Doppler Ultrasound of the Umbilical Artery: Clinical Application

Ultrassonografia Doppler da artéria umbilical: Aplicação clínica

Ana Sá Rocha[1] Ana Rosa Araújo Andrade[2] Maria Lúcia Moleiro[2] Luís Guedes-Martins[1,2,3,4]

[1] Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal
[2] Departamento da Mulher e da Medicina Reprodutiva, Centro Materno Infantil do Norte, Centro Hospitalar Universitário do Porto EPE, Porto, Portugal
[3] Departamento da Mulher e da Medicina Reprodutiva, Centro Materno Infantil do Norte, Unidade de Investigação e Formação, Porto, Portugal
[4] Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal

Address for correspondence Ana Sá Rocha, MD, R. Jorge de Viterbo Ferreira, 228, 4050-313, Porto, Portugal (e-mail: rochasaana@gmail.com).

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Abstract

Objective To provide a survey of relevant literature on umbilical artery Doppler ultrasound use in clinical practice, technical considerations and limitations, and future perspectives.

Methods Literature searches were conducted in PubMed and Medline, restricted to articles written in English. Additionally, the references of all analyzed studies were searched to obtain necessary information.

Results The use of this technique as a routine surveillance method is only recommended for high-risk pregnancies with impaired placentation. Meta-analyses of randomized trials have established that obstetric management guided by umbilical artery Doppler findings can improve perinatal mortality and morbidity. The values of the indices of Umbilical artery Doppler decrease with advancing gestational age; however, a lack of consensus on reference ranges prevails.

Conclusion Important clinical decisions are based on the information obtained with umbilical artery Doppler ultrasound. Future efforts in research are imperative to overcome the current limitations of the technique.

Keywords
- doppler
- placenta
- umbilical artery
- fetal surveillance
- placental insufficiency

Resumo

Objetivo Compilar informação relevante proveniente da literatura atual sobre a ultrassonografia Doppler das artérias umbilicais (AUs) na prática clínica, considerações e limitações técnicas e perspectivas futuras.

Métodos A pesquisa bibliográfica foi realizada nos bancos de dados PubMed e Medline e restringiu-se a artigos escritos na língua inglesa. Recorreu-se também à bibliografia dos artigos selecionados, quando necessário, para obter informação relevante.

Resultados A utilização desta técnica como método de vigilância de rotina está apenas recomendada em gravidezes de alto risco com disfunção placentar. Metanálises

Palavras-chave
- doppler
- placenta
- artéria umbilical
- vigilância fetal
- insuficiência placentária

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de estudos randomizados mostraram que o seguimento obstétrico baseado nos achados do Doppler da artéria umbilical pode melhorar a mortalidade e a morbilidade perinatal. É consensual que os valores dos índices Doppler da AU decrescem com o avanço da idade gestacional. No entanto, há ainda muita incerteza quanto aos valores de referência.

Conclusão As informações obtidas através da AU Doppler US são a base para muitas decisões clínicas importantes. Trabalhos de investigação nesta área são essenciais para tentar colmatar atuais limitações da técnica.

Introduction

The umbilical arteries (UAs) play a key role in the regulation of the fetoplacental circulation. In the UAs, nerve regulation is absent and its tonus depends uniquely on locally released or circulating vasoactive substances, as well as on ions, such as calcium (Ca^{2+}) and potassium (K^{+}).[1–7] They lead the deoxygenated blood from the fetus to the placenta during systole and diastole, and together with the umbilical vein, which conducts the blood on the opposite direction, the exchange of nutrients, respiratory gases, and metabolites between the mother and the fetus, is guaranteed.[8]

To ensure normal intrauterine growth, there are some conditions that must be met: normal umbilical cord architecture and function; adequate placental perfusion; a healthy fetus and a favorable maternal condition; availability of nutrients and absence of pregnancy-related or non-related diseases.[1,8,9] Any abnormality in any of these prerequisites can potentially lead to intrauterine growth restriction (IUGR), with its inherent increased risk of perinatal mortality and morbidity in the short and long term.[1,9–14]

The main cause of IUGR is placental insufficiency,[9] which is associated with an increased resistance to blood flow in the placental vasculature, restricting the blood supply to the fetus and inducing compensatory responses with hemodynamic changes.[9,15,16] The onset of IUGR can occur anytime during pregnancy, and strict fetal surveillance is required after the diagnosis to determine when staying in the womb represents a greater risk of adverse perinatal outcomes than being born.[10,17–20]

Doppler ultrasound (US) of the UA provides useful information regarding the blood flow features within the arteries and is a well-established surveillance method in high-risk pregnancies due to impaired placentation.[11,20–22] In high-risk pregnancies, it is estimated that the use of Doppler US has allowed a decrease in the risk of perinatal death by $\sim$ 29%.[20]

The physical principle behind the Doppler US technology is named after The Doppler Effect, which is defined as the variation in the frequencies transmitted to and received from US waves between two objects when at least one is moving.[23,24] In obstetrics, the constant object is the transducer, and the red blood cells of the uterofetoplacental circulation are the shifting reflectors that produce the returning signal echoes.[23]

