

REVIEW

Umbilical vein blood flow: State-of-the-art

Moira Barbieri MD¹  | Daniela Denis Di Martino MD, PhD¹  |
 Enrico Mario Ferrazzi^{1,2}  | Tamara Stampalija MD, PhD^{3,4} 

¹Department of Mother, Child and Neonate, Fondazione IRCCS Ca' Granda Ospedale Policlinico di Milano, Milan, Italy

²Department of Clinical and Community Sciences, University of Milan, Milan, Italy

³Unit of Fetal Medicine and Prenatal Diagnosis, Institute for Maternal and Child Health IRCCS "Burlo Garofolo", Trieste, Italy

⁴Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy

Correspondence

Tamara Stampalija, Unit of Fetal Medicine and Prenatal Diagnosis, Department of Mother and Neonate, Institute for Maternal and Child Health, IRCCS "Burlo Garofolo", Via dell'Istria, 65/1, 34137, Trieste, Italy.

Email: tamara.stampalija@burlo.trieste.it

Abstract

Placental blood supply to the fetus can be measured by evaluating the umbilical vein blood flow. Despite its potential application in healthcare, the umbilical vein blood flow volume is still used only in research setting. One of the reasons is a concern regarding its reproducibility, partly due to technology issues. Nowadays, technology improvements make this evaluation accurate and reproducible. The aim of this review is to refresh basic elements of the physiology of umbilical vein blood flow and its analysis. Its evaluation in normal and abnormal fetal growth is also discussed.

KEYWORDS

Doppler ultrasound, fetal growth, fetal growth restriction, umbilical vein blood flow volume

1 | INTRODUCTION

Fetal growth is a result of the fetal, maternal, and placental compartments integration. Indeed, fetal growth is determined by the individual fetal genetic growth potential and anthropometric factors, but fetal nutrition is the result of the balance between fetal demands and maternal-placental availability of nutrients and oxygen. An altered availability of nutrients can lead to fetal growth trajectory alterations, both in excess or in defect. For example, placental insufficiency can cause fetal growth restriction while an excessive availability of nutrients, as in diabetes, can cause excessive intrauterine growth leading to a large-for-gestational age fetus. In this context, both the umbilical vein and the placenta play a key role as the sole sources of nutrition for the fetus.

1.1 | Anatomy pills

The placenta is a transient fetal organ, and its development is determined both by maternal hemodynamics and by immune response to

invading fetal syncytiotrophoblast cells into the decidua and spiral arteries.¹ The functional structures that allow the maternal-fetal exchanges are chorionic villus. The fetus is connected to the placenta by the umbilical cord, in which three blood vessels run: one umbilical vein and two umbilical arteries (Figure 1). The umbilical vein is a thin-walled vessel with poor muscle structure that originates on the fetal face of the placenta, and it enters the abdominal wall at the umbilical ring. It is typically protected by the two umbilical arteries spiraling around it and by the Wharton jelly, and carries blood rich in oxygen and nutrients, while the umbilical arteries carry venous blood.

The intrahepatic part of the umbilical vein branches the left hepatic vein while the mainstream flow joins the portal vein to form the portal sinus to feed both the right liver circulation or to be directly shunted by the ductus venosus into the inferior vena cavae. The shape of ductus venosus is that of trumpet-shaped narrow vessel, or asymmetrical clepsydra³ that streams the umbilical vein blood flow via inferior vena cavae to the medial part of the right atrium, toward the left heart via the foramen ovale. From the left ventricle the oxygenated blood preferentially reaches the brain.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2023 The Authors. *Journal of Clinical Ultrasound* published by Wiley Periodicals LLC.

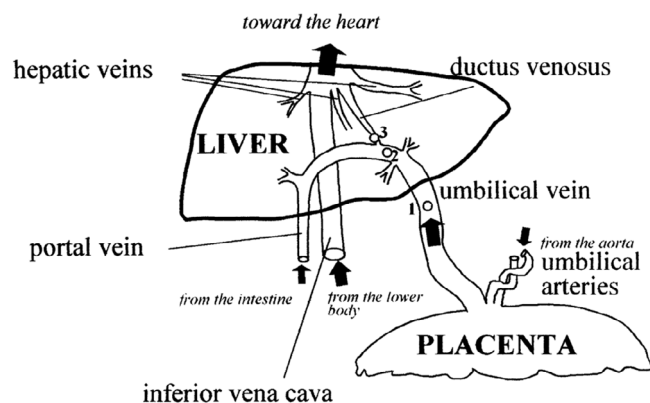


FIGURE 1 A model of the fetal circulation from Bellotti et al.²

1.2 | Technical aspects

Umbilical vein blood flow is generally obtained by using the following formula:

$$\text{Umbilical vein blood flow} = \text{cross sectional area} \times \text{mean velocity} \times 60$$

where the blood flow is expressed in ml/min, the cross-sectional area is expressed in mm² and is usually calculated as $\pi \times \text{radius}^2$, and the mean velocity is computed as mm/s.

