Assessment of umbilical arterial and venous flow using color Doppler

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ABSTRACT

Objective   *To estimate the umbilical artery and vein blood volume flow using B-mode and Doppler ultrasound in the second and third trimesters of pregnancy.*

Design   *This was a cross-sectional study of 129 singleton, healthy pregnancies at 23–33 weeks' gestation. The umbilical artery and vein cross-sectional area, time-averaged velocity and pulsatility index were measured in a free loop of cord, and the fetal weight was estimated. Ranges for each parameter were obtained; from these the blood flow for the vein and artery was calculated, and the average flow corrected for fetal weight was derived.*

Results   *The median time for examination was 6 min. The mean cross-sectional area and time-averaged velocity for both the vein and artery increased linearly with gestation. The umbilical artery flow correlated closely with the average vein flow (r = 0.9, p < 0.001). There was a significant, though poor, inverse correlation between the umbilical artery pulsatility index and the average umbilical flow (r = −0.25, p < 0.05). The average umbilical flow (calculated from the mean of arterial and venous flow), corrected for estimated fetal weight, decreased from 189.2 ml/kg per min at 23 weeks to 176.2 ml/kg per min at 33 weeks' gestation.*

Conclusion   *The estimates of fetal umbilical flow obtained by this Doppler method are consistent with previously published data. Averaging the arterial and venous flow is theoretically advantageous in reducing the inherent errors in estimating either the arterial or the venous flow. This method of measuring umbilical flow may have clinical potential in assessing fetal health and disease processes.*

INTRODUCTION

Doppler ultrasound examination of the umbilical artery is used widely as a non-invasive method for assessment of fetal blood flow. Analysis of flow velocity waveforms gives measures of impedance and velocity. A physiologically more important parameter than impedance is volume flow, but this measurement is technically difficult to obtain in the fetus, owing to the caliber and curvature of the vessels and fetal movements.

Several authors have attempted to quantify umbilical venous blood flow using invasive *in utero* isotope injections[1] and *ex utero* thermodilution methods[2,3]. From the early 1980s onwards, the combination of B-mode ultrasonography and pulsed Doppler has been used to measure intra-abdominal umbilical venous flow[4–7], although its use has not gained widespread acceptance in obstetric sonography. This may be because the more precise techniques require 10–30 min per examination, specialized ultrasound equipment and, in certain cases, immersion of the patient in a waterbath[5,8].

We describe a further adaptation of this technique that uses commercially available color Doppler and high-resolution gray-scale ultrasound to measure both venous and arterial flow through the umbilical cord. The umbilical cord is unique in that the flow through the two arteries must be more or less equivalent to that of the vein. The two flow measurements can therefore be compared directly at a given time. In this study of healthy pregnancies between 23 and 33 weeks' gestation, we sought to compare umbilical artery and vein flow, and derive a mean flow correcting for estimated fetal weight. We also present our cross-sectional reference ranges for umbilical artery and vein cross-sectional area and time-averaged velocity.

PATIENTS AND METHODS

We recruited 129 healthy women, with no evidence of hypertension, diabetes or other cardiovascular condition. All were undergoing routine ultrasound examinations of a singleton pregnancy in the range of 23–33 weeks' gestation and in none was there evidence of fetal abnormalities. No cases of two-vessel umbilical cord were included in the study. In all cases, fetal biometry was between the 5th and

95th centiles for abdominal circumference, head circumference, biparietal diameter and femur length, with normal amniotic fluid and normal umbilical artery Doppler pulsatility index (PI) (< 95th centile). Estimated fetal weight[9] was obtained at the time of umbilical volume flow measurement (or within 1 week by extrapolation from the appropriate centile of estimated fetal weight).

Women underwent ultrasound examination by one of two operators, C.L. or G.A. An Acuson Aspen ultrasound system with a 3.5-MHz curvilinear probe (Acuson, Mountainview, CA) was used for all examinations. The umbilical cord was visualized in cross-section in a free loop and magnified to the maximum possible extent. In most cases, the cord appearance was of the characteristic two arteries and one vein. At least two measurements were made of the cross-sectional area of both the vein and the artery, if necessary by using different sections of cord. The ellipse function allowed a directly derived internal cross-sectional area to be obtained for each vessel. These measurements were averaged to give a mean arterial and venous cross-sectional area. We did not attempt separate measurements of velocity and cross-sectional area for each of the umbilical arteries; instead, we measured the areas and velocities several times to obtain a mean for each.

For time-averaged velocity measurements for both artery and vein, at least two arterial and two venous measurements were recorded. Measurements were made in accordance with the manufacturer's guidelines for this, as follows.

(1) Cord vessels were visualized in longitudinal section in the absence of fetal movements or breathing. In all cases the angle of insonation was less than 60°.

(2) Care was taken to avoid contamination of the waveform with other signals, either above or below the baseline, and only waveforms with a high signal-to-noise ratio were accepted. The sample volume was adjusted to insonate the whole width of the vessel.

(3) At least three consecutive arterial waveforms were obtained. Calipers were placed to allow time-averaged velocity measurements to be made with angle correction.

Similarly, venous waveforms were obtained and, because of the uniformity of flow (absence of pulsations), the maximum extent of the waveform was measured, with care taken to avoid arterial contamination.

Arterial flow was calculated by the equation:

$$\text{Total umbilical artery flow (ml/min)} =$$
$$\text{mean arterial time-averaged velocity (cm/s)} \times$$
$$\text{mean cross-sectional area (cm}^2) \times 2 \times 60$$

Venous flow was calculated similarly:

$$\text{Total umbilical vein flow (ml/min)} =$$
$$\text{Mean venous time-averaged velocity (cm/s)} \times$$
$$\text{mean cross-sectional area (cm}^2) \times 60$$

Average flow was calculated from the mean of the venous and the arterial flow:

$$\text{Average flow (ml/min)} =$$
$$\text{(total venous flow + total arterial flow)/2}$$

Average flow corrected for estimated fetal weight was calculated:

$$\text{Average flow corrected for estimated fetal weight}$$
$$\text{(ml/kg per min)} = \text{average flow (ml/min)/estimated fetal}$$
$$\text{weight (kg)}$$

Data were analyzed by the Statistical Package for Social Sciences (SPSS). The data for all parameters were tested for normality. Reference ranges and the 5th, 50th and 95th centiles are shown. A p value of < 0.05 was regarded as significant.

RESULTS

All subjects were between 23 and 33 weeks' gestation; the median gestation at examination was 28 weeks. The Doppler flow examination took 3–10 min, with a median of 6 min. Intraobserver variability was calculated from three measurements obtained consecutively by each operator (C.L. and G.A.) for the following parameters: umbilical vein time-averaged velocity, umbilical vein area, umbilical artery time-averaged velocity and umbilical artery area (Table 1). The two observers performed blinded measurements independently on a minimum of six subjects; the interobserver variability data are shown in Table 2.

There was a significant increase with gestation in umbilical artery area from 0.05 ± 0.01 cm^2 at 23 weeks to 0.10 ± 0.01 cm^2 at 33 weeks ($r = 0.69$, $p < 0.001$; Figure 1) and umbilical vein area from 0.20 ± 0.7 cm^2 at 23 weeks to

Table 1 Intraobserver variability

	Degrees of freedom	Mean square	Estimated standard deviation
Umbilical vein TAV			
observer 1	12	38.8	1.3
observer 2	7	1.2	1.1
Umbilical vein area			
observer 1	15	1389.4	37.3
observer 2	9	1549.4	39.4
Umbilical artery TAV			
observer 1	13	6.5	2.6
observer 2	8	11.2	3.4
Umbilical artery area			
observer 1	21	139.1	11.8
observer 2	12	799.8	28.3

TAV, time-averaged velocity

Table 2 Interobserver variability

	n	Mean average	Mean difference	95% limits of agreement
Umbilical vein TAV	6	10.2	1.1	−5.5, 7.8
Umbilical vein area	7	35.5	−0.3	−5.0, 4.2
Umbilical artery TAV	7	20.4	−2.3	−10.3, 5.7
Umbilical artery area	7	9.2	0.1	−4.3, 4.6

TAV, time-averaged velocity

0.46 ± 0.7 cm^2 at 33 weeks ($r = 0.79$, $p < 0.001$; Figure 2). Umbilical artery time-averaged velocity increased significantly from 16.33 ± 3.4 cm/s at 23 weeks to 19.78 ± 3.4 cm/s at 33 weeks ($r = 0.33$, $p < 0.001$; Figure 3) and umbilical vein time-averaged velocity from 8.16 ± 2.24 cm/s at 23 weeks to 10.79 ± 2.25 at 33 weeks ($r = 0.38$, $p < 0.001$; Figure 4).

There was a significant increase in umbilical arterial flow from 112.66 ± 58.32 ml/min at 23 weeks to 256.46 ± 58.9 ml/min at 33 weeks ($r = 0.66$, $p < 0.001$; Figure 5) and umbilical vein flow from 95.04 ± 64.8 ml/ min at 23 weeks to 303.28 ± 63.8 ml/min at 33

weeks ($r = 0.76$, $p < 0.001$; Figure 6). A close correlation was demonstrated between arterial flow and venous flow over the gestation range 23–33 weeks ($r = 0.9$, $p < 0.001$; Figure 7). Umbilical artery pulsatility index showed an inverse correlation with average volume flow ($r = -0.25$, $p < 0.05$; Figure 8).

Average flow was calculated from the mean of venous and arterial flow. Average flow per unit of estimated fetal weight showed a non-significant reduction from 189.17 ± 51 ml/kg per min at 23 weeks to 176.17 ± 51 ml/kg per min at 33 weeks ($r = 0.1$, $p = 0.11$; Figure 9).
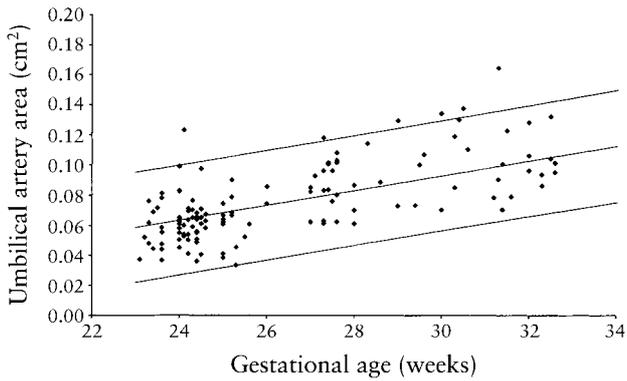

Figure 1 Normal range of umbilical artery area from 23 to 33 weeks of gestation
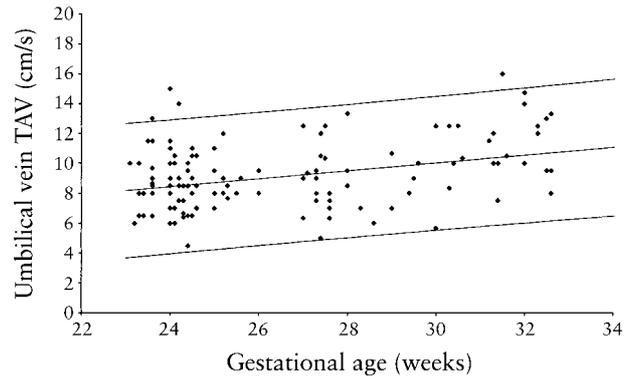

Figure 4 Normal range of umbilical vein time-averaged velocity (TAV) from 23 to 33 weeks of gestation
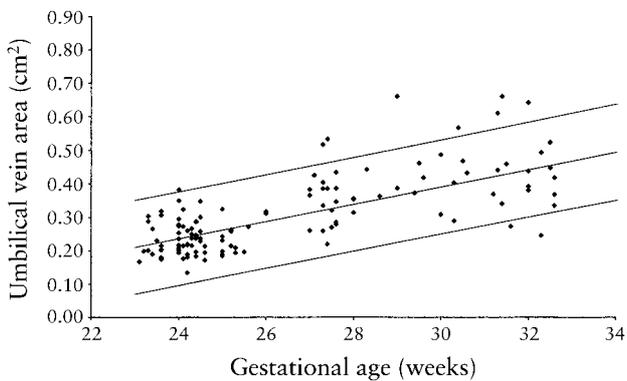

Figure 2 Normal range of umbilical vein area from 23 to 33 weeks of gestation
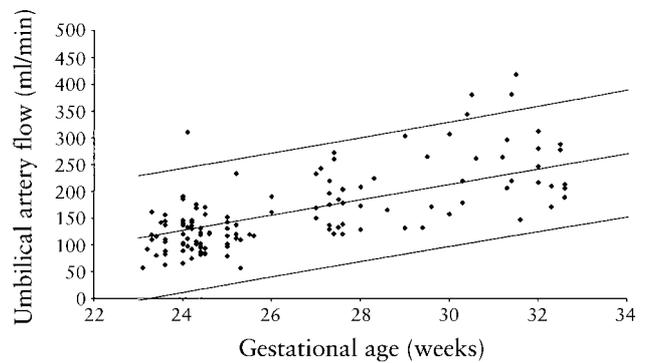

Figure 5 Normal range of umbilical artery flow from 23 to 33 weeks of gestation
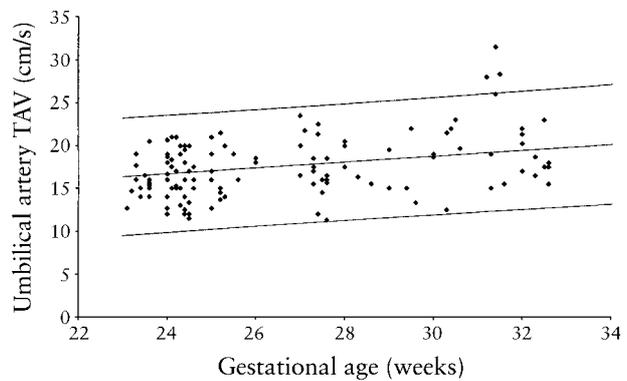

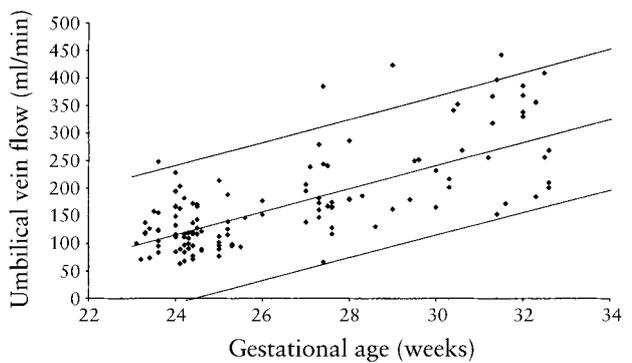**Figure 3** Normal range of umbilical artery time-averaged velocity (TAV) from 23 to 33 weeks of gestation
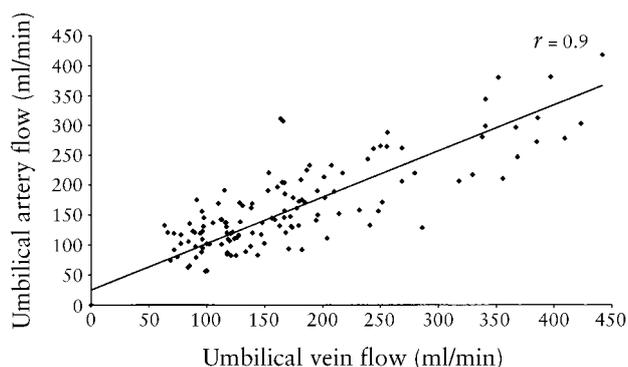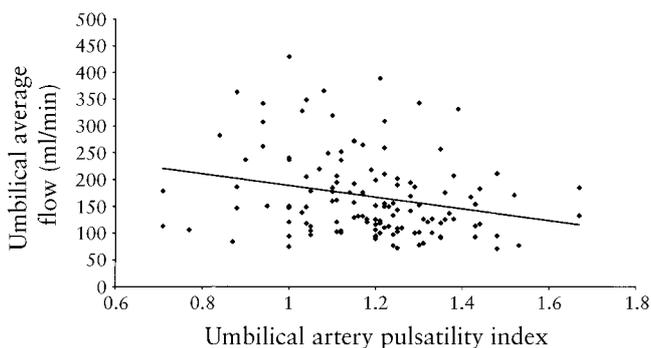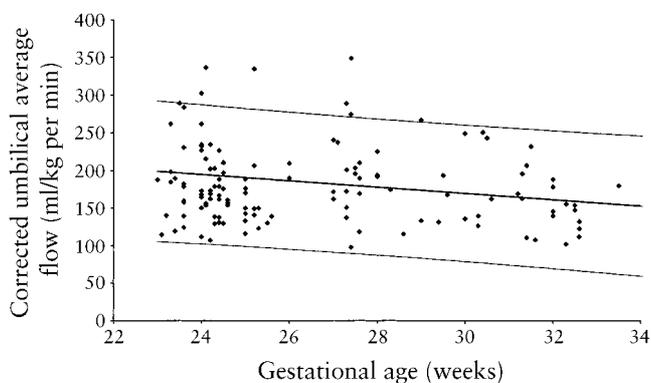

Figure 6 Normal range of umbilical vein flow from 23 to 33 weeks of gestation

Figure 7 Correlation between umbilical vein flow and umbilical artery flow

Figure 8 Correlation between umbilical artery pulsatility index and umbilical average flow

Figure 9 Normal range of umbilical average flow corrected for estimated fetal weight, from 23 to 33 weeks of gestation

DISCUSSION

This study has demonstrated results for average umbilical flow per unit weight that are comparable to, although higher than, those of previous studies measuring umbilical vein flow in the fetus (Table 3). These data most closely resemble those of Gill and colleagues[5] who reported intra-abdominal umbilical vein blood flow per unit weight to be 120 ml/kg per min at 35 weeks' gestation, and the estimate of Kuenzel and colleagues[7] of 143 ml/kg per min at term (based on an average birth weight of 3.6 kg). The flow volume estimate from this study gives an average of the arterial and venous flow (per unit estimated fetal weight) of 176 ml/kg per min at 33 weeks. Assuming that the linear reduction in flow per unit weight holds for later gestations, extrapolating our regression line would give an estimate for umbilical flow of approximately 168 ml/kg per min at term. It must be stated, however, that we estimated fetal weight sonographically by the Hadlock formula[9]; the error of this method may be in the region of 15%.

Ex utero umbilical vein thermodilution studies cannot be compared directly with *in utero* flow measurements as the seconds following delivery are associated with rapid closure of the umbilical vein[2,3]. Xenon radioisotope injection into the intervillous space can be a major source of error through incorrect injection technique or placental heterogeneity[1].

This work departs from previous studies in that we combined blood flow measurements for both the arteries and vein in the same umbilical cord to give an estimation of average flow. For reasons apparent later in this discussion, this is likely to minimize the error associated with measuring both the low velocities found in the vein and the small diameters associated with the artery. The flow through the umbilical artery closely matched that in the vein within the gestation range studied (r = 0.9). The vein flow was, however, slightly higher than the arterial flow. This may be explained by the fact that, although the high-pass filter was reduced to its minimum, it would artificially elevate the mean measured velocity in the vein, leading to an apparently slightly higher velocity.

The increase in flow throughout gestation was more dependent on the increase in vessel cross-sectional area than on the mean velocity (Figures 1–4). Furthermore, in common with the findings of other authors[5], the increase in umbilical flow with gestation was outstripped by an

Table 3 Umbilical flow studies of other authors

Authors	Gestation range (weeks)	Method	Approximate umbilical blood flow (ml/kg per min)
Stembera *et al.* (1965)[3]	(term)	thermodilution at delivery	75 (venous)
Clavero *et al.* (1973)[1]	39–40	xenon injection into intervillous space	27–56* (venous)
McCallum (1977)[2]	37–42	thermodilution at delivery	40–70† (venous)
Eik-Nes *et al.* (1980)[4]	32–41	Doppler	105 (venous)
Jouppila and Kirkinen (1983)[6]	30–36	Doppler	100 (venous)
Gill *et al.* (1984)[5]	22–40	Doppler	90–120 (venous)
Kuenzel *et al.* (1992)[7]	37–40	Doppler	143 (arterial)

*Approximated from original paper by assuming that fetoplacental volemia at term is approximately 340 ml; †derived from the original paper by dividing ml/min by birth weight

increase in fetal weight, thus leading to an effective reduction in umbilical flow per unit weight in later gestation. This implies reduced tissue perfusion in the later gestations, perhaps explaining the redistribution phenomenon that is seen with oxygenated blood preferentially directed through the heart to the fetal brain and associated with reduced cerebral impedance[10]. Another possible explanation would be the presence of more effective tissue perfusion and metabolism later in pregnancy, leading to a relatively lower tissue demand for blood flow.

The umbilical artery exhibits low pulsatility and low resistance flow under normal conditions. Indices such as S/D ratio, resistance index and pulsatility index are easily measured, because they do not require Doppler angle correction, but are altered by changes to both the proximal and the distal vasculature and blood flow. Neither index was designed for use in obstetrics; the pulsatility index was developed to evaluate proximal changes in resistance as a result of stenosis[11] and the resistance index to examine changes distal to the common carotid artery[12]. These indices have limited sensitivity to moderate changes in distal resistance in low-impedance vascular beds; large changes in vascular resistance may not be reflected by changes in the pulsatility index[13,14]. The complex relationship between input pressure pulsatility, impedance and distal resistance produces changes that defy simple analysis of the umbilical artery flow velocity waveform.

There is therefore no good reason why pulsatility and resistance indices should be particularly sensitive in measuring differences in fetoplacental blood flow in normal pregnancy. It is therefore not surprising that this study has demonstrated a relatively poor relationship between pulsatility index and volume flow in the umbilical artery. *In vitro* tests have shown that Doppler can produce consistent and reliable results under controlled conditions in measuring the volume flow of vessels including the carotid, renal, mesenteric and uterine arteries[15–17]. The technique requires measurement of vessel size (either as a diameter or the cross-sectional area) and of mean velocity in the vessel; these measurements are major sources of error[18,19].

Area measurement is influenced by image resolution and accuracy of cursor placement, obliquity of diameter/cross-sectional measurement and the pulsatility of the artery. The small diameter of the umbilical arteries makes quantification of cross-sectional area difficult, whether by B-mode or M-mode imaging[20]. The finite pulse length causes echoes to appear longer than the interfaces from which they are scattered or reflected. If a measurement of only diameter is used, the slice thickness can cause underestimation of the diameter, as echoes are obtained from an arc of the vessel wall rather than from opposite surfaces. Since slice thickness focusing for most array transducers is fixed, compensation may be made by measuring from the more superficial edge of each wall[21]. Therefore, we measured cross-sectional area using the center of each wall echo as the basis from which to draw a circle. Our M-mode umbilical artery tracings indicate that diameter changes in the cardiac cycle were too low to be measurable and changes in cross-sectional area were not observed in cine-loop analysis

of the image. This suggests that errors due to changes in area through the cardiac cycle were negligible.

Velocity measurement is influenced by non-uniform insonation of the vessel under investigation, insonation of adjacent vessels, inaccurate beam/flow angle correction and high-pass filter setting. Inherent inaccuracies of the Doppler measurement system were reduced to a minimum by adjusting to the manufacturer's recommended settings. The umbilical arteries and veins are small and curved, making angle correction more difficult than for a straight vessel. The beam/flow angle was kept in most cases to within 30°, and in all cases within 60° to ensure that small errors in angle correction were well tolerated. The Doppler filter was kept at its lowest setting. The vessels are closely adjacent and, despite efforts to insonate a single vessel only, there is the risk that unintended insonation of a second vessel detracts from or adds to the mean velocity recorded. The small size of the vessels does mean, however, that flow is likely to be uniformly insonated across their area.

In the measurements made, we assumed that the limited resolution of mean velocity resulted in better accuracy of measurement of arterial velocity than for venous, where the velocities are lower. However, the smaller size of the arteries tended to produce greater errors in cross-sectional area measurement than in the vein. This led us to take the mean of arterial and venous flow measurements to derive a weight-corrected mean flow parameter in an effort to reduce to a minimum the errors with measuring either artery or vein flow alone.

In conclusion, we have demonstrated that it is possible to obtain measurements of volume flow in the umbilical cord, corrected for weight, that are consistent with previously reported results using Doppler ultrasound. Our method has acceptable intra- and interobserver variability, does not require extreme skill or specialized ultrasound apparatus, and is not particularly time intensive, the median examination time being 6 min. As has previously been suggested, umbilical volume flow calculation may be particularly useful in pathological states such as intrauterine growth restriction or rhesus isoimmunization[5,8]. Further work is needed to investigate whether umbilical volume flow or the pulsatility index is the more accurate index of fetoplacental vascular perfusion.

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