

Umbilical Artery Half-Peak Systolic Velocity Deceleration Time in Fetal Growth Restriction

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Key Words

Umbilical artery · Impedance indices · Doppler · Fetal growth restriction · Perinatal death · Half-peak systolic velocity deceleration time

Abstract

Objective: To study the umbilical artery (UA) half-peak systolic velocity deceleration time (hPSV-DT) in pregnancies complicated by fetal growth restriction (FGR). **Methods:** The study included 266 singleton, high-risk pregnancies with an estimated fetal weight <10th percentile, which were examined between 24 and 40 weeks' gestation and delivered within a week from the last ultrasound evaluation. UA hPSV-DT was measured with Doppler ultrasound in the same wave used to measure the pulsatility index. UA hPSV-DT values were correlated with perinatal outcome. **Results:** UA hPSV-DT <5th percentile was found in 87 and 98% of fetuses with moderate and severe FGR, respectively. 94% of fetuses with a UA hPSV-DT <90 ms had poor perinatal outcome including perinatal death or prolonged admission to the neonatal intensive care unit. None of the fetuses had a UA hPSV-DT <70 ms. Perinatal death occurred in 39 fetuses; UA hPSV-DT was abnormal in all of them, with 95% of these fetuses having values of ≤ 120 ms. In the group of fetuses with absent/reverse end-diastolic velocity in the UA, the perinatal mortal-

ity rate was 51% for those with a UA hPSV-DT ≤ 90 ms and only 23% for those having a UA hPSV-DT >90 ms ($p < 0.01$). **Conclusions:** UA hPSV-DT seems to be a useful technique in the evaluation of pregnancies at risk for FGR and perinatal death. Additionally, hPSV-DT was shown to be a good predictor of perinatal death, with values of <90 ms corresponding to imminent risk of intrauterine demise and values of <70 ms being likely to be incompatible with intrauterine life.

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Introduction

Placental insufficiency is a key event in several fetal conditions characterized by histological changes in the placenta and progressive increase in placental vascular resistance leading to fetal growth restriction (FGR), hypoxia, and perinatal death [1–6]. Umbilical artery (UA) Doppler flow velocimetry provides important information for assessing placental vascular resistance during the second half of pregnancy and thus helps clinicians in the management of pregnancies at risk for FGR [7–10]. The incorpo-

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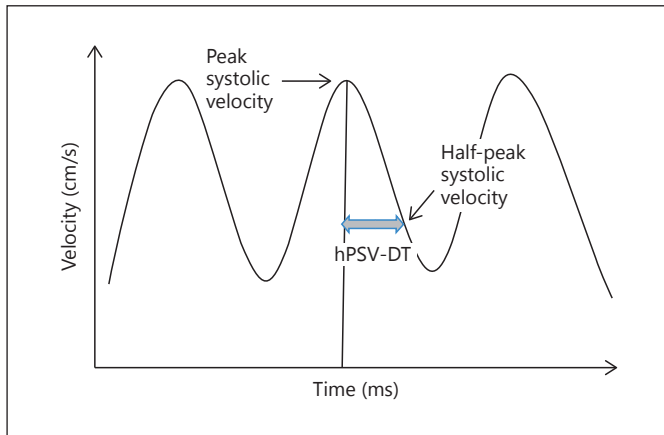


Fig. 1. Schematic representation of hPSV-DT.

ration of this technique into clinical practice has shown to improve perinatal outcomes in pregnancies with FGR, whereas the adjunct value of middle cerebral artery, ductus venosus, and cerebroplacental Doppler indexes is still under discussion [11–15].

