival. If such challenges are main-

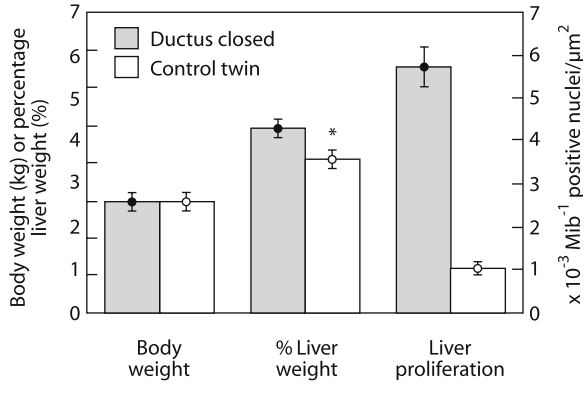

Fig. 28.5. Experimentally occluded ductus venosus in fetal lambs leads to an increased umbilical flow through the liver, increased signs of proliferative activity (*right ordinate*), and increased liver growth (*left ordinate*). (From [54])

tained over a longer period, adaptational mechanisms come into play, reducing the metabolic requirements, and the circulatory redistribution partially returns to normal patterns [61, 62].

Portal Watershed Area

Since blood from the umbilical vein and blood from the main portal stem both supply the liver, there is a watershed area in the liver between the two sources in the right liver. Conventionally umbilical blood supplies the left liver, the ductus venosus, and flows through the left portal branch to join with the blood from the main portal stem as the blood flows into the right portal branch (Fig. 28.3); thus, in the human fetus under physiological conditions in late pregnancy, the left half of the liver receives pure umbilical blood while the right half receives a 50% mixture of umbilical and splanchnic blood [26, 63]; however, during hypovolemia this distributional pattern is shifted to the left. During experimental hemorrhage, less umbilical blood is provided to keep up the pressure in the portal system with the perfusion of the liver and ductus venosus. An increasing component of splanchnic blood from the main portal stem fills up the left portal branch and an increasing proportion of the ductus venosus blood flow will be of splanchnic origin [44, 47, 48]. The phenomenon of shift of the watershed to the left has been observed in the human fetus as well [64, 65], but with no proof that the underlying cause was hypovolemia.

Porto-Caval Pressure Gradient

The position between the umbilical vein (i.e., portal sinus) and the IVC makes the blood flow in the ductus venosus an important indicator of the porto-caval pressure gradient that perfuses the liver tissue [10, 66]. The absolute blood velocity has been suggested as a marker of fetal portal hypertension seen during fetal liver diseases (e.g., lymphoproliferative infiltration, virus infections, mitochondrial diseases). The simplified Bernoulli equation is suggested for the estimation of the pressure gradient [10] (Δp; in mm Hg) based on the maximum trace of the ductus venosus blood velocity (V_{DV}) and the velocity in the umbilical vein (V_{UV}) measured in m/s:

$$\Delta p = 4\left((V_{DV})^2 - (V_{UV})^2\right)$$

It has been estimated that the energy dissipation at the isthmus does not exceed 30%, which makes the calculation a fairly reliable pressure estimate [67, 68] in spite of the possible pressure regain expected to occur during velocity retardation as the blood approaches the heart. Up to now, the diagnostic possibilities of this concept have not been explored to any extent.

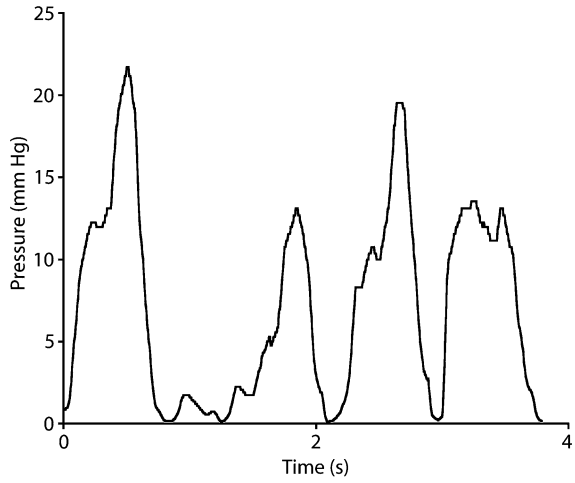

Fig. 28.6. Pressure difference between the lungs and abdomen during fetal respiratory activity at 39 weeks of gestation. It is based on the assumption that the close proximity to the diaphragm makes the ductus venosus blood velocity an indicator of the difference in pressure above and below the liver. The pressure is calculated from the velocities using the simplified Bernoulli equation. (From [10])

Fetal Respiratory Force

Since the liver and its venous confluence is situated just beneath the diaphragm, the ductus venosus blood flow velocity also reflects the abdomino-thoracic pressure gradient. This gradient varies during fetal respiratory movements and is calculated to reach more than 20 mmHg during maximal excursions (Fig. 28.6). The estimations are based on the Bernoulli equation in the same manner as above. The low velocities in the umbilical vein do not influence the calculations and can be left out. Again, this concept is another example of possible diagnostic ductus venosus examination hardly explored.

