Comparison of Variations Between Spectral Doppler and Gaussian Surface Integration Methods for Umbilical Vein Blood Volume Flow

Jonathan M. Rubin, MD, PhD, Sibo Li, PhD, J. Brian Fowlkes, PhD, Shriram Sethuraman, PhD, Oliver D. Kripfgans, PhD, William Shi, PhD, Marjorie C. Treadwell, MD, James R. Jago, PhD, Ronald D. Leichner, Stephen Z. Pinter, PhD

Objectives—We are studying a new method for estimating blood volume flow that uses 3-dimensional ultrasound to measure the total integrated flux through an ultrasound-generated Gaussian surface that intersects the umbilical cord. This method makes none of the assumptions typically required with standard 1-dimensional spectral Doppler volume flow estimates. We compared the variations in volume flow estimates between techniques in the umbilical vein.

Methods—The study was Institutional Review Board approved, and all 12 patients gave informed consent. Because we had no reference standard for the true umbilical vein volume flow, we compared the variations of the measurements for the flow measurement techniques. At least 3 separate spectral Doppler and 3 separate Gaussian surface measurements were made along the umbilical vein. Means, standard deviations, and coefficients of variation (standard deviation/mean) for the flow estimation techniques were calculated for each patient. $P < .05$ was considered significant.

Results—The ranges of the mean volume flow estimates were 174 to 577 mL/min for the spectral Doppler method and 100 to 341 mL/min for the Gaussian surface integration (GSI) method. The mean standard deviations (mean $\pm$ SD) were 161 $\pm$ 95 and 45 $\pm$ 48 mL/min for the spectral Doppler and GSI methods, respectively ($P < .003$). The mean coefficients of variation were 0.46 $\pm$ 0.17 and 0.18 $\pm$ 0.14 for the spectral Doppler and GSI methods respectively ($P < 0.002$).

Conclusions—The new volume flow estimation method using 3-dimensional ultrasound appears to have significantly less variation in estimates than the standard 1-dimensional spectral Doppler method.

Key Words—color Doppler; Doppler; power Doppler; umbilical cord blood flow; umbilical vein volume flow

Received February 26, 2020, from the Department of Radiology, University of Michigan, Ann Arbor, Michigan, USA (J.M.R., J.B.F., O.D.K., S.Z.P.); Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Michigan, USA (M.C.T.); and Philips Research North America, Cambridge, Massachusetts, USA (S.L., S.S., W.S., J.R.J., R.D.L.). Manuscript accepted for publication June 21, 2020.

This work was partially supported by National Institutes of Health grants R21HD095501-01A1 and 5R01HD097756-01 and was performed in conjunction with and was partially supported by Philips Healthcare (Bothell, WA).

Address correspondence to Jonathan M. Rubin, MD, PhD, Department of Radiology, University of Michigan, 3208C Medical Sciences Building 1, 1301 Catherine St, Ann Arbor, MI 48109, USA.

E-mail: jrubin@med.umich.edu

Abbreviations

2D, 2-dimensional; 3D, 3-dimensional; GSI, Gaussian surface integration

doi:10.1002/jum.15411

Umbilical cord blood flow has been considered the physiologic analog in fetuses to cardiac output in adults, and studies have shown the potential of true umbilical cord blood flow in the early diagnosis of fetal conditions such as intrauterine growth restriction and preeclampsia.[1–11] Unfortunately, umbilical cord blood flow measurements are rarely used in clinical practice. This is because they are difficult and tedious to perform and require multiple unjustified assumptions to make the

flow estimate.[12–15] Since standard blood flow estimates are based on both measurements of the vessel diameter from 2-dimensional (2D) B-mode ultrasound images to calculate the cross-sectional area and 1-dimensional spectral Doppler imaging for making mean velocity estimates, these flow measurements are angle dependent, flow geometry dependent, and vessel cross-section shape dependent. Accumulations of errors in these measurements lead to large errors in blood flow estimates.[13]