UA Doppler indices that are traditionally used for assessing placental vascular resistance include the pulsatility index (PI), resistance index, and systolic/diastolic ratio. The UA half-peak systolic velocity deceleration time (hPSV-DT) is a new Doppler velocimetry index based on the time it takes the UA to halve its maximum systolic velocity (fig. 1) [16]. We have previously reported normative data for UA hPSV-DT showing increasing linear values as pregnancy progresses and demonstrated the potential utility of this technique in evaluating placental vascular resistance in fetuses with bradyarrhythmia [16]. As expected, UA hPSV-DT was inversely proportional to UA PI, suggesting that UA hPSV-DT measures the compliance of the placenta and, as such, increased placental vascular resistance manifests as a decrease in UA hPSV-DT [16]. In pregnancies with increasing placental vascular resistance – and therefore decreasing compliance – the diastolic flow velocity in the UA decreases rapidly, resulting in a short deceleration period. Similar concepts have been used in pediatric and fetal cardiological evaluation, namely the ‘systolic velocity half time’ in the descending aorta of children with coarctation of the aorta [17] and the ‘intermediate diastolic velocity’ of the atrioventricular valves of fetuses with FGR [18]. However, we are not aware of any mathematical or experimental information on the diastolic phase of the fetal arteries that can explain this phenomenon in detail.

Table 1. Obstetric conditions affecting the study group

Pathology	n	%
Fetal growth restriction only	164	61.7
Preeclampsia	50	18.8
Chronic hypertension	22	8.3
Another hypertensive disorder	10	3.8
Previous fetal demise	5	1.9
Lupus	4	1.5
Nephropathy	2	0.8
Other	9	3.4
Total	266	100

To date, no information on the usefulness of UA hPSV-DT in high-risk pregnancies has been reported. We hypothesized that abnormal UA hPSV-DT, as an indicator of increased placental vascular resistance, could be associated with increased risk of FGR and perinatal death. The aim of this study was therefore to examine UA hPSV-DT in pregnancies with FGR, with special focus in those cases ending in perinatal death.

Subjects and Methods

The study group was prospectively recruited from pregnant women attending the Ultrasound Unit, Department of Obstetrics and Gynecology, San Juan de Dios Hospital, which is a teaching hospital of tertiary level. High-risk patients were mainly referred for evaluation, management, and delivery because of suspected FGR or medical and obstetrical conditions associated with placental insufficiency. This study was approved by the local Institutional Review Board, and all patients gave consent for ultrasound examination, including Doppler studies of the fetoplacental circulation. Pregnancies that met the following inclusion criteria were eligible for the current study: (1) singleton live fetus; (2) gestational age between 23 and 40 weeks’ gestation; (3) reliable gestational age confirmed by first-trimester ultrasound examination; (4) estimated fetal weight <10th percentile for gestational age calculated using the formula of Hadlock et al. [19] and plotted against the nomogram for birth weight in Chilean newborns [20], and (5) absence of associated fetal malformation, chromosomal abnormality, and congenital infection at the time of the scan or at delivery.

All patients underwent a detailed scan for fetal biometry, anatomical survey and UA Doppler flow velocimetry. All examinations were carried out by 1 of 3 independent maternal-fetal medicine specialists with at least 5 years of experience performing obstetric scans using high-resolution ultrasound equipment with color Doppler (Sonoace 8000 EX, Sonoace 8800 MT; Medison, Seoul, Korea, and Philips HD9, Amsterdam, The Netherlands). UA Doppler flow waveforms were obtained during fetal apnea, absent fetal movement, and at an insonation angle of <45° until a minimum of three similar waves were documented on the screen.