Postnatal Physiology

After birth, the ductus venosus is obliterated within 1–3 weeks (Fig. 28.7) [69, 70]. Interestingly, the high blood velocity seen prenatally seems to be maintained during that period [70], reflecting the fact that the portal perfusion pressure for the liver circulation is maintained. Observations of prematurely born neonates show that the ductus remains patent longer than in infants born at term [71, 72]. The hypothesis that a patent ductus venosus represents a bypass of the liver in the first weeks of postnatal life to the extent that it influences the clearance rate has been addressed by assessing the galactose concentration in prematurely born neonates [73]. No effect of the patent ductus was found, but the degree of shunting in the ductus venosus was not quantified. The ductus

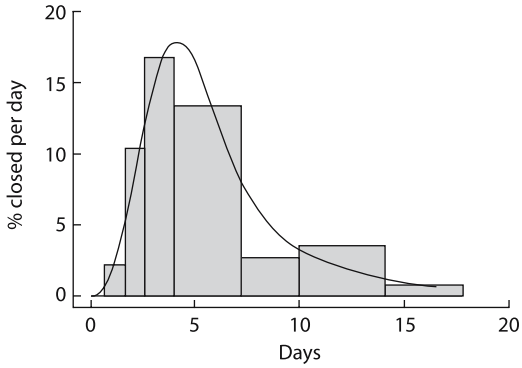

Fig. 28.7. Distribution of closing times of the ductus venosus in healthy neonates. The *bars* represent the percentage closure per day and the curve represents the fitted log logistic distribution. (From [70])

venosus stays open longer also in infants with congenital heart defects or persistent pulmonary hypertension [8], and the waveforms in these cases resemble those seen in abnormal cases prenatally; thus, the ductus venosus velocimetry has been suggested as a diagnostic adjuvant during the first weeks of postnatal life as well.

Ultrasound Imaging and Insonation

A sagittal anterior insonation offers the best visualization of the ductus venosus (Fig. 28.8) [5, 9]. To assess its course and diameters, the perpendicular insonation through the fetal liver suits best. An oblique transverse section may be more convenient in some fetal positions but rarely offers visualization of the entire length of the vessel.

Color Doppler is an indispensable help in identifying the high velocity at the isthmus of the ductus (Fig. 28.9). With modern equipment the identification can be done from any direction but requires an appropriate setting of filters and ranges to distinguish the typical high velocity of the ductus venosus from velocities in neighboring vessels.

For the pulsed Doppler measurements the sagittal anterior or posterior insonation offers the best control of angle. The anterior insonation from below the fetal umbilicus (Fig. 28.9), or the posterior from the level of the chest, gives insonations that hardly require angle correction. If such insonations are not possible, then the oblique transverse section through the fetal abdomen will provide a good visualization of the ductus venosus inlet but less control of the insonation angle. For the measurement of waveforms this should suffice.

Sample volume should be kept wide to ensure the recording of the maximum velocity during the heart cycle. This holds true for the second half of pregnancy; however, during early pregnancy the sample volume has to be reduced to fit with the geometrical details in order to reduce interference of velocities of the umbilical vein, the proximal portion of the ductus, or neighboring veins and arteries. This is particularly important during the atrial contraction phase

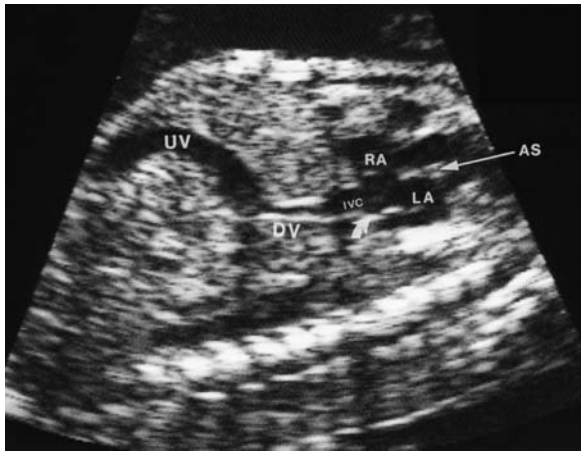

Fig. 28.8. Sagittal ultrasound insonation shows the ductus venosus (*DV*) connecting the umbilical vein (*UV*) to the proximal portion of the inferior vena cava (*IVC*) in a fetus of 18 weeks' gestation. Note how the continuation of the DV follows the posterior wall of the IVC and the foramen ovale valve (*curved arrow*) into the left atrium (*LA*) and behind the atrial septum (*AS*; *arrow*). *RA* right atrium

