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REVIEW

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

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## 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 clepsydra[3] 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.

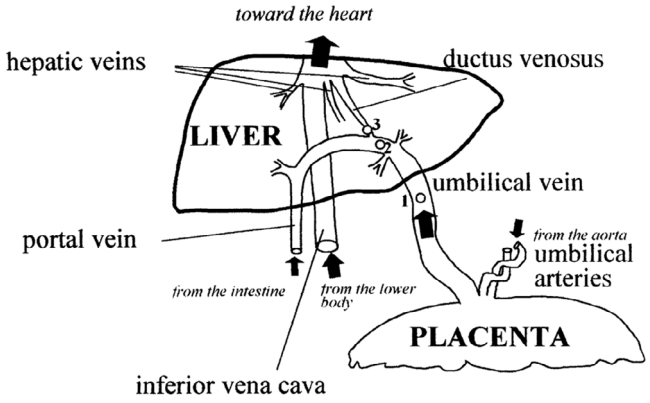


**FIGURE 1** A model of the fetal circulation from Bellotti et al.[2]

## 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 $mm^2$ 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 loop[4–10] 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.

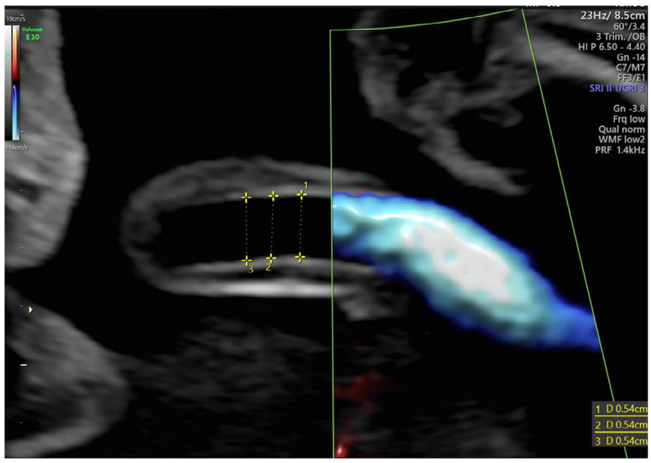

**FIGURE 2** The ultrasound measurement of umbilical vein diameter at a free-floating portion of the umbilical vein. The measurement of the three diameters is represented and the average value is used for formula calculation

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 × 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 vein[20] (Figure 4). Pennati and coworkers[20] 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-abdominal[11–16] or free-floating[4–10] 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 × mean velocity × 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

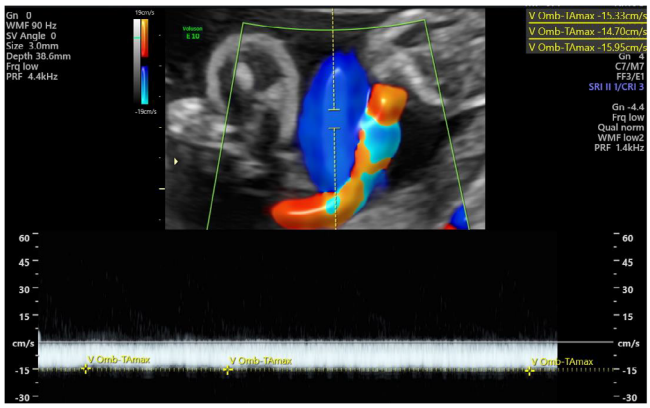


**FIGURE 3** The ultrasound measurements of umbilical vein blood flow velocity, for the calculation of the umbilical vein blood flow volume

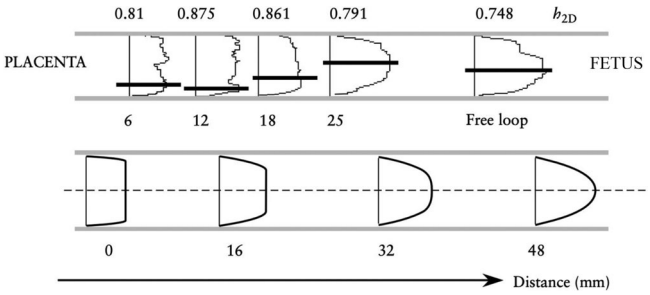


**FIGURE 4** Comparison between the umbilical vein velocity profiles recorded at different distances from the placental insertion and those derived from the fluid-dynamic theory of a fluid passing from a reservoir into a cylindrical tube[20]

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 pregnancy[6] (i.e., from 63 ml/min at 20 weeks to 373 ml/min at 38 weeks[8]) (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 diameter[31] 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