We have been developing a method for estimating blood volume flow that uses a process that has none of the limitations described above.[11,16–18] The method is angle independent, flow profile independent, and vessel geometry independent. It uses a technique developed by the mathematician Carl Friedrich Gauss, which defines blood flow as the integral of the total flux across a vessel. The method requires a 3-dimensional (3D) ultrasound acquisition to define a C-surface across the ultrasound field that intersects the vessel of interest. The method, originally defined in 1979, has been used to determine cardiac output, flows through transjugular intrahepatic portosystemic shunts, and umbilical vein blood flow.[18–25] The C-surface is acquired such that all of the ultrasound Doppler velocity components from the transducer are perpendicular to the C-surface.[16]

Given the many sources of error inherent in the spectral Doppler volume flow technique, we wanted to determine whether the variations among estimates of umbilical vein volume flow would be different between the flow measurement techniques. We, therefore, designed a study to test this.

Materials and Methods

This was a University of Michigan Institutional Review Board–approved (HUM00075665) prospective study in which all patients gave written informed consent. All examinations were performed at the University of Michigan Von Voigtlander Women's Hospital. The study was limited to women who had high-risk gestations and were hospitalized during pregnancy. Since all of these patients were hospitalized under observation, they were not pressed for time and were very willing to participate in our study. Twelve women between the gestational ages of 24 weeks and 35 weeks 5 days were included in the study. Each patient had a singleton gestation. The demographics of the included patients are shown in Table 1.

Scans were performed with an EPIQ 7 ultrasound scanner (Philips Healthcare, Bothell, WA) using a 2D array transducer, either an X6-1 or XL14-3. The choice of transducer depended on scanning-related issues, such as the body habitus and depth to the sampling site along the umbilical vein, and the availability of a specific transducer. Across all patients' volume flow measurements, there were 25 spectral Doppler

Table 1. Patient Descriptions

Patient	Reason(s) for Hospitalization	Method of Delivery	Gestational Age at Delivery, wk + d	Birth Weight, g	Sex
1	Autoimmune neutropenia, history of preeclampsia, history of cervical incompetence, prior cesarean delivery	Cesarean	39 + 2	3795	Male
2	Severe preeclampsia	Cesarean	34 + 0	2130	Male
3	Placenta accreta, bleeding, hysterectomy	Cesarean	37 + 0	2845	Female
4	Elevated blood pressure	Cesarean	31 + 1	975	Male
5	Gestational diabetes, at risk for preeclampsia, β-thalassemia	Cesarean	39 + 1	2935	Female
6	Severe IUGR, preeclampsia	Cesarean	32 + 3	1505	Female
7	Severe IUGR, preeclampsia	Cesarean	28 + 5	670	Female
8	Severe preeclampsia, multiple congenital anomalies	Cesarean	33 + 6	1760	Male
9	Systemic lupus	Vaginal	37 + 1	2730	Male
10	Severe preeclampsia	Vaginal	36 + 4	2075	Male
11	Chronic hypertension	Cesarean	36 + 6	3335	Male
12	Chronic hypertension with preeclampsia	Cesarean	36 + 6	2177	Female

IUGR indicates intrauterine growth restriction.

estimates made with the XL14-3, 18 spectral Doppler estimates made with the X6-1, 22 Gaussian surface integration (GSI) estimates made with the XL14-3, and 18 GSI estimates made with the X6-1. In 1 patient, measurements were made only with the X6-1; 6 had only XL14-3 measurements; and 5 had both X6-1 and XL14-3 measurements. These are shown in Table 2. One spectral Doppler measurement with the X6-1 was excluded because of a lack of angle correction and diameter measurement.

At least 6 separate volume flow measurements were made along the umbilical vein in each case. One measurement was made by the standard spectral Doppler technique in which a straight segment of the umbilical vein was identified. A Doppler sample volume was placed in the vein with the range gate extended across the vein's lumen; an angle-corrected Doppler spectrum was obtained; and the mean velocity through the range gate was measured over time. The umbilical vein diameter was measured across the vessel perpendicular to the angle correction marker. When necessary, color Doppler imaging was used to define the margins of the vessel when the vessel was in an orientation not perpendicular to the sound field. Spectral Doppler volume flow was calculated as

$$Q = \pi(d/2)^2 < v >,$$

where Q is volume flow; d is the diameter of the umbilical vein as shown along the segment of vein being analyzed; and $< v >$ is the mean velocity of the blood at the site of measurement. This calculation was performed on the ultrasound scanner itself. Each Doppler measurement, including vessel diameter, angle correction, and site of measurement, was assessed by 2 observers (J.M.R. and S.Z.P.), and both observers had to agree on the measurement before it was recorded. For each of the spectral Doppler volume flow estimates made on the ultrasound machine, the observers could see what measurement was recorded on screen.