Spectral Doppler US is a speed-time spectral recording, presenting as flow velocity waveforms (FVWs).[25] It enables the quantification of the peak systolic velocity (PSV) and of the end-diastolic velocity (EDV) of blood flow within the UA, with which three indices can be obtained: the pulsatility index (PI), the resistance index (RI), and the systolic/diastolic ratio (S/D).[26,27] These indices are considered to be indirect measures of the resistance to blood flow of the placental vasculature.[1,11,28–30] Therefore, values not expected for the gestational age indicate placental dysfunction and fetal distress.[15,26,28,31]

The UA Doppler US is widely used in fetal surveillance because it is a noninvasive, economical, simple, and reproducible method.[8,12,13,15] However useful, this technic has some limitations, including the potential to cause considerable anxiety in families and clinicians, further diagnostic testing, and early (possibly very preterm) birth.[11] Moreover, it has been found that many studies reporting reference ranges for UA Doppler are based in methodologies with much heterogeneity.[20,31]

The aim of the present review is to provide a survey of the relevant literature on UA Doppler US in the clinical practice, its technical considerations and limitations, and to explore future perspectives.

Methods

The present research aimed to include studies that focused on the applicability of UA Doppler US in pregnancy management. To compose the present review, thorough literature searches were conducted in the PubMed and Medline databases, restricted to articles written in the English language. The screening of articles was performed using the following terms from the Medical Subject Heading of the Index Medicus as keywords: *Doppler ultrasound* AND/OR *umbilical artery*. The list of obtained articles was revised and the ones dealing with placental evaluation, placental insufficiency, fetal/pregnancy surveillance, and IUGR were chosen for further revision. Articles found by cross-referencing that met the inclusion criteria were also included.

All identified studies were screened for these inclusion criteria: (1) published in English (2) with full-text available, (3) UA Doppler US application in pregnancy.

A selection of the articles was performed. First, articles were filtered by reviewing titles and abstracts using the same

inclusion criteria. Second, the remaining articles were accessed based on the full text. Studies that did not meet all the inclusion criteria were excluded.

Results

Umbilical Artery Waveform Analysis

Concerning the UA, the standard Spectral Doppler US FVW pattern presents as a "sawtooth" pattern, revealing a unidirectional, continuous, and pulsatile flow toward the placenta (►**Fig. 1**). Its pattern can be distinguished from that of the umbilical vein since the UV FVW are continuous and non-pulsatile throughout the cardiac cycle.[32,33] In the "sawtooth" pattern of the UA, the highest point corresponds to the PSV, the lowest point corresponds to the EDV, and TAV stands for time-averaged velocity. These parameters enable the calculation of three indices: S/D Ratio: PSV/EDV; PI: (PSV - EDV)/TAV; RI: (PSV - EDV) / PSV.[23] In the clinical practice, the PI is the most commonly used.[34]

In low-risk pregnancies, the fetoplacental circulation presents itself with a placental high resistance to flow until the 20th week; thereafter, it gradually decreases and becomes a low-resistance system.[8] This phenomenon occurs from the end of the 2nd trimester due to the progressive placental villi maturation, greater width and wall compliance of the umbilical vessels along with greater fetal cardiac output and blood pressure.[35,36] Consequently, an acceleration in the EDV occurs and a proportional decrease in the three indices mentioned above is expected.[37] A deviation from the expected indices may signal an underlying placental dysfunction, and it indicates an increased risk of fetal demise,[31,38–40] regardless of the Doppler technique used.[35,41]

Pathological UA FVW has a progressive pattern of alterations, depending on the severity of the disorder: the EDV of the waveform becomes reduced (positive end-diastolic velocities [PEDV]), might disappear (absent end-diastolic velocities [AEDV]) (►**Fig. 2**), and can even reverse (reversed end-diastolic velocities [REDV]) (►**Fig. 3**), while PSV is not affected.[37,40,42] In these cases, the PI is more indicated for the interpretation of FVW findings[35] and it starts to increase only when 40% of the placental vascular tree remains functioning.[43]

While an AEDV flow before the 15th week is a normal physiological finding,[44] a REDV flow during the 1st trimester is associated with chromosomal abnormalities, fetal cardiovascular defects, and significant mortality.[45–49] However, as stated by Bellver et al.,[50] the latter "is not always an ominous sign."

Once present, the AEDV can stabilize or gradually evolve to REDV.[51] In a small number of cases, an AEDV can ameliorate and normalize spontaneously around the 27th week of gestation, although it is still unknown how to predict in which fetuses it will happen.[51] Antenatal administration of betamethasone to IUGR fetuses with absent or reversed end-diastolic velocity (AREDV) has also been correlated with the returning of the EDV and the stabilization of the resistance in the ductus venosus. By converting the AREDV to a normal flow, the outcome greatly improves, reverting the constant hypoxemia and acidosis to a better oxygenative status.[52] However, this positive effect of betamethasone is not seen in all cases, and the favorable response of the responding fetuses has not yet been understood.[52]