Table 2. UA hPSV-DT and PI according to birth weight classification

	AGA		Moderate FGR		Severe FGR		Total	
	%	n	%	n	%	n	%	n
Normal UA hPSV-DT	36.2	29/80	13.5*	19/141	2.2*	01/45	18.4	49/266
Abnormal UA hPSV-DT	63.8	51/80	86.5*	122/141	97.8*	44/45	81.6	217/266
Abnormal UA hPSV-DT, delivery <34 weeks	80.6	29/36	94.6*	88/93	96.4*	27/28	91.7	144/157
UA hPSV-DT <120 ms	30	24/80	50.4*	71/141	68.9*	31/45	47.4	126/266
Normal UA PI	70	56/80	45.4*	64/141	28.9*	13/45	50	133/266
Abnormal UA PI	30	24/80	54.6*	77/141	71.1*	32/45	50	133/266
UA AREDV	10	8/80	31.2*	44/141	53.3*	24/45	28.6	76/266
Mean GA, weeks	34		32.5		30.8*		32.7	
Mean birth weight, g	2,017		1,454*		1,063*		1,557	

GA = Gestational age; abnormal hPSV-DT = <5th percentile; abnormal PI = >95th percentile. * $p < 0.01$ vs. AGA.

The wave with the highest systolic velocity and least noise was selected for measuring the UA PI using the built-in program software. Subsequently, the same wave was used for measuring UA hPSV-DT as previously reported [16]. The intraobserver and interobserver variability for UA hPSV-DT measurement was 7.4 and 10.7%, respectively [16].

Information obtained with the conventional Doppler ultrasound examination was available to the clinicians for subsequent prenatal care; however, UA hPSV-DT values were kept in a database and not reported to the attending physician. UA PI values >95th percentile, according to the nomogram reported by Arduini and Rizzo [21], were considered abnormal, and UA hPSV-DT values <5th percentile, according to the nomogram previously published by our group [16], were considered abnormal. Only fetuses whose last Doppler study was performed within 7 days before birth were included in the analysis. At delivery, newborn infants were classified into three groups according to birth weight [20]: adequate for gestational age (AGA; birth weight >10th percentile); moderate FGR (birth weight between the 10th and 3rd percentile), and severe FGR (birth weight <3rd percentile).

Statistical analyses were performed using the χ^2 test with Yates' correlation when the sample size was smaller than 5 cases, likelihood ratio calculation, and receiver operating characteristic (ROC) curves. A p value of <0.05 was considered statistically significant.

Results

During the study period from 2009 to 2013, 383 patients met the inclusion criteria. Patients who were delivered in another institution or those whose birth occurred >7 days after the last ultrasound examination ($n = 117$) were subsequently excluded, resulting in 266 patients included in the current analysis.

Table 1 shows the obstetric conditions affecting these 266 patients: 164 (62%) had isolated FGR and 102 (38%)

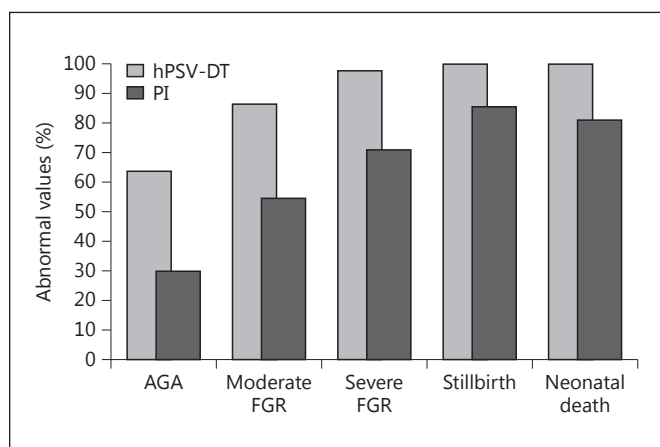


Fig. 2. Frequency of abnormal UA hPSV-DT and PI according to birth weight classification and perinatal death.

had other associated clinical conditions, mainly pre-eclampsia or chronic hypertension. At delivery, 80 (30%) newborns were classified as AGA, 141 (53%) as moderate FGR, and 45 (17%) as severe FGR. The distribution of UA hPSV-DT and PI according to birth weight is shown in table 2 and figure 2. Fetuses with both moderate and severe FGR had a statistically higher frequency of abnormal UA PI and UA hPSV-DT compared to AGA fetuses ($p < 0.01$). Overall, the UA hPSV-DT values were abnormal in 89% (166/186) of fetuses with FGR compared to 64% (51/80) of AGA fetuses ($p < 0.01$). When this group was subdivided into moderate and severe FGR, the UA hPSV-DT values were abnormal in 87% (122/141) and 98%