There are few crucial aspects that have to be fulfilled in order to obtain an adequate and reproducible measurement.

1.2.1 | Measurement of the umbilical vein

The umbilical vein can be measured both on a free loop⁴⁻¹⁰ or at the intra-abdominal tract,¹¹⁻¹⁶ with the ultrasound beam perpendicular to the longest axis and on a magnified ultrasound image of the vessel. The external perimeter of the umbilical vein can be manually circled, and the cross-sectional area can be automatically calculated by the ultrasound software.¹⁷⁻¹⁹ Alternatively, the average of three diameter measurements can be used to obtain the internal diameter (Figure 2). The diameter should be measured inner-to-inner and the brightest reflected echoes of the wall indicate the best perpendicular section. Great care should be dedicated to the measurement of the umbilical vein' diameter, since the cross-sectional area is computed as $\pi \times \text{radius}^2$ (equal to $\pi \times \text{diameter}/2$), where any error is squared and amplified. However, present ultrasound machines allow clinicians to optimize the resolution of the diameter' measurement.

1.2.2 | Mean velocity measurement

To measure the mean velocity, the ultrasound probe has to be tilted in order to obtain a longitudinal section of the vessel. The measurement has to be performed in conditions of fetal rest with the angle of insonation as close as possible to 0°, with a maximum correction of the angle below 30° (Figure 3). Measurements with an angle above 30° should be discharged.

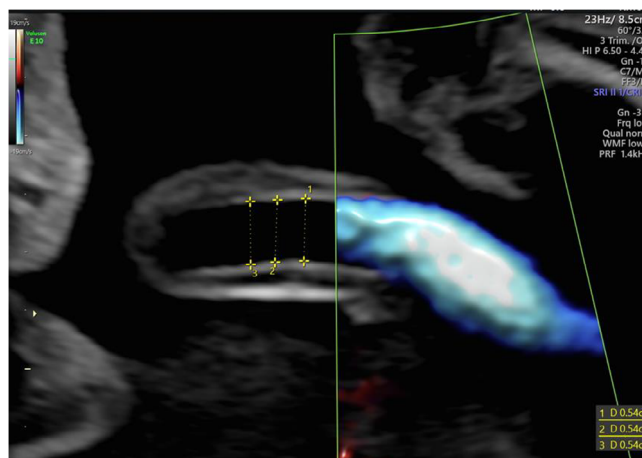


FIGURE 2 The ultrasound measurement of umbilical vein diameter at a free-floating portion of the umbilical vein. The measurement of the three diameters is represented and the average value is used for formula calculation

The most common method of estimating the mean blood flow velocity is its extraction from the intensity-weighted mean velocity. The ideal model of blood flow is a parabolic flow uniformly distributed along the vessel and not conditioned by Doppler low pass filters; in these conditions, the mean velocity represents the half of peak velocity (mean velocity = peak velocity \times 0.5).

Different parabolic shapes of the umbilical vein blood flow have been reported suggesting a higher coefficient for measurement performed at a free-loop of the umbilical cord and away from the placenta and/or from the intra-abdominal fetal tract of the umbilical vein²⁰ (Figure 4). Pennati and coworkers²⁰ suggested that the correction coefficient to be used should not always be 0.5 as changes from site to site. However, so far, the mostly adopted coefficient is 0.5. The consequence is that the choice of the sampling site is important and should be made a priori in order to make the results reproducible and comparable.

Two main sampling sites have been proposed: the intra-abdominal¹¹⁻¹⁶ or free-floating⁴⁻¹⁰ portion of the umbilical vein. Measurements performed at the intra-abdominal portion are easier to reproduce thanks to its relatively fixed location. However, fixed fetal position, bone shadowing and other technical aspects might represent an important obstacle for intra-abdominal evaluation. These limitations are easily overcome when the measurements is performed at the free-floating portion of the umbilical cord. On the other side, due to its motility and length, doubts have been raised regarding the difficulties in standardizing the measurement site.²¹⁻²³

1.2.3 | Experimental research

In an experimental study the “cross sectional area \times mean velocity \times 0.5” formula was applied to fetal lambs and compared to measurements obtained by invasive diffusion technique.⁸ Ultrasound and diffusion technique assessment for umbilical vein blood flow pro kg were

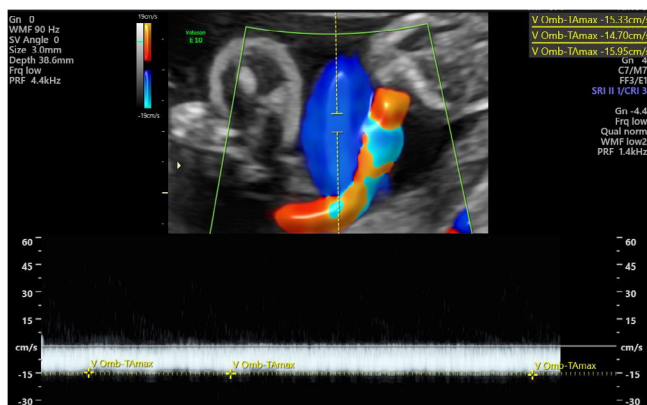


FIGURE 3 The ultrasound measurements of umbilical vein blood flow velocity, for the calculation of the umbilical vein blood flow volume