We attempted as best as possible to pair spectral Doppler measurements with GSI measurements at similar sites along the umbilical cord. However, because of differences in the acquisition methods, identical sites for each method could not always be used. Fortunately, volume flow should be the same at all locations along the cord such that the variation on measures should be indicative of the associated errors and not the absolute position along the cord.

Spectral Doppler measurements are made in a longitudinal orientation with the direction of the cord positioned parallel to the scan head face (Figure 1). For the GSI method, the cord is more or less directed toward the scan head so the beam can be swept across the cord (Figure 1). The orientation is not absolutely critical, since the method is angle independent as long as a Doppler shift can be obtained across the flow. Changes in fetal position also made it impossible to absolutely scan at the same location for both the spectral Doppler and GSI methods. Ultimately, as mentioned, at least 6 separate measurements of volume flow were made in each case. Three patients had an additional spectral Doppler measurement not paired with a GSI measurement, and 1 patient had an additional GSI measurement not paired with a spectral Doppler measurement (Table 2).

The GSI volume flow method itself has been described previously.[16] However, briefly, a segment of the umbilical cord is identified such that a C-surface can be defined across the ultrasound beam that intersects the umbilical vein, and the surface is defined as being equidistant along all of the ultrasound beams from the scan head surface. This particular Gaussian surface is not unique and is defined so that all of the Doppler vectors are perpendicular to the surface. This is perfect for calculating flow by using Gauss's divergence theorem (Equation 1). To do this, a 2D ultrasound array sweeps the beam across the blood vessel, making a Doppler estimate for each beam as it intersects the vessel cross section. The area of each beam's cross section where it intersects the umbilical vein multiplied by the mean Doppler shift at that position represents the local flux. The sum of all of these local fluxes across the vein is equal to volume flow. This is represented by the following equation and is known as Gauss's divergence theorem:

$$Q = \oint \mathbf{v} \cdot d\!\!\!/ A, \qquad (1)$$

where Q is volume flow, and v is the velocity of blood passing through a small area component, dA. In this case, dA corresponds to the beam cross-section; • is

Table 2. Volume Flow Data and Analysis

Patient	Transducer	Gaussian Surface, mL/min				Mean, mL/min	Standard deviation, mL/min	CV	Spectral Doppler, mL/min				Mean, mL/min	Standard deviation, mL/min	CV
1	XL14-3	230	246	229	x	235	9.5	0.041	562	959	209	x	577	375.2	0.651
2	X6-1	290	220	240	x	250	36.1	0.144	107	374	417	x	299	167.9	0.561
3	XL14-3	544	209	246	x	333	183.7	0.552	603	285	537	x	475	167.8	0.353
4	XL14-3	186	203	187	x	192	9.5	0.050	94	243	234	x	190	83.5	0.439
5	XL14-3	289	318	417	x	341	67.1	0.197	328	472	370	274	361	83.8	0.232
6	XL14-3	266	217	331	x	271	57.2	0.211	368	111	396	x	292	157.1	0.539
7	XL14-3	122	110	110	x	114	6.9	0.061	166	235	180	187	192	30.0	0.156
8	X6-1/XL14-3	90	83	123	104	100	17.6	0.176	207	113	202	x	174	52.9	0.304
9	X6-1/XL14-3	120	209	138	166	158	38.8	0.245	114	137	191	478	230	168.5	0.732
10	X6-1/XL14-3	218	222	263	x	234	24.9	0.106	313	434	156	585	372	182.0	0.489
11	X6-1/XL14-3	233	335	284	323	294	46.0	0.157	220	856	443	418	484	267.2	0.552
12	X6-1/XL14-3	261	230	218	164	218	40.5	0.185	591	184	572	354	425	193.5	0.455

Measured volume flow data from 12 patients using the Gaussian surface method and the spectral Doppler method. Each patient had at least 3 Gaussian surface measurements and at least 3 spectral Doppler measurements of the umbilical vein volume flow in their umbilical cord. Four patients had 4 Gaussian surface measurements, and 6 had 4 spectral Doppler measurements. When only 3 measurements were made in a particular category, an x was inserted into the empty slot. CV indicates coefficient of variation.

the dot product, which ensures that the velocity component being measured is perpendicular to the small area component, and the dot product $v \bullet dA$ is the local flux. For ultrasound, the velocity component in the dot product is along the ultrasound beam, which removes the need to angle correct the measurement.[16]

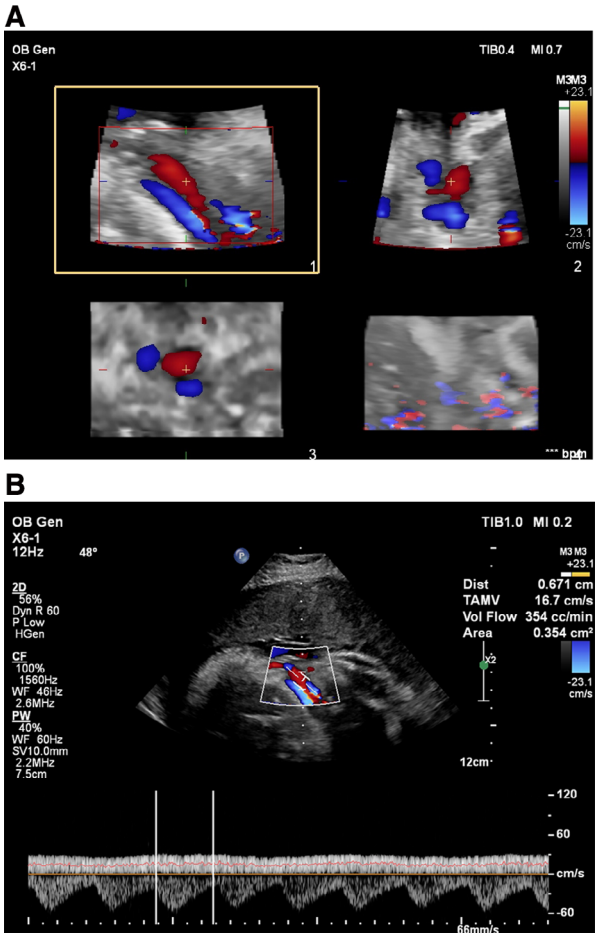
The only remaining issue is partial volume correction, which is required, since some of the area elements are partly in flowing blood and partly outside the lumen. To fully count these areas would cause an overestimate of the measurement. Partial volume correction is accomplished by using power Doppler ultrasound in which the power in each area element is normalized by the power in area elements from the center of the vein that are fully in blood. The fraction of flowing blood in the area element is applied as a weighting factor to the flux to compensate for partial volume in the area.[16,26,27] The distribution of power values that correspond to 100% blood are assigned fractional pixel weighting $w = 1$; partial-volume pixel values are assigned fractional pixel weights of $0 < w < 1$; and background pixels are assigned $w = 0$. These weightings are obtained from a histogram composed of power Doppler values produced from several C-surface slices above, below, and including the surface of interest.[28] The partial volume weights are generated from this histogram.

At least 20 samples, ie, 20 3D volumes, of umbilical vein flow were acquired at each position; the mean flow calculated from these samples was used as the flow measurement at each position. With a 2D array ultrasound transducer, it generally took on the order of 5 to 10 seconds to acquire a multivolume data set at each position.

All the GSI volume flow estimates were calculated offline by an algorithm developed by Philips Healthcare. The operators (J.M.R. and S.Z.P.), were totally blinded to these results. The spectral Doppler estimates were processed by volume flow software on the EPIQ 7 scanner, and the operators knew the results at the time of measurement.

A mean umbilical vein volume flow estimate using the spectral Doppler method and the GSI method was made for each sampling position. Since the mean blood flow in the umbilical cord has to be the same at all positions, we averaged the estimates of each method to get the overall mean estimate for each patient. We then calculated the standard

Figure 1. A, Color flow images of the vessels in the umbilical cord in one of the sampling positions for patient 12 in this study. The umbilical arteries are blue and the umbilical vein is red. A + is positioned in the umbilical vein identifying a 3D point that coincides in the 3 acquired views. Image 1 is an image along the length of the vein and one of the arteries. Image 2 is perpendicular to image 1. It would correspond to a transverse image if image 1 is a longitudinal image of the umbilical vein and umbilical arteries. Image 3 is the C-surface or Gaussian surface image from which volume flow is calculated. Summing the local flux measurements across the vein (red) in this image produces a volume flow estimate. Image 4 corresponds to a 3D rendering in which the vessels are poorly visualized. This view is not used when positioning the cord in the C-surface or for volume flow measurement. Color bar indicates velocity in centimeters per second. **B**, Color flow image and angle-corrected spectral Doppler estimate for volume flow in patient 12. The angle correction (48°) and vessel diameter (0.671 cm) estimates are shown. The venous spectral trace with the mean estimate represented by the orange line through the venous trace is shown at the bottom of the image. The white vertical bars on the trace indicate the time interval used for averaging. The volume flow estimate is 354 mL/min and is computed by using the average flow velocity (time-averaged mean velocity, 16.7 cm/s) and the area estimate based on the diameter measurement (0.354 cm^2). Color bar indicates velocity in centimeters per second.



deviation of the overall mean estimate, and finally, we calculated a coefficient of variation (standard deviation/overall mean) for each patient.

Comparisons of the mean standard deviations and mean coefficients of variation for both volume flow determination methods were made by paired *t* tests. $P < .05$ was considered significant.

Results

Twelve patients were scanned in this study (Table 2). The ranges of the mean umbilical vein volume flow estimates in these 12 patients were 174 to 577 mL/min for the spectral Doppler method and 100 to 341 mL/min for the GSI method. However, since we did not know the true umbilical vein flows in any of these cases, we instead compared the variations in the flow estimates. The mean standard deviation (mean ± SD) for the spectral Doppler method was 161 ± 95 mL/min, whereas the mean standard deviation for the GSI method was 45 ± 48 mL/min. This difference was highly significant ($P < .003$). The standard deviation magnitude could vary depending on how large the estimated mean value was, and as stated above, we did not know the true mean flow values. To account for this, we also compared the coefficients of variation of each of the estimates. The mean coefficient of variation for the spectral Doppler method was 0.46 ± 0.17, whereas the mean coefficient of variation for the GSI method was 0.18 ± 0.14. This difference was again highly significant ($P < .002$).

Discussion

Umbilical cord volume flow estimates have been referred to as "… a dream comes true …" for fetal assessments.[29] However, given the stated significance of the measurement, volume flow measurements are rarely performed during fetal surveys. A continuation of the above quote by Ferrazzi: "… but now for some standardization"[29] and a quote from Parra-Saavedra et al sum up the problem: "Through the years the repeated attempts to make umbilical flow a relevant clinical parameter have failed, probably due to large measurement variation (particularly in diameter

assessment) and the time-consuming technique."[12] Given that, for umbilical cord volume flow estimates to become a standard part of the obstetric armamentarium, a much more reliable and efficient method needs to be implemented.

We have been working on a method that overcomes many of the problems associated with the standard spectral Doppler estimate of volume flow.[16] The method is angle independent, flow profile independent, and vessel geometry independent. The method also does not require a caliper measurement of the umbilical vein's diameter. The technique requires a 3D ultrasound acquisition to define a 2D Gaussian surface that intersects the umbilical vein. Modern 3D color Doppler (velocity) ultrasound with simultaneous power Doppler imaging has made such measurements possible, and with a 2D ultrasound array transducer, such flow measurements could be performed in near real time once implemented on a clinical scanner. At a sampling rate of about 4 volumes per second, a mean volume flow measurement based on 20 flow estimates can be made in 5 seconds.

However, given concerns similar to those of Parra-Saavedra et al,[12] if the repeatability of the spectral Doppler method is a major issue, and if the GSI method could not improve on spectral Doppler's poor repeatability, then enthusiasm for the new method would be limited. On the basis of that, we performed our small study, which definitely suggests that the GSI volume flow quantification method is more repeatable than the spectral Doppler method. In fact, the GSI method had a coefficient of variation that was less than half that of the spectral Doppler method. This was not a surprise, since multiple sources of error that corrupt the spectral Doppler method do not affect the GSI method. In addition, acquisitions are straightforward, since the umbilical cord can be intersected in almost any arbitrary orientation and at any location along the cord as long as Doppler shifts are detectable. The potential rapidity of the acquisitions would make annoying problems such as fetal movement during scanning much less of an issue.

One of the advantages of volume flow measurement is that the average volume flow does not vary along the umbilical cord. This has to be the case, since there are no feeding or draining vessels entering or leaving the umbilical arteries or vein along the cord.[30] Therefore, any blood that enters and leaves the cord comes in at one end and leaves at the other. There are no branch vessels to divert the flow. There can be variations in instantaneous flow such as pulsations in the arteries, but the average must be the same. Thus, variations in mean volume flow estimates must be due to the measurement technique itself, such as incorrect assumptions, measurement inaccuracies, technical difficulties such as bad Doppler angles, etc. This also holds true on a physiologic basis, so it does not matter whether the flow is normal. Either way, the flow has to be the same along the cord. That is why we thought in this study that we could study umbilical vein flows in women with high-risk pregnancies.

There were some limitations to this study. First, the number of patients was relatively small. However, the difference in the mean coefficients of variation between the methods was large, with a Cohen effect size of 1.81, so we were sufficiently powered even with the 12 patients studied. The post hoc power for this study for $P < .05$, our significance threshold, was 0.80. However, given the small size of this study and the unusual population of high-risk patients, the findings herein should be validated in larger studies. Another potential issue was that all of the patients in this study were inpatients and had complications of pregnancy. This would definitely be an issue if we were investigating and comparing normal umbilical cord flow values between the spectral Doppler method and the GSI method. However, we were only interested in the precision of the flow measurements made by the techniques, so the absolute flow rates were not an issue. Next, since the spectral Doppler volume flow estimates were calculated on the ultrasound machine, the operators were not blinded. However, all of the GSI calculations were performed offline, and both observers were blinded to those. Since the focus of the study was on precision, not accuracy (the correct answer was not known), the observers could not know which measurement set was the more precise, ie, had the least variation, until after offline calculation of the GSI estimates. We therefore believe that the comparison of the precision of the techniques is valid. Follow-up studies to confirm this finding might still be in order, however.

Finally, we had no truth data for the flow in the umbilical vein, and frankly, multiple studies demonstrating umbilical venous flow by ultrasound did not have truth data in humans either.[1–6,8,9,11] It would be unethical to place a flow cuff around the umbilical cord in humans. Therefore, normal values are typically based on ranges defined by clinical experiences. That is not to say that the GSI flow method is not accurate. Multiple evaluations of the GSI method in phantoms and animals have shown excellent accuracies even in circumstances in which the standard Doppler method would likely fail because of flow situations that do not adhere to the strict assumptions made with that technique.[17,31]

In conclusion, this study suggests that the GSI 3D approach to flow quantification is much more precise than the current spectral Doppler method. Furthermore, it is not hard to believe that flow measurements using this method will be easier to perform than those with the spectral method, particularly since the requirements of angle correction and vessel diameter measurement are no longer necessary. Given the improved ease of use and better precision of the GSI measurement, normal and abnormal umbilical vein volume flow ranges will need to be clinically defined, just as they have been defined for blood flow parameters such as resistive indices, pulsatility indices, and systolic/diastolic ratios.[32] There should be definite interest in defining these ranges, since multiple early clinical studies have shown the ability of volume flow measurements to make accurate diagnostic predictions regarding conditions such as intrauterine growth restriction and preeclampsia.[1–11] Hopefully, these incentives will lead to umbilical cord volume flow measurements becoming a part of standard fetal surveys.

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