Table 3. UA hPSV-DT and PI in cases of perinatal death

	Stillbirth		Neonatal death		Perinatal death		Alive at discharge	
	%	n	%	n	%	n	%	n
Normal UA hPSV-DT	0	0/15	0	0/24	0*	00/39	21.6	49/227
Abnormal UA hPSV-DT	100	15/15	100	24/24	100*	39/39	78.4	178/227
UA hPSV-DT <120 ms	93.3	14/15	95.8	23/24	94.9*	37/39	39.2	89/227
Normal UA PI	20	3/15	20.8	5/24	20.5*	08/39	55.1	125/227
Abnormal UA PI	80	12/15	79.2	19/24	79.5*	31/39	44.9	102/227
UA AREDV	80	12/15	70.8	17/24	74.4*	29/39	20.7	47/227
Birth weight classification								
No FGR	6.7	1/15	12.5	3/24	10.3*	04/39	33.5	76/227
Moderate FGR	26.7	4/15	54.2	13/24	43.6*	17/39	54.6	124/227
Severe FGR	66.7	10/15	33.3	8/24	46.2*	18/39	11.9	27/227
Mean GA, weeks	25.5		26.6		26.2*		33.8	
Birth weight, g								
Mean	496		632		580*		1,725	
Range	280–760		390–980		280–980		540–3,080	

Abnormal UA hPSV-DT = <5th percentile; abnormal UA PI = >95th percentile; GA = gestational age. * $p < 0.01$, difference between babies alive at discharge and fetuses that suffered perinatal death.

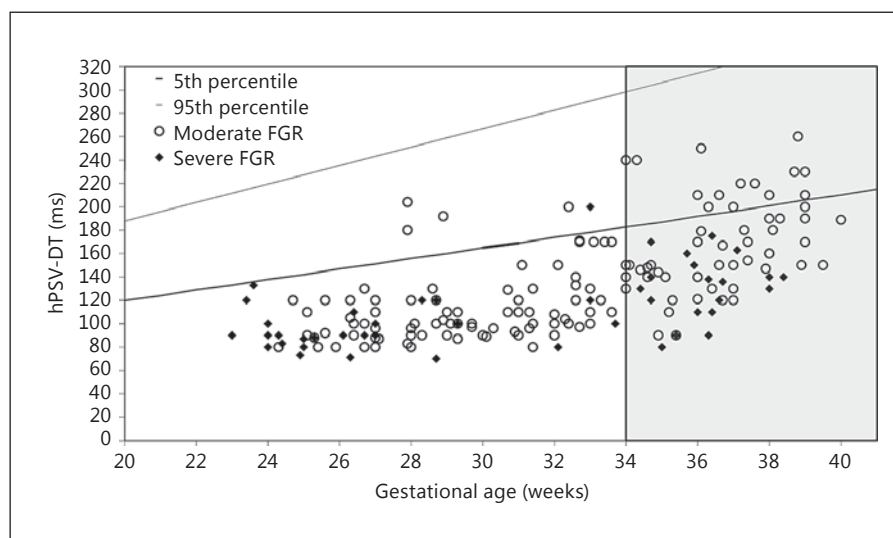


Fig. 3. UA hPSV-DT in fetuses with moderate and severe FGR. Gray zone = Delivery after 34 weeks' gestation.

(44/45) of the cases, respectively. However, in fetuses with FGR delivered at or before 34 weeks, the percentage of fetuses with abnormal UA hPSV-DT values increased to 95% (103/109; fig. 3). The percentage of cases with abnormal UA PI values was lower than that of cases with abnormal UA hPSV-DT values in the FGR group (59 vs. 89%; $p < 0.01$; fig. 2).