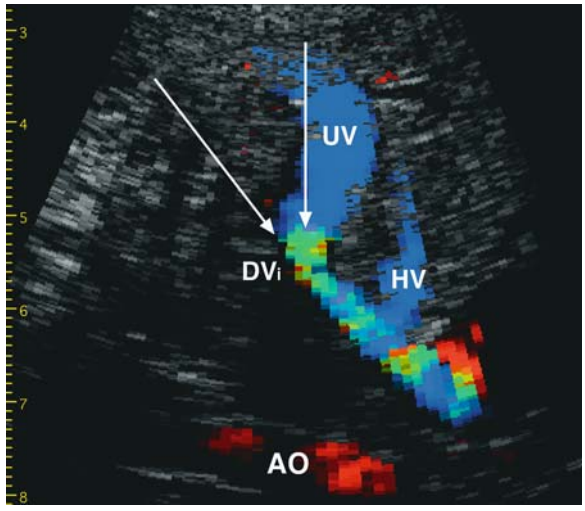

Fig. 28.9. Color Doppler helps identifying the isthmic inlet of the ductus venosus (*DVi*). The preferred insonation for Doppler recording is along or between the *arrows*. Note that the aliasing starts already in the umbilical vein (*UV*) in front of the inlet, the reason being that the blood starts to accelerate before reaching the isthmus. *AO* descending aorta, *HV* middle hepatic vein

since a zero velocity or inverted velocity, which is commonly used for diagnostic purposes [74–79], may be masked.

Angle of insonation and angle correction need particular attention. Transducers commonly used by obstetricians are broad with a flat or curved surface. Compared with sector scanners, these transducers make it harder to achieve an insonation along the ductus venosus with zero or near-zero angle correction. If the recording of absolute velocities has any diagnostic consequence, there is much to gain from getting accustomed to sector scanners so commonly used in cardiology. As mentioned, the sagittal insonation offers the best control of angle, but an oblique transverse interrogation may, in favorable positions, be a good alternative. The angle of insonation should always be documented. In case a curvature has developed centrally to the isthmus, a tangential insonation to this curvature ensures correct insonation and no need of angle correction.

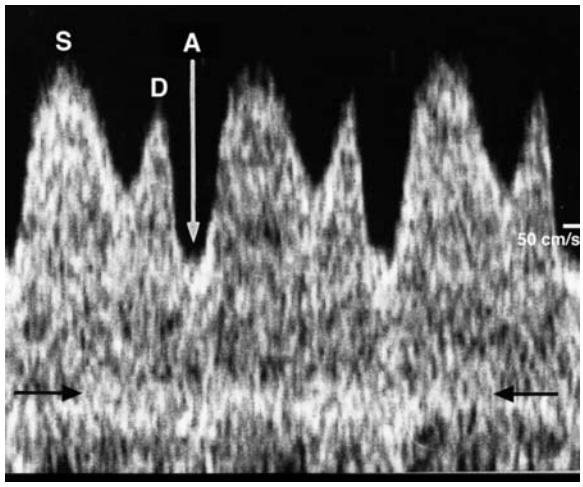

Fig. 28.10. Doppler recording of the blood velocity at the isthmus of the ductus venosus at 33 weeks of gestation. Typically there is high velocity during the entire cardiac cycle with a peak during systole (*S*), another peak during passive diastolic filling (*D*), and deflection (*white arrow*) during atrial contraction (*A*). The velocity of the interfering umbilical vein is faintly seen between *black arrows*

Normal Ductus Venosus Blood Velocity

Typically, the ductus venosus blood flow has a high velocity during the entire cardiac cycle compared with neighboring veins at the corresponding gestational age (Fig. 28.10) [5, 6, 9, 80–82]. Starting in early pregnancy (e.g., 10 weeks of gestation) the velocity increases until reaching a plateau at 22 weeks [81, 82]. For the rest of the pregnancy the peak velocity ranges between 40 and 85 cm/s (Fig. 28.11) [5, 6, 80, 81]. Some variation in reference ranges is seen, probably depending on equipment, insonation techniques, angle correction, and population.