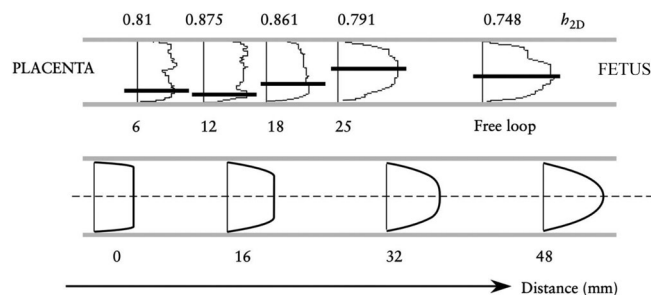


FIGURE 4 Comparison between the umbilical vein velocity profiles recorded at different distances from the placental insertion and those derived from the fluid-dynamic theory of a fluid passing from a reservoir into a cylindrical tube²⁰

comparable (211 ± 19 and 206 ± 38 ml/min/kg; $p = 0.9$). On the same set of animals, a comparison between ultrasound Doppler indices and steady-state diffusion technique was performed yielding virtually identical results (207 ± 9 vs. 208 ± 7 ml/min/kg).²⁴ Moreover, the umbilical vein blood flow was strictly correlated with the weight of the cotyledons serving each vein.

Umbilical vein blood flow was found to be significantly reduced in lambs affected by fetal growth restriction compared to controls (129 ± 15 vs. 176 ± 13 ml/min/kg; $p < 0.05$).²⁵ A reduced maximum and weighted mean velocity in pregnant sheep was found to be associated with maternal hypoxemia.²⁶

1.3 | Umbilical vein blood flow in normal pregnancy

A progressive and exponential increase in placental blood flow in the human fetus can be observed throughout gestation. Several studies^{4-9,12-14,16,27-29} obtained an estimate of the umbilical vein blood flow.^{21,30} The absolute blood flow volume in umbilical vein increases

around 7-fold in the second half of the pregnancy⁶ (i.e., from 63 ml/min at 20 weeks to 373 ml/min at 38 weeks⁸) (Figure 5; *data unpublished, presented at ISUOG World Congress 2022*). This increase throughout gestation seems to be mainly due to the increase in vessel diameter, and to the lesser extent to the mean velocity. The umbilical vein diameter increases approximately from 4 mm at 20 weeks to 8 mm at 38 weeks while the velocity increases from 0.08 to 0.1 m/s.¹⁰

Contrary to the absolute value, the umbilical vein blood flow if normalized per kg of fetal weight, decreases throughout gestation (Figure 5; *data unpublished, presented at ISUOG World Congress 2022*).^{5,8,13}

1.3.1 | Reproducibility

There are few critical aspects of the umbilical vein blood flow quantification that raised concerns regarding its accuracy and reproducibility.²¹⁻²³ The first report that dealt with the measurements of the umbilical vein blood flow volume date back the 80s of the last century.³⁰⁻³³ Measurements were obtained on the intrahepatic tract of the umbilical vein. Figure 6 shows an example of pioneering measurement of umbilical vein diameter³¹ compared to more recent assessment. There is no doubt that the poor resolution of ultrasound technology of that time penalized the use of this parameter.