In our study group, 39 fetuses died in the perinatal period, including 15 intrauterine deaths and 24 neonatal deaths (table 3). The vast majority died because they were

extremely premature (mean 26.2 weeks' gestation) or had very low birth weight (mean 580 g). In 90% (35/39) of the cases, perinatal death was associated with FGR. Figure 2 and table 3 display the values of the UA Doppler flow velocimetry in these cases. The UA PI and UA hPSV-DT were abnormal in 80 and 100% of the pregnancies ending in intrauterine death, respectively. Among neonatal deaths, the UA PI and UA hPSV-DT were abnormal in 79 and 100% of the cases, respectively ($p < 0.05$ compared with surviving fetuses).

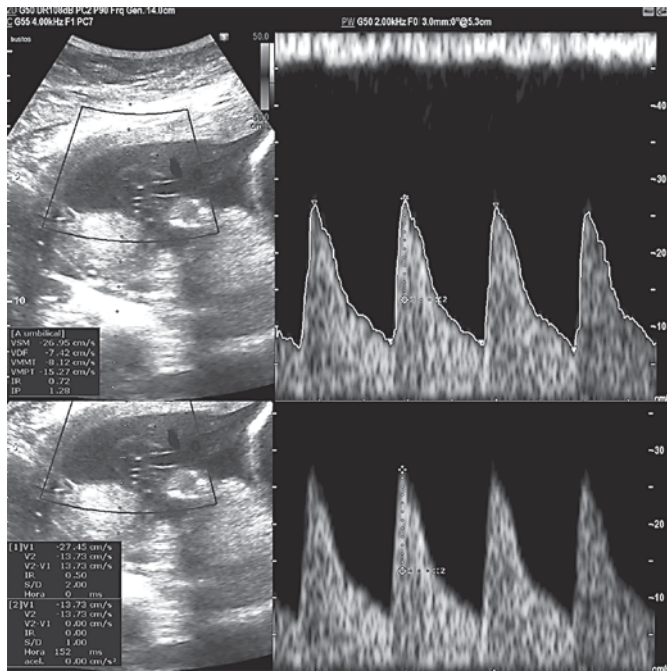


Fig. 4. Representative spectral Doppler waveforms in a 29-week fetus with severe FGR show a normal UA PI of 1.28 but an abnormal hPSV-DT of 152 ms. Note the narrow blood flow waveforms. The newborn infant weighed 685 g and survived.

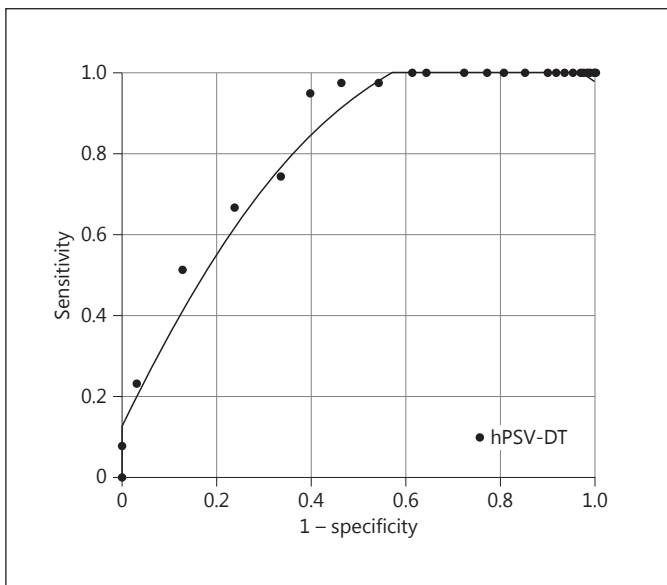


Fig. 5. The ROC curve for UA hPSV-DT in 39 fetuses ultimately ending in perinatal death. The area under the curve was 0.888.