The velocity pattern reflects the cardiac cycle with a peak during systole, another during passive diastolic filling and a nadir during active diastolic filling (atrial contraction; Fig. 28.10). Typically, the nadir during atrial contraction does not reach the zero line during the second half of pregnancy, in contrast to other precordial veins; however, below 15 weeks of gestation, an increasing number of zero or below-zero

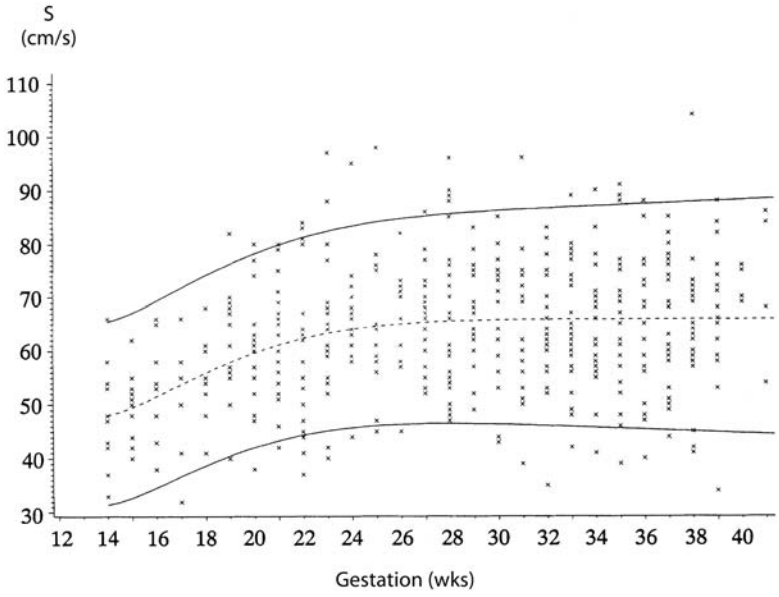

Fig. 28.11. Cross-sectional reference ranges for the systolic peak velocity (*S*) in the ductus venosus with the 5th, 50th, and 95th percentile. (From [81])

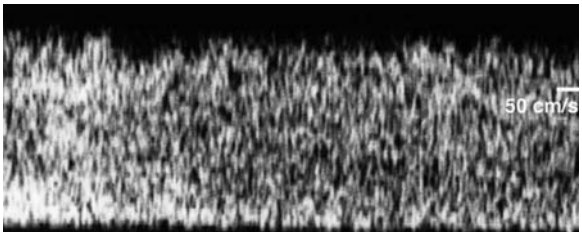

Fig. 28.12. Doppler recording of the blood velocity at the isthmus of the ductus venosus at 32 weeks of gestation shows no pulsation. The phenomenon occurs in 3% of all recordings in low-risk pregnancies. (See Chap. 5 for explanation)

velocities are observed in normal fetuses [14]. Reference ranges have been established for all the components of the wave as well as for the time-averaged maximum velocity during the entire cardiac cycle [5, 80–82]. The time-averaged weighted mean velocity is typically 0.7 of the maximum velocity. The relationship is established by mathematical modeling, and experimental and clinical observations, and is a quite useful information when calculating volume flow [68, 83–86].

It is important to acknowledge the wide normal variation of the waveform. Most reference ranges have not taken that into account, and some have. In 11% of the recording no second velocity peak will be found during the passive diastolic filling [9], and in 3% of all recordings there will be no well-defined nadir visible (Fig. 28.12) [9]. These patterns reflect the wide range of geometrical variation possible in the normal fetus. Squeezing of the ductus venosus outlet or the IVC at the level of the diaphragm will cause an increased wave reflection with less or no pulse wave transmitted into the ductus venosus resulting in nonpulsatile velocity recording at the isthmus (see Chap. 5) [14, 87]. While this is a fairly common phenomenon in normal fetuses, there are no data on its occurrence in the compromised pregnancy; however, based on experience, it must be rare.

Absolute blood velocity thus has the advantage of directly reflecting both the porto-caval pressure gradient that drives the liver perfusion [10] and the cardiac events that modify the velocity waveform [5]; however, both the type of equipment used by the obstetrician and their tradition of examination technique have made the angle-independent waveform analysis the preferred method compared with the more demanding absolute velocity recording, but not without some loss in diagnostic information.

Waveform Analysis: Indices

To give an angle-independent evaluation, ratios of various components of the waveform during the heart cycle have been suggested (Table 28.2). Some of these ratios are used also for other fetal veins and in analysis of arterial blood velocities. The indices that include the entire heart cycle are more robust and are thus recommended for general use. The pulsatility index for veins (PIV) [80] is probably the most widely used index (Fig. 28.13).