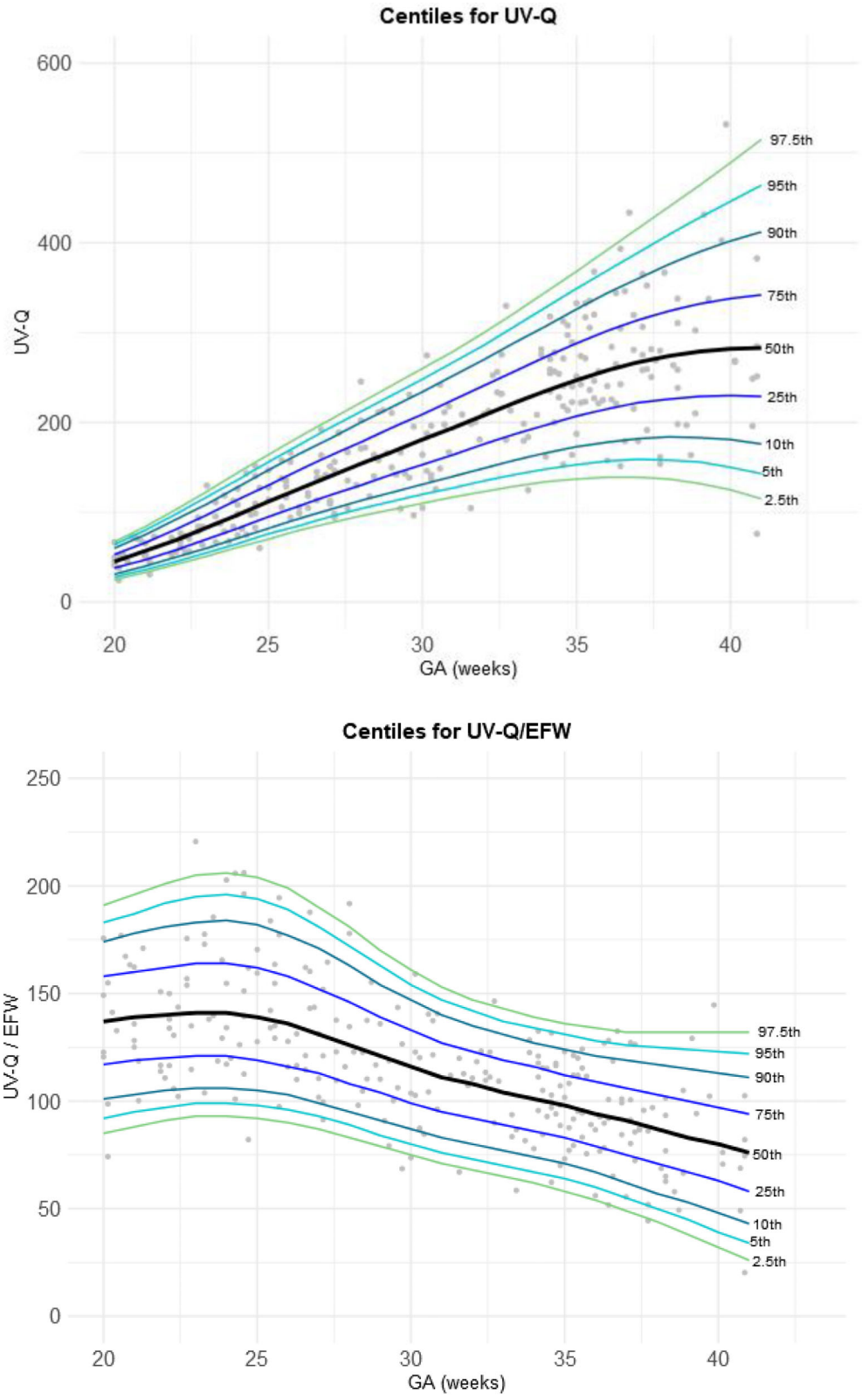


**FIGURE 5** Centiles for: (A) umbilical vein blood flow volume (UV-Q); and (B) umbilical vein blood flow volume normalized for estimated fetal weight (UV-Q/EFW) derived by our cohort of uncomplicated pregnancies. *Source*: Data presented at ISUOG World Congress 2022