All fetuses with a normal UA PI and normal UA hPSV-DT ($n = 49$) survived. The subgroup of fetuses with a normal UA PI and abnormal UA hPSV-DT ($n = 84$) included 8 perinatal deaths. In these cases, the spectral Doppler showed a narrow wave, which was objectively demonstrated as a shortened UA hPSV-DT in all cases (fig. 4). All fetuses with an abnormal UA PI ($n = 133$) had an abnormal UA hPSV-DT, and 31 of these fetuses died in the perinatal period. In the subgroup of fetuses with absent/reverse end-diastolic velocity (AREDV) in the UA ($n = 76$), the sensitivity for detecting perinatal death was 80% for stillbirths and 71% for neonatal deaths. Moreover, in this group, perinatal death occurred in 51% (19/37) of fetuses with a UA hPSV-DT ≤ 90 ms and in only 23% (9/39) of fetuses with a UA hPSV-DT > 90 ms ($p < 0.01$).

The ROC curve analysis of the UA hPSV-DT revealed a maximum discriminatory value of 110 ms and area under the curve of 0.888 (fig. 5). It is noteworthy that, despite our previous finding that UA hPSV-DT increases as pregnancy progresses [16], the UA hPSV-DT values were very similar in those pregnancies complicated by perinatal death, regardless of gestational age. In fact, 49% of the perinatal deaths had a UA hPSV-DT ≤ 90 ms and 46% had a UA hPSV-DT between 90 and 120 ms (fig. 6).

Fetuses with a UA hPSV-DT < 90 ms ($n = 46$) had poor perinatal outcomes, including 41% ($n = 19$) of the fetuses that died in the perinatal period and 50% ($n = 23$) that had prolonged admission to neonatal intensive care unit. For UA hPSV-DT ≤ 90 ms, the likelihood ratio for perinatal death was 9.22 (95% confidence interval: 4.9–17.4), and the negative likelihood ratio for UA hPSV-DT values ≥ 120 ms was 0.08 (95% confidence interval: 0.02–0.33; table 4). There were no cases with UA hPSV-DT < 70 ms.

Discussion

This study is the first to report the value of UA hPSV-DT in the evaluation of pregnancies with FGR and in those fetuses that ultimately died in the perinatal period. Our findings demonstrate that fetuses with FGR have an increased rate of abnormal UA hPSV-DT values compared to AGA fetuses, with 90% having values < 5 th percentile. Our results also show that the more severe the FGR, the more abnormal the UA hPSV-DT. This trend is even more pronounced in pregnancies with early-onset FGR, i.e. those presenting before 34 weeks' gestation.

According to our findings, there was also a strong correlation between perinatal death and abnormal UA hPSV-DT. This strongly suggests that abnormal UA hPSV-DT