The waveform reflects cardiac events, i.e., the intra-cardiac pressure variation, which is emitted into the precordial venous system as a pulse wave. As mentioned above, using the waveform as the only analysis of the velocity means disregarding the porto-caval pressure gradient reflected in the absolute

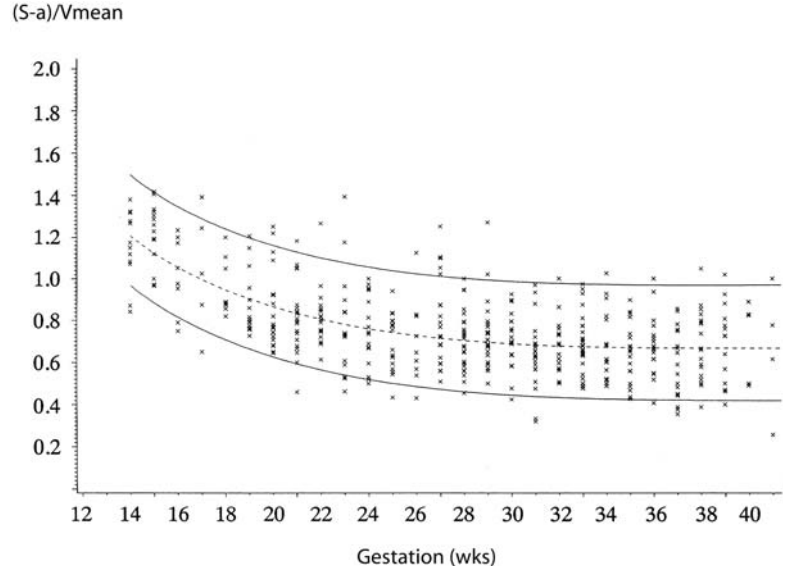

Fig. 28.13. Cross-sectional reference ranges for the pulsatility index for veins ($(S\text{-}a)/V_{mean}$). (From [81])

Table 28.2. Indices suggested for the waveform analysis of the ductus venosus blood flow velocity. Some of the indices are suggested also for other veins. *A* minimum velocity during atrial contraction (a-wave), *D* peak velocity during ventricular diastole, *S* peak velocity during ventricular systole, V_{ta} time-averaged maximum velocity

Index	Author/date	Reference
$\frac{V_{ta}}{S}$	Kiserud et al. (1991)	[5]
$\frac{S}{D}$	Huisman et al. (1992)	[6]
$\frac{S}{A}$	Oepkes et al. (1993)	[128]
$\frac{S-A}{S}$	DeVore and Horenstein (1993)	[129]
$\frac{S-A}{D}$	Hecher et al. (1994)	[80]
$\frac{S-A}{V_{ta}}$	Hecher et al. (1994)	[80]

velocity. At a very acute angle of insonation an increased error assessing the lowest velocity during atrial contraction may make the waveform less reliable.

Interpretation of the Waveform

The Atrial Contraction Wave

The atrial contraction wave (a-wave) is the single most important part of the waveform from a diagnostic point of view. The augmented atrial contraction wave signifies an increased end-diastolic filling pressure in the heart, which may be induced by an increased distension of the atria leading to an augmented contraction (the Frank-Starling effect) commonly seen in cases with increased preload or congestive heart failure [88–94]. An increased afterload can also lead to a reinforced a-wave (Fig. 28.14) [95–99]. Experimentally imposed hypoxic insult has been shown to cause an increased a-wave in late pregnancy [86, 100, 101], but also at mid-gestation and in early pregnancy [102]. In case of the latter, the effect is believed to be primarily a direct hypoxic effect on the myocardium. In late pregnancy, the effect is predominantly orchestrated via immediate neural responses and secondary endocrine effects on cardiac rhythm and contractility as well as on peripheral vascular impedance [45, 103, 104].

Heart rate is an important determinant for the precordial venous waveforms [92]. A slowing of the heart rate permits a more pronounced venous filling and increased distension of the myocardium resulting in augmented atrial contraction. The effect is seen in fetal bradycardic conditions.