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

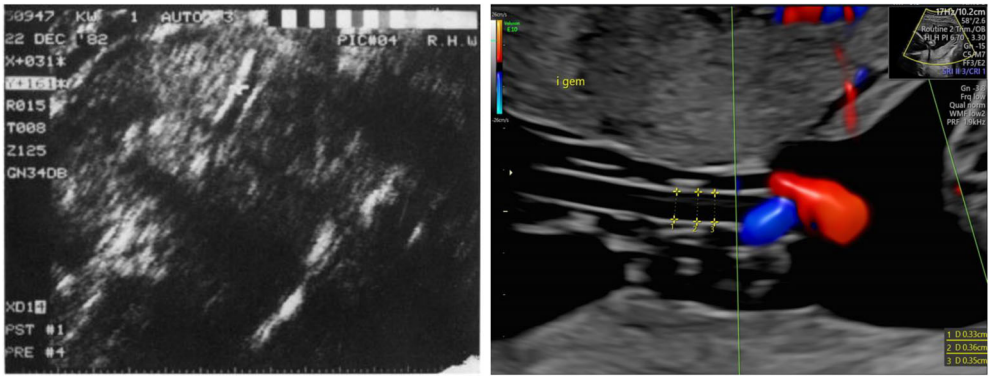


**FIGURE 6** Differences in imaging resolution thanks to the improvement of ultrasound equipment. The image on the left was derived from Gill et al.[31]

**TABLE 1** Reproducibility of the umbilical vein blood flow volume calculation

| | UV diameter or cross-sectional area | | Mean velocity | | Absolute flow | |
|---|---|---|---|---|---|---|
| | Intra-observer coefficients of variation | Inter-observer coefficients of variation | Intra-observer coefficients of variation | Inter-observer coefficients of variation | Intra-observer coefficients of variation | Inter-observer coefficients of variation |
| Barbera et al.[8] | 3.3% | 2.9% | 9.7% | 7.9% | 10.9% | 12.7% |
| Boito et al.[6] | 9.1% | - | 12% | - | 11.9% | - |

fetuses with serum pregnancy-associated plasma protein-A concentration below 0.3 multiples of the median.[36] Among pregnancies with low serum pregnancy-associated plasma protein-A levels, a significant decreased umbilical vein blood flow was found in fetuses with a birth weight below 10th centile and development of umbilical artery pulsatility index above 95th centile,[36] thus, supporting the hypothesis that Doppler parameters are already altered in the first trimester of pregnancy.[36,37] Moreover, Rigano and co-workers[38] showed in a longitudinal study that the umbilical vein blood flow, normalized for estimated fetal weight, was reduced from the second trimester in 15 of 21 fetal growth restricted fetuses. By the time of delivery, 16 of these fetuses had umbilical vein blood flow below the 10th percentile. Recent evidence showed that reduced umbilical vein blood flow is also associated with cardiac remodeling in fetal growth restriction.[39] Particularly, in pregnancies complicated by fetal growth restriction, there was a positive correlation between the sphericity index (calculated as the ratio between the end-diastolic mid-basal-apical and transverse lengths) and the umbilical vein blood flow normalized for abdominal circumference. This association is even more important if we consider the numerous evidence in support of the *fetal programming* according to which the cardiovascular changes that occurred the prenatal era can persist in later stages of life, thus, determining an increase in cardiovascular morbidity in adulthood.[40,41]

The association between the umbilical vein blood flow and alteration in fetal growth was also supported by a study of placental specimens from singleton pregnancies with confirmed birth weight below the 10th percentile[42]: 51 placentae exhibited histological findings consistent with placental under-perfusion and the reduction of umbilical vein blood flow was evident in case of under-perfused placenta.

A prospective study on a cohort of fetuses with late fetal growth restriction[43] showed that umbilical vein blood flow normalized for abdominal circumference at the time of diagnosis had a higher prediction value for adverse outcome than cerebro-placental ratio.

A study by Hamidi et al.[44] found that, although absolute umbilical vein blood flow was not decreased in small-for-gestational age fetuses, the number of fetuses with an abnormal umbilical vein blood flow below the 10th percentile, both absolute and normalized for abdominal circumference, was increased compared to controls. Thus, the authors speculate that umbilical vein blood flow may be a more sensitive indicator of fetal distress, even in case of "constitutionally" small fetuses. In conclusion, several studies showed a reduced umbilical vein blood flow in fetal growth restriction.[21,38,43,45] These results were also confirmed by magnetic nuclear imaging hemodynamics[46] in late fetal growth restriction[40] and open a window of opportunity for its use in the diagnosis and/or management of fetal growth restriction, but further studies are needed.

### 1.4.2 | Fetal macrosomia

It has been also reported that umbilical vein blood flow is increased in pregnancies complicated by fetal macrosomia[47,48] providing increased liver perfusion particularly in the second half of the pregnancy. In a cohort of 29 healthy non-diabetic pregnant women who gave birth to neonates with birth weight above 90th centile, Ebbing and colleagues[48] found that umbilical vein blood flow was higher and, not only, both the ductus venosus systolic blood velocity and the left portal vein blood velocity were found to be significantly higher during the second half of pregnancy. Recently, based on these premises, Rizzo et al.[47] computed the performance of different models in predicting fetal macrosomia; while the models including estimated fetal weight and maternal factors had an area under the curve (AUC) of 0.724 (95%

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 postnatal 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.

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## 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.

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