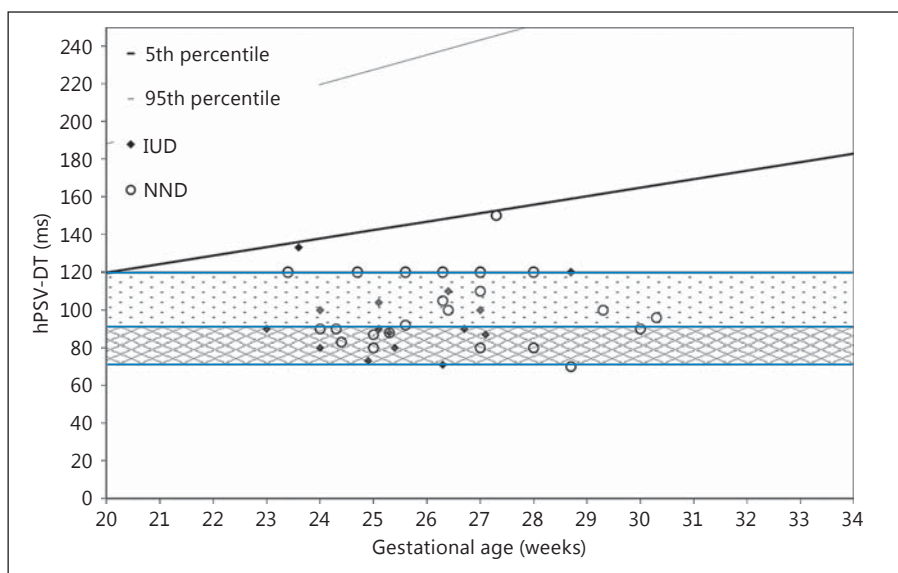


Fig. 6. The UA hPSV-DT in 39 fetuses ultimately ending in perinatal death. IUD = Intrauterine death; NND = neonatal death; dotted zone = 90–120 ms; diamond zone = 70–90 ms.

Table 4. Likelihood ratios (LR) of UA hPSV-DT and PI for perinatal mortality

	+LR	-LR
Abnormal UA hPSV-DT	1.27 (1.19–1.36)	0, NC
UA hPSV-DT <90 ms	9.22 (4.87–17.44)	0.54 (0.39–0.74)
UA hPSV-DT <120 ms	2.45 (2.05–2.93)	0.08 (0.02–0.33)
Abnormal UA PI	1.77 (1.43–2.19)	0.37 (0.2–0.7)
UA AREDV	4.12 (2.95–5.74)	0.31 (0.18–0.54)

Figures in parentheses indicate 95% confidence intervals. Abnormal UA hPSV-DT = <5th percentile; abnormal UA PI = >95th percentile; NC = not calculable.

is related to increased placental vascular resistance, which in turn will lead to subsequent FGR and perinatal death. Indeed, the vast majority of fetuses who ultimately died had abnormal UA hPSV-DT values (between 70 and 120 ms in 95% of the cases), with 95% of the fetuses with a UA hPSV-DT <90 ms being severely compromised. Additionally, there was no single case of UA hPSV-DT <70 ms, suggesting that values below this limit are likely to be incompatible with intrauterine life.

An important observation in our study was that UA hPSV-DT might be useful for the assessment of fetuses with AREDV in the UA. Currently, end-diastolic velocities in the UA are reported qualitatively as present, absent, or reverse [22, 23]. Nevertheless, it is likely that the degree of deterioration with AREDV is variable, but there is no

technique to quantify this observation. In the AREDV group, 51% of fetuses with a UA hPSV-DT <90 ms died in the perinatal period compared to only 23% of those with values >90 ms. Thus, UA hPSV-DT might be a quantitative technique that can be followed over time and could be useful in the surveillance of fetuses with AREDV. Further studies should establish the role of UA hPSV-DT in assisting in the decision of when to deliver fetuses with severe IUGR, especially those with AREDV. Based on the current data, the following guideline is proposed: if the UA hPSV-DT is between 90 and 120 ms, consider delivering the fetus soon; with a UA hPSV-DT between 70 and 90 ms (critical zone), the fetus should be delivered immediately.

In conclusion, our results show that FGR severity is correlated with progressive decrease in UA hPSV-DT, a trend that is even more pronounced before 34 weeks' gestation. UA hPSV-DT is also a good predictor of perinatal death. Additionally, it seems to provide a quantitative measurement that might be useful in the surveillance of fetuses with AREDV, with a UA hPSV-DT value of <90 ms probably indicating that the fetus is at imminent risk of intrauterine death. Additionally, no fetuses in this study had a UA hPSV-DT value <70 ms, indicating that values below this limit are probably incompatible with intrauterine life. Finally, this study suggests that UA hPSV-DT is an index of placental vascular resistance that could be useful in the evaluation of fetuses at risk for placental insufficiency, FGR and perinatal death and should be considered as an adjunct to UA PI in the assessment of these high-risk fetuses.

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Disclosure Statement

The authors report no conflicts of interest.

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