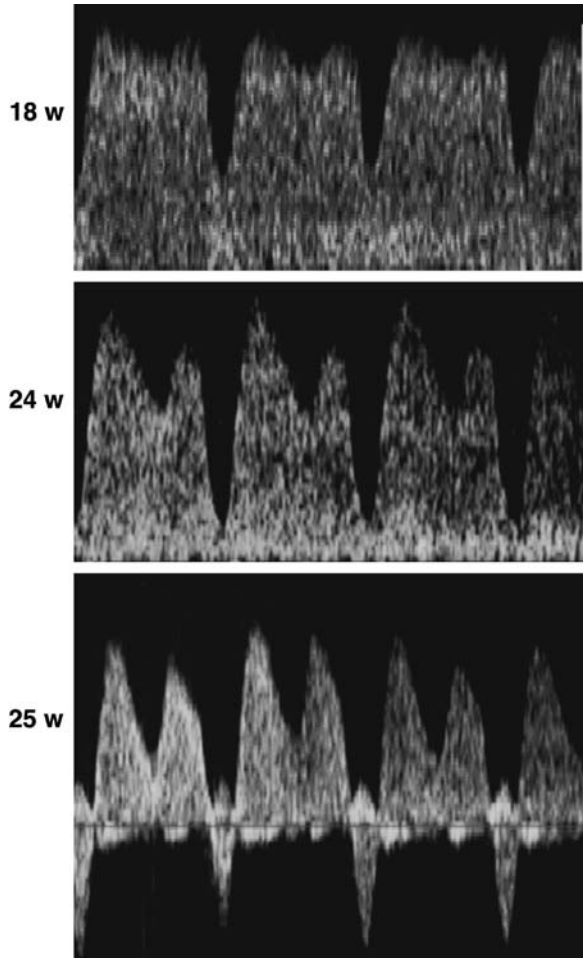

Fig. 28.14. A case of progressive placental compromise and growth restriction shows normal ductus venosus blood flow at 18 weeks with a normal a-wave (*upper panel*). At 24 weeks the augmented a-wave was apparent (*middle panel*). At 25 weeks a further deterioration was seen with a reversed a-wave and an increasing dichotomy between the systolic and diastolic peak (*lower panel*)

An increased venous return causes a more pronounced myocardial distension, and a correspondingly augmented a-wave. Typically, this occurs in the twin–twin transfusion syndrome with one of the fetuses being overloaded through placental communications [105]. Arterio-venous malformations in the placenta, fetal liver, fetal brain, or the increased load due to cystic adenomatoid lung malformations are other examples of conditions causing an increased venous return.

Hyperkinetic circulation, such as in fetal anemia, also increases the preload, and the a-wave [106]. With the deterioration of cardiac function, i.e., congestive heart failure, the sign of augmented a-wave becomes

more marked, with the minimum velocity reaching zero line or below, even in late pregnancy.

Compliance of the heart is reflected in the a-wave. The reduced compliance of the myocardium in cardiomyopathies, myocarditis (e.g., parvovirus B19 infection), hypoxemia, and acidosis is commonly associated with a deepened a-wave (Fig. 28.14). The compliance can also be influenced by extra-cardiac restrictions in the chest (see Chap. 5). Normally, the absence of free air during intrauterine life makes the entire vascular system, including the heart, less compliant than after birth. In addition, increased pressure in the fetal chest (e.g., large tumors, pleural effusions, or tracheal atresia) could lead to further restriction of the cardiac excursions and made visible in the a-wave.

A significant tricuspid or mitral regurgitation, or both, may contribute to a rapidly increasing volume and pressure in the atria thus causing an augmented a-wave.

Timing of the atrial contraction is also an important determinant for the magnitude of the a-wave. The various patterns found in arrhythmias are particularly instructive [107–109]. In its simplest form, the wave of a supraventricular extrasystole may hardly be visible in the ductus venosus Doppler recording, whereas the atrial contraction following the compensatory postictal pause has been given the extra time and load of volume to cause an augmented a-wave. An even more amplified version of the a-wave is seen in cases of atrioventricular block. When the atrial contraction coincides with the ventricular systole, the atrioventricular valves are closed and the compliance correspondingly reduced, the result being a stronger pulse-wave directed into the precordial veins, including the ductus venosus. During tachycardia the timing of the atrial contraction, the size of the atria, whether the atrioventricular valves are open, the momentary degree of filling, the functional condition of the myocardium itself, and probably details of where the contraction starts and how it propagates determine the details of the a-wave [109].

In recent years the a-wave has been the focus in the search for methods of surveillance of patients with placental compromise. Short-time variation of the computerized CTG and the a-wave (or its effect on the pulsatility indices) showed late changes compared with umbilical artery pulsatility and changes in the middle cerebral artery (Fig. 28.15) [110–112]. The sign seems easier to interpret in pregnancies before 32 weeks of gestation than after; thus, it has become a promising method for serial observations in order to determine timing of delivery of the growth-restricted fetus. Since the ductus venosus velocity pattern is an instantaneous reflection of the cardiac function, these changes are probably useful signs in other conditions where the fetus is at risk as well.