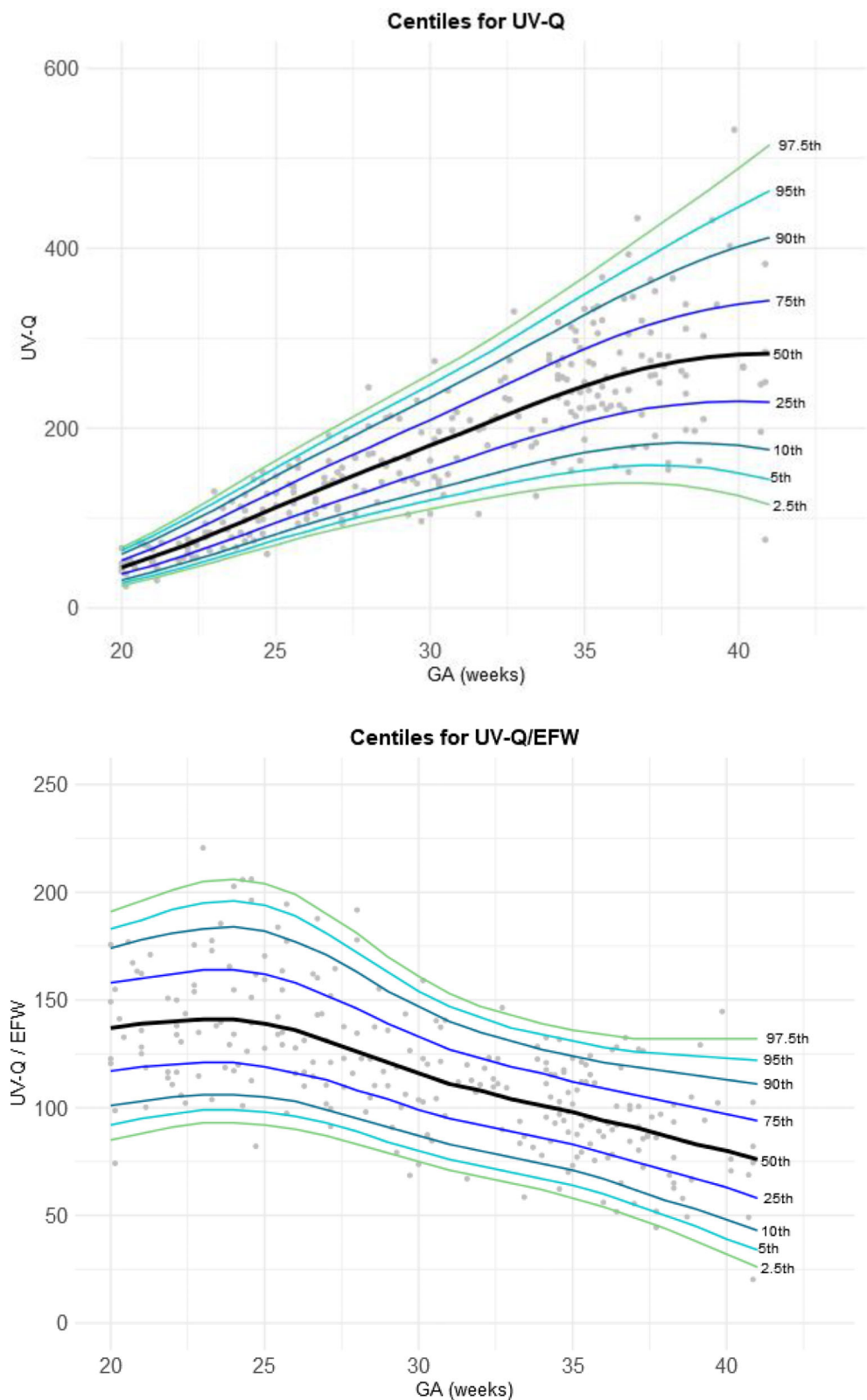
Table 1 reports the inter- and intra-observer coefficients of variation of the umbilical vein diameter, mean velocity, and absolute value. Figueras et al.³⁴ reported the reproducibility of the assessment of umbilical vein blood flow by two operators: the intra-observer intraclass correlation coefficient (ICCs) (95% CI) for the diameter, mean velocity and umbilical vein blood flow were 0.7 (0.5-0.8), 0.6 (0.4-0.7), and 0.5 (0.3-0.8) respectively, while the inter-observer ICCs were 0.6 (0.3-0.7), 0.5 (0.2-0.6), and 0.6 (0.4-0.7) respectively. The same results were obtained by other authors.^{6,8,10} Therefore, the limitations that have been raised over time regarding the accuracy and reproducibility of umbilical vein blood flow can be easily overcome by practice, by improved image and Doppler quality and by the adoption of a standardized technique.^{24,34,35}

1.4 | Umbilical vein blood flow volume in fetal growth

1.4.1 | Fetal growth restriction

Fetal growth is closely linked to placental circulation; thus, it is not surprising that umbilical vein blood flow may be altered in fetuses who suffer from fetal growth restriction. Our group found that the umbilical vein blood flow velocity was significantly reduced in case of fetal growth restriction throughout the gestation compared to normally growing fetuses,²¹ suggesting that it may be useful predictor of fetal growth. In growth restricted fetuses the umbilical vein blood

FIGURE 5 Centiles for: (A) umbilical vein blood flow volume (UV-Q); and (B) umbilical vein blood flow volume normalized for estimated fetal weight (UV-Q/EFW) derived by our cohort of uncomplicated pregnancies. Source: Data presented at ISUOG World Congress 2022



flow normalized for estimated fetal weight was 98 ± 19 ml/min/kg compared to 117 ± 30 in the control group ($p < 0.001$).²¹ Growth restricted fetuses that showed also abnormal heart rate before elective delivery had even a larger difference in umbilical vein blood flow

values compared to control group (63 ± 22 vs. 124 ± 30 ml/min/kg; $p < 0.001$).²¹

Umbilical vein blood flow has been also investigated during the first trimester of pregnancy (from 11^{+0} to 13^{+6} weeks of gestation) in

CI 0.69–0.80) and 0.770 (95% CI 0.63–0.82) respectively, the addition of umbilical vein blood flow assessed at 36 weeks of pregnancy significantly improved the detection of fetuses with a birth weight above 4000 grams (AUC of 0.851 (95% CI 0.73–0.9)). Moreover, Rizzo et al.⁴⁹ found that umbilical vein blood flow was associated independently with large-for-gestational age fetuses, even if measured at 11–14 weeks of gestation, thus, improving the prediction of large-for-gestational age at birth.