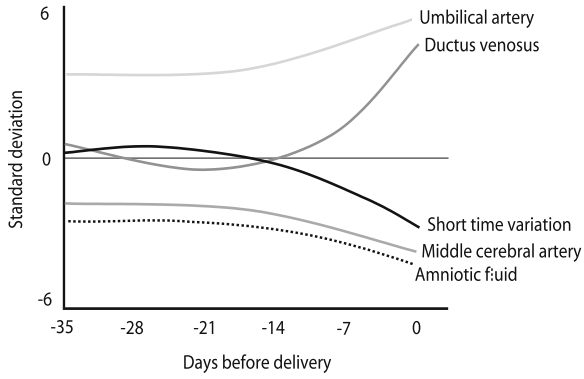

Fig. 28.15. Serial observations of cases with severe intrauterine growth restriction delivered 32 weeks of gestation. Changes in the pulsatility index of the umbilical and middle cerebral arteries and oligohydramnios are common findings 3–5 weeks before delivery. Alterations in the ductus venosus waveform and short time variation are notable during the last 2 weeks before delivery, indicating that these two parameters may be suitable for the final tuning of time of delivery. (Modified from [20])

Systolic Wave

Conventionally, the systolic peak during ventricular contraction is smooth and rounded (Fig. 28.16). Changes in myocardial function are reflected also in this part of the cardiac cycle. In conditions of reduced compliance, both of extracardiac and cardiac origin, the downstroke of the velocity becomes more acute (Fig. 28.16). This is particularly apparent during the deterioration seen in placental compromise [7, 113]. Increased afterload combined with an increased degree of hypoxemia and acidosis drives the myocardial function toward less compliance. The visible result is the acute up- and downstroke of the systolic peak and a corresponding dissociation between the systolic and diastolic peak (Fig. 28.16). A similar effect can be achieved by the externally increased pressure on the heart, and thus correspondingly reduced compliance (see Chap. 5). The increased blood volume and atrial pressure caused by a regurgitation of the atrioventricular valves causes an augmented a-wave; however, the more extensive the regurgitation is, the more rapid the atrial filling will be, and the earlier in the heart cycle the impact will come. In cases of Ebstein anomaly this may lead to an early downstroke during ventricular systole.

Pitfalls

For the beginner, sampling the velocity in a neighboring vein, or including interference from the IVC or other vessels, may falsely give the impression of an abnormal ductus venosus recording. The velocity in the hepatic veins tends to be more acute and, partic-

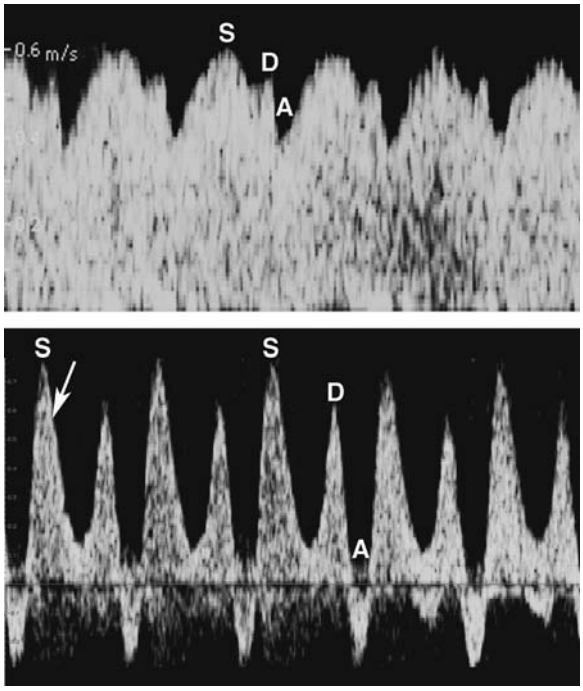

Fig. 28.16. Conventionally, the systolic peak (*S*) is smooth signifying good atrial compliance (*upper panel*). Increased stiffness of the myocardium due to hypoxia and acidosis, such as in advanced placental compromise, results in a rapid downstroke (*arrow*) of the S (*lower panel*). Typically the waveform is transformed into acute velocity changes and a dissociation between S and diastolic peak (*D*). The augmented a-wave (*A*) reaching below zero is a common part of the pattern

ularly during the second trimester, the veins have a zero or reversed velocity during atrial contraction. Before leaping to a conclusion, it is prudent to reproduce the recording in a renewed insonation. It is also helpful to know that the augmented pulsatility in the ductus venosus commonly has a corresponding pulsatile flow in the umbilical vein. If the insonation makes the identification of the ductus venosus less certain, the pulsatility and a-wave should be checked in more accessible precordial veins such as the IVC or hepatic veins.

The pulsatile flow in the left portal vein is the mirror image of the ductus venosus waveform [64]. One of the consequences is that the a-wave occurs not as a nadir but as a peak (see Chap. 5). The simultaneous sampling of the ductus venosus inlet and the left portal vein could then cause a masking of the true nadir in the ductus venosus. Masking may also be the case during simultaneous sampling at the isthmus of the ductus venosus and the umbilical vein where the pulsatility usually is less pronounced. This is a common problem in early pregnancy.

Local changes of no pathological significance may influence the waveform. The fetal position may be such a factor. A fetus bending forward, particularly in the extreme situations of oligohydramnios, may squeeze the IVC, the outlet, or the entire length of the ductus venosus to the extent that most of the wave is reflected and the recorded wave at the inlet has lost pulsation (see Chap. 5). In 3% of pregnancies this normal phenomenon may be observed. Usually, a change in fetal position within the next minutes is accompanied with the restoration of pulsatile flow velocity.

A normal ductus venosus does not exclude abnormal physiology. All the factors determining the waveform should be taken into consideration when interpreting the velocity recording, e.g., a metabolic error of the myocardium may not necessarily be reflected in an abnormal waveform in the ductus venosus if the heart has compensated for the increased stiffness of the muscle by increasing the cardiac volume and thus improving the compliance.

Increased vascular resistance in the fetal liver tissue may cause portal hypertension and ascites. Examining exclusively the waveform of the ductus venosus using indices may not reveal any abnormality since the waveform predominantly reflects cardiac function. It is a common error not to notice the absolute velocities, which may exceed 1 m/s and signify portal hypertension in such cases [66].

Reproducibility

In experienced hands a recording of the ductus venosus blood velocimetry is achieved in almost all women both in early and late pregnancy, even with substandard equipment. The limits of agreement for intra-observer variation are [–13; 12 cm/s] for the systolic peak, and [–15; 12 cm/s] during the a-wave [9]. The reproducibility is better for the indices than for the absolute velocity recordings [81]. That is due to the extra challenge it takes to record absolute velocities at a zero- or low angle of insonation, a less important detail when using the waveform analysis.

Doppler assessment of the ductus venosus during early pregnancy seems to have a reduced reproducibility, particularly for the peak systolic and the nadir during a-wave during transabdominal scanning at 10–14 weeks of gestation. The coefficient of variation for systolic and end-diastolic velocity was 19% and 29%, respectively [114]. The coefficient for the PIV was better, 9%. These results were reproduced in another study but with somewhat better numbers [115].

The normal ranges for absolute velocities were reasonably reproduced in the pioneering studies [5, 9, 80, 81]. When recording Doppler signals without the control of color Doppler, the velocities appeared to be

slightly less, possibly due to less control of the correct insonation angle. For the pulsatility indices there is little variation from study to study.

Fetal movements and respiratory exercise could have a profound impact on the ductus venosus blood flow velocity and should carefully be avoided for the standard evaluation.

Agenesis of the Ductus Venosus

An increasing number of case reports link agenesis of the ductus venosus to fetal demise, hydrops fetalis, asphyxia, vascular and cardiac anomalies, and chromosomal aberrations [116–125]. This has led to the recommendation of an extended scan if the ductus venosus is not identified. It is likely that agenesis occurs more commonly in connection with chromosomal aberrations and anomalies, but so far there are no statistics to prove it. Some have taken the presence of ductus venosus agenesis in hydrops and intrauterine demise as an indication that a patent ductus venosus is vital for intrauterine development; however, it can be argued that the ductus venosus agenesis was discovered in these fetuses after a primary finding had made an extended ultrasound scan necessary or during post-mortem examination. In a recent study of 203 normal pregnancies one fetus had agenesis [11]. Perinatal outcome was uneventful for this fetus with a birth weight at the 39th percentile and a normal ponderal index.

Experimental occlusion of the ductus venosus in fetal sheep led to increased umbilical vein pressure and hepatic venous flow but otherwise had no impact on regional blood distribution [126]; however, such an occlusion has a considerable impact on liver cell proliferation and IGF-2 production, and thus growth [54, 55].

There is an interesting set of observations of agenesis in fetuses with porto-caval shunts, or similar shunts, draining umbilical venous blood directly to the central veins or heart [125]. These fetuses seem to be in the position of not being able to develop the ductus venosus or to close the ductus as a compensatory mechanism. Many of these fetuses have a hyperkinetic circulation, possibly in an attempt to keep up portal pressure and liver perfusion.

This is not in contradiction to the concept that the ductus venosus is an important fetal shunt. Instead, the story unfolds with the ductus venosus having at least two functions. In the long run, the regulation of the umbilical liver perfusion is crucial for fetal development and growth; however, during acute challenges of hypoxemia or hypovolemia, the priority of the liver is temporarily reduced to permit life-saving maneuvers of maintaining oxygenated blood to the heart and brain, or as some physiologists have put it: "The fetal dilemma: spare the brain and spoil the liver" [127].

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