1.4.3 | Toward the term

Lower umbilical vein blood flow values have been found also in normally grown fetuses that underwent intrapartum distress^{50–52} with a higher rate of emergency caesarean section or instrumental delivery, thus, suggesting a potential role for umbilical vein blood flow in prediction of distress in labor.⁵³ According to Parra-Saavedra et al.,⁵⁴ fetuses with an umbilical vein blood flow volume below 68 ml/min/kg had twice the risk of non-reassuring fetal status in induced labor. If we go back to 1987, the umbilical vein blood flow volume measured 2 days before delivery in late fetal growth restriction was 68 ml/min/kg.⁵⁵ This value is very similar to one we observed in early fetal growth restriction with abnormal heart rate (63 ml/min/kg).²¹

Umbilical vein blood flow was found to be significantly lower in late-term appropriate for gestational age fetuses that had a drop in abdominal circumference compared to those that did not reduce their growth velocity [184 ml/min (IQR 143–225) and 55 ml/min/kg (IQR 42–66) versus 234 ml/min (IQR 184–278) and 64 ml/min/kg (IQR 50–75); $p < 0.05$].⁵² Taken together, these results would suggest a potential role of umbilical vein blood flow assessment in stunted fetal growth. Interestingly, umbilical vein blood flow was lower in fetuses that required formula milk supplementation at birth compared to those that did not require any supplementation [203 ml/min (IQR 154–240) and 56 ml/min/kg (IQR 44–66) versus 230 ml/min (IQR 178–277) and 62 ml/min/kg (IQR 47–74); $p < 0.05$].⁵² A possible explanation might be that, due to lower umbilical vein blood flow, there is a lower nutrient and oxygen delivery that may lead to decreased fetal energy reserves, and as such to require complementary feeding in the immediate post-natal life.⁵⁶ It is still not known what kind of implication the exposition to varying degrees of oxygen and nutrient deprivation may have on the fetus and its growth velocity, but the latter has been shown to be associated with adverse perinatal outcome even in the absence of Doppler abnormalities.⁵⁷ If further studies confirm umbilical vein blood flow to be associated with adverse fetal and neonatal outcomes,⁵⁸ this information might be combined with other Doppler and biophysical indices for risk stratification assessment.

2 | CONCLUSION

The umbilical vein blood flow cast an important background of studies that make its role in poor oxygenation and hypo-nutrition intuitive. This should encourage further investigation on the potential role of umbilical vein blood flow assessment in clinical setting.

ACKNOWLEDGMENTS

Open access funding provided by BIBLIOSAN.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ORCID

Moira Barbieri  <https://orcid.org/0000-0002-9273-505X>

Daniela Denis Di Martino  <https://orcid.org/0000-0003-1541-5236>

Enrico Mario Ferrazzi  <https://orcid.org/0000-0001-5243-0537>

Tamara Stampalija  <https://orcid.org/0000-0002-9080-3848>

REFERENCES

- Tay J, Masini G, McEniery CM, et al. Uterine and fetal placental Doppler indices are associated with maternal cardiovascular function. *Am J Obstet Gynecol*. 2019;220(1):96.e1–96.e8. doi:10.1016/j.ajog.2018.09.017
- Bellotti M, Pennati G, de Gasperi C, Bozzo M, Battaglia FC, Ferrazzi E. Simultaneous measurements of umbilical venous, fetal hepatic, and ductus venosus blood flow in growth-restricted human fetuses. *Am J Obstet Gynecol*. 2004;190(5):1347–1358.
- Ferrazzi E, Lees C, Acharya G. The controversial role of the ductus venosus in hypoxic human fetuses. *Acta Obstet Gynecol Scand*. 2019;98(7):823–829. doi:10.1111/aogs.13572
- Boito SM, Struijk PC, Ursem NTC, Stijnen T, Wladimiroff JW. Assessment of fetal liver volume and umbilical venous volume flow in pregnancies complicated by insulin-dependent diabetes mellitus. *BJOG*. 2003;110(11):1007–1013.
- Flo K, Wilsgaard T, Acharya G. Longitudinal reference ranges for umbilical vein blood flow at a free loop of the umbilical cord. *Ultrasound Obstet Gynecol*. 2010;36(5):567–572. doi:10.1002/uog.7730
- Boito S, Struijk PC, Ursem NTC, Stijnen T, Wladimiroff JW. Umbilical venous volume flow in the normally developing and growth-restricted human fetus. *Ultrasound Obstet Gynecol*. 2002;19(4):344–349. doi:10.1046/j.1469-0705.2002.00671.x
- Bellotti M, Pennati G, de Gasperi C, Battaglia FC, Ferrazzi E. Role of ductus venosus in distribution of umbilical blood flow in human fetuses during second half of pregnancy. *Am J Physiol Heart Circ Physiol*. 2000;279(3):H1256–H1263. doi:10.1152/ajpheart.2000.279.3.H1256
- Barbera A, Galan HL, Ferrazzi E, et al. Relationship of umbilical vein blood flow to growth parameters in the human fetus. *Am J Obstet Gynecol*. 1999;181(1):174–179. doi:10.1016/S0002-9378(99)70456-4
- Sutton MSJ, Theard MA, Bhatia SJS, Plappert T, Saltzman DH, Doubilet P. Changes in placental blood flow in the normal human fetus with gestational age. *Pediatr Res*. 1990;28(4):383–387. doi:10.1203/00006450-199010000-00016
- Lees C, Albaiges G, Deane C, Parra M, Nicolaidis KH. Assessment of umbilical arterial and venous flow using color Doppler. *Ultrasound Obstet Gynecol*. 1999;14(4):250–255. doi:10.1046/j.1469-0705.1999.14040250.x
- Widnes C, Flo K, Wilsgaard T, Odibo AO, Acharya G. Sexual dimorphism in umbilical vein blood flow during the second half of pregnancy: a longitudinal study. *J Ultrasound Med*. 2017;36(12):2447–2458. doi:10.1002/jum.14286
- Rizzo G, Rizzo L, Aiello E, Allegra E, Arduini D. Modelling umbilical vein blood flow normograms at 14–40 weeks of gestation by quantile

- regression analysis. *J Matern Fetal Neonatal Med.* 2016;29(5):701-706. doi:10.3109/14767058.2015.1019855
13. Acharya G, Wilsgaard T, Rosvold Berntsen GK, Maltau JM, Kiserud T. Reference ranges for umbilical vein blood flow in the second half of pregnancy based on longitudinal data. *Prenat Diagn.* 2005;25(2):99-111. doi:10.1002/pd.1091
 14. Kiserud T, Rasmussen S, Skulstad S. Blood flow and the degree of shunting through the ductus venosus in the human fetus. *Am J Obstet Gynecol.* 2000;182(1):147-153. doi:10.1016/S0002-9378(00)70504-7
 15. Tchirikov M, Rybakowski C, Hüneke B, Schoder V, Schröder HJ. Umbilical vein blood volume flow rate and umbilical artery pulsatility as 'venous-arterial index' in the prediction of neonatal compromise. *Ultrasound Obstet Gynecol.* 2002;20(6):580-585. doi:10.1046/j.1469-0705.2002.00832.x
 16. Tchirikov M, Rybakowski C, Hüneke B, Schröder HJ. Blood flow through the ductus venosus in singleton and multifetal pregnancies and in fetuses with intrauterine growth retardation. *Am J Obstet Gynecol.* 1998;178(5):943-949. doi:10.1016/S0002-9378(98)70528-9
 17. Togni FA, Araujo E, Vasques FAP, Moron AF, Torloni MR, Nardoza LMM. The cross-sectional area of umbilical cord components in normal pregnancy. *Int J Gynecol Obstet.* 2007;96(3):156-161. doi:10.1016/j.ijgo.2006.10.003
 18. Cromi A, Ghezzi F, di Naro E, Siesto G, Bergamini V, Raio L. Large cross-sectional area of the umbilical cord as a predictor of fetal macrosomia. *Ultrasound Obstet Gynecol.* 2007;30(6):861-866. doi:10.1002/uog.5183
 19. Ghezzi F, Raio L, Günter Duwe D, Cromi A, Karousou E, Dürig P. Sonographic umbilical vessel morphometry and perinatal outcome of fetuses with a lean umbilical cord. *J Clin Ultrasound.* 2005;33(1):18-23. doi:10.1002/jcu.20076
 20. Pennati G, Bellotti M, de Gasperi C, Rognoni G. Spatial velocity profile changes along the cord in normal human fetuses: can these affect Doppler measurements of venous umbilical blood flow? *Ultrasound Obstet Gynecol.* 2004;23(2):131-137. doi:10.1002/uog.938
 21. Ferrazzi E, Rigano S, Bozzo M, et al. Umbilical vein blood flow in growth-restricted fetuses. *Ultrasound Obstet Gynecol.* 2000;16(5):432-438. doi:10.1046/j.1469-0705.2000.00208.x
 22. Kiserud T, Acharya G. The fetal circulation. *Prenat Diagn.* 2004;24(13):1049-1059. doi:10.1002/pd.1062
 23. Pennati G, Bellotti M, Ferrazzi E, Bozzo M, Pardi G, Fumero R. Blood flow through the ductus venosus in human fetus: calculation using Doppler velocimetry and computational findings. *Ultrasound Med Biol.* 1998;24(4):477-487. doi:10.1016/S0301-5629(98)00011-8
 24. Galan HL, Jozwik M, Rigano S, et al. Umbilical vein blood flow determination in the ovine fetus: comparison of Doppler ultrasonographic and steady-state diffusion techniques. *Am J Obstet Gynecol.* 1999;181(5):1149-1153. doi:10.1016/S0002-9378(99)70098-0
 25. Padoan A, Regnault T, DeVrijer B, et al. Endothelial nitric oxide synthase in uteroplacental vasculature in an ovine model of IUGR. *Am J Obstet Gynecol.* 2004;189(6):s193.
 26. Kiserud T, Jauniaux E, West D, Ozturk O, Hanson MA. Circulatory responses to maternal hyperoxaemia and hypoxaemia assessed non-invasively in fetal sheep at 0.3-0.5 gestation in acute experiments. *BJOG.* 2001;108(4):359-364. doi:10.1111/j.1471-0528.2001.00096.x
 27. Tchirikov M, Strohnner M, Förster D, Hüneke B. A combination of umbilical artery PI and normalized blood flow volume in the umbilical vein: venous-arterial index for the prediction of fetal outcome. *Eur J Obstet Gynecol Reprod Biol.* 2009;142(2):129-133. doi:10.1016/j.ejogrb.2008.10.015
 28. Wang L, Zhou Q, Zhou C, et al. Z-score reference ranges for umbilical vein diameter and blood flow volume in normal fetuses. *J Ultrasound Med.* 2022;41(4):907-916. doi:10.1002/jum.15774
 29. DeVore GR, Epstein A. Computing Z-score equations for clinical use to measure fetal umbilical vein size and flow using six independent variables of age and size. *J Ultrasound Med.* 2022;41(8):1949-1960. doi:10.1002/jum.15872
 30. Sauters JB, Wright N, Lewis KO. Measurement of human fetal blood flow. *BMJ.* 1980;280(6210):283-284. doi:10.1136/bmj.280.6210.283
 31. Gill RW, Kossoff G, Warren PS, Garrett WJ. Umbilical venous flow in normal and complicated pregnancy. *Ultrasound Med Biol.* 1984;10(3):349-363. doi:10.1016/0301-5629(84)90169-8
 32. Jouila P, Kirkinen P. Umbilical vein blood flow as an indicator of fetal hypoxia. *BJOG.* 1984;91(2):107-110. doi:10.1111/j.1471-0528.1984.tb05891.x
 33. RLA E, JWK R. Quantitative measurement of fetal blood flow using Doppler ultrasound. *BJOG.* 1985;92(6):600-604. doi:10.1111/j.1471-0528.1985.tb01398.x
 34. Figueras F, Fernández S, Hernández-Andrade E, Gratacós E. Umbilical venous blood flow measurement: accuracy and reproducibility. *Ultrasound Obstet Gynecol.* 2008;32(4):587-591. doi:10.1002/uog.5306
 35. Schmidt KG, di Tommaso M, Silverman NH, Rudolph AM. Doppler echocardiographic assessment of fetal descending aortic and umbilical blood flows. Validation studies in fetal lambs. *Circulation.* 1991;83(5):1731-1737. doi:10.1161/01.CIR.83.5.1731
 36. Rizzo G, Capponi A, Pietrolucci ME, Capece A, Arduini D. First-trimester umbilical vein blood flow in pregnancies with low serum pregnancy-associated plasma protein-A levels: an early predictor of fetal growth restriction. *Ultrasound Obstet Gynecol.* 2010;36(4):433-438. doi:10.1002/uog.7699
 37. Proctor LK, Toal M, Keating S, et al. Placental size and the prediction of severe early-onset intrauterine growth restriction in women with low pregnancy-associated plasma protein-A. *Ultrasound Obstet Gynecol.* 2009;34(3):274-282. doi:10.1002/uog.7308
 38. Rigano S, Bozzo M, Ferrazzi E, Bellotti M, Battaglia FC, Galan HL. Early and persistent reduction in umbilical vein blood flow in the growth-restricted fetus: a longitudinal study. *Am J Obstet Gynecol.* 2001;185(4):834-838. doi:10.1067/mob.2001.117356
 39. Rizzo G, Mattioli C, Mappa I, et al. Hemodynamic factors associated with fetal cardiac remodeling in late fetal growth restriction: a prospective study. *J Perinat Med.* 2019;47(7):683-688. doi:10.1515/jpm-2019-0217
 40. Cruz-Lemini M, Crispi F, Valenzuela-Alcaraz B, et al. Fetal cardiovascular remodeling persists at 6 months in infants with intrauterine growth restriction. *Ultrasound Obstet Gynecol.* 2016;48(3):349-356. doi:10.1002/uog.15767
 41. Crispi F, Bijlens B, Figueras F, et al. Fetal growth restriction results in remodeled and less efficient hearts in children. *Circulation.* 2010;121(22):2427-2436. doi:10.1161/CIRCULATIONAHA.110.937995
 42. Parra-Saavedra M, Croveto F, Triunfo S, et al. Association of Doppler parameters with placental signs of underperfusion in late-onset small-for-gestational-age pregnancies. *Ultrasound Obstet Gynecol.* 2014;44(3):330-337. doi:10.1002/uog.13358
 43. Rizzo G, Mappa I, Bitsadze V, et al. Role of Doppler ultrasound at time of diagnosis of late-onset fetal growth restriction in predicting adverse perinatal outcome: prospective cohort study. *Ultrasound Obstet Gynecol.* 2020;55(6):793-798. doi:10.1002/uog.20406
 44. Hamidi OP, Driver C, Steller JG, et al. Umbilical venous volume flow in late-onset fetal growth restriction. *J Ultrasound Med.* 2022;22. doi:10.1002/jum.15993 [In Press].
 45. Rigano S, Bozzo M, Padoan A, et al. Small size-specific umbilical vein diameter in severe growth restricted fetuses that die *in utero*. *Prenat Diagn.* 2008;28(10):908-913. doi:10.1002/pd.2054
 46. Zhu MY, Milligan N, Keating S, et al. The hemodynamics of late-onset intrauterine growth restriction by MRI. *Am J Obstet Gynecol.* 2016;214(3):367.e1-367.e17. doi:10.1016/j.ajog.2015.10.004
 47. Rizzo G, Mappa I, Bitsadze V, Khizroeva J, Makatsarya A, D'Antonio F. The added value of umbilical vein flow in predicting fetal macrosomia

- at 36 weeks of gestation: a prospective cohort study. *Acta Obstet Gynecol Scand.* 2021;100(5):900-907. doi:[10.1111/aogs.14047](https://doi.org/10.1111/aogs.14047)
48. Ebbing C, Rasmussen S, Kiserud T. Fetal hemodynamic development in macrosomic growth. *Ultrasound Obstet Gynecol.* 2011;38(3):303-308. doi:[10.1002/uog.9046](https://doi.org/10.1002/uog.9046)
 49. Rizzo G, Mappa I, Bitsadze V, et al. Role of first-trimester umbilical vein blood flow in predicting large-for-gestational age at birth. *Ultrasound Obstet Gynecol.* 2020;56(1):67-72. doi:[10.1002/uog.20408](https://doi.org/10.1002/uog.20408)
 50. Prior T, Mullins E, Bennett P, Kumar S. Umbilical venous flow rate in term fetuses: can variations in flow predict intrapartum compromise? *Am J Obstet Gynecol.* 2014;210(1):61.e1-61.e8. doi:[10.1016/j.ajog.2013.08.042](https://doi.org/10.1016/j.ajog.2013.08.042)
 51. Prior T, Mullins E, Bennett P, Kumar S. Prediction of fetal compromise in labor. *Obstet Gynecol.* 2014;123(6):1263-1271. doi:[10.1097/AOG.0000000000000292](https://doi.org/10.1097/AOG.0000000000000292)
 52. Stampalija T, Monasta L, Barbieri M, et al. Late-term fetuses with reduced umbilical vein blood flow volume: an under-recognized population at increased risk of growth restriction. *Eur J Obstet Gynecol Reprod Biol.* 2022;272:272-187. doi:[10.1016/j.ejogrb.2022.03.032](https://doi.org/10.1016/j.ejogrb.2022.03.032)
 53. Kiserud T. Re: umbilical vein flow and perinatal outcome in term small-for-gestational-age fetuses. M. Parra-Saavedra, F. Crovetto, S. Triunfo, S. Savchev, G. Parra, M. Sanz, E. Gratacos and F. Figueras. *Ultrasound Obstet Gynecol* 2013; 42: 189-195. *Ultrasound Obstet Gynecol.* 2013;42(2):130. doi:[10.1002/uog.12553](https://doi.org/10.1002/uog.12553)
 54. Parra-Saavedra M, Crovetto F, Triunfo S, et al. Added value of umbilical vein flow as a predictor of perinatal outcome in term small-for-gestational-age fetuses. *Ultrasound Obstet Gynecol.* 2013;42(2):189-195. doi:[10.1002/uog.12380](https://doi.org/10.1002/uog.12380)
 55. Laurin J, Lingman G, Marsál K, Persson PH. Fetal blood flow in pregnancies complicated by intrauterine growth retardation. *Obstet Gynecol.* 1987;69(6):895-902.
 56. di Naro E, Raio L, Ghezzi F, et al. Longitudinal umbilical vein blood flow changes in normal and growth-retarded fetuses. *Acta Obstet Gynecol Scand.* 2002;81(6):527-533.
 57. Stampalija T, Wolf H, Mylrea-Foley B, et al. Reduced fetal growth velocity and weight loss are associated with adverse perinatal outcome in fetuses at risk of growth restriction. *Am J Obstet Gynecol.* 2022;S0002-9378(22)00477-X. doi:[10.1016/j.ajog.2022.06.023](https://doi.org/10.1016/j.ajog.2022.06.023)
 58. Figueras F, Cruz-Martinez R, Sanz-Cortes M, et al. Neurobehavioral outcomes in preterm, growth-restricted infants with and without prenatal advanced signs of brain-sparing. *Ultrasound Obstet Gynecol.* 2011;38(3):288-294. doi:[10.1002/uog.9041](https://doi.org/10.1002/uog.9041)

How to cite this article: Barbieri M, Di Martino DD, Ferrazzi EM, Stampalija T. Umbilical vein blood flow: State-of-the-art. *J Clin Ultrasound.* 2023;51(2):318-325. doi:[10.1002/jcu.23412](https://doi.org/10.1002/jcu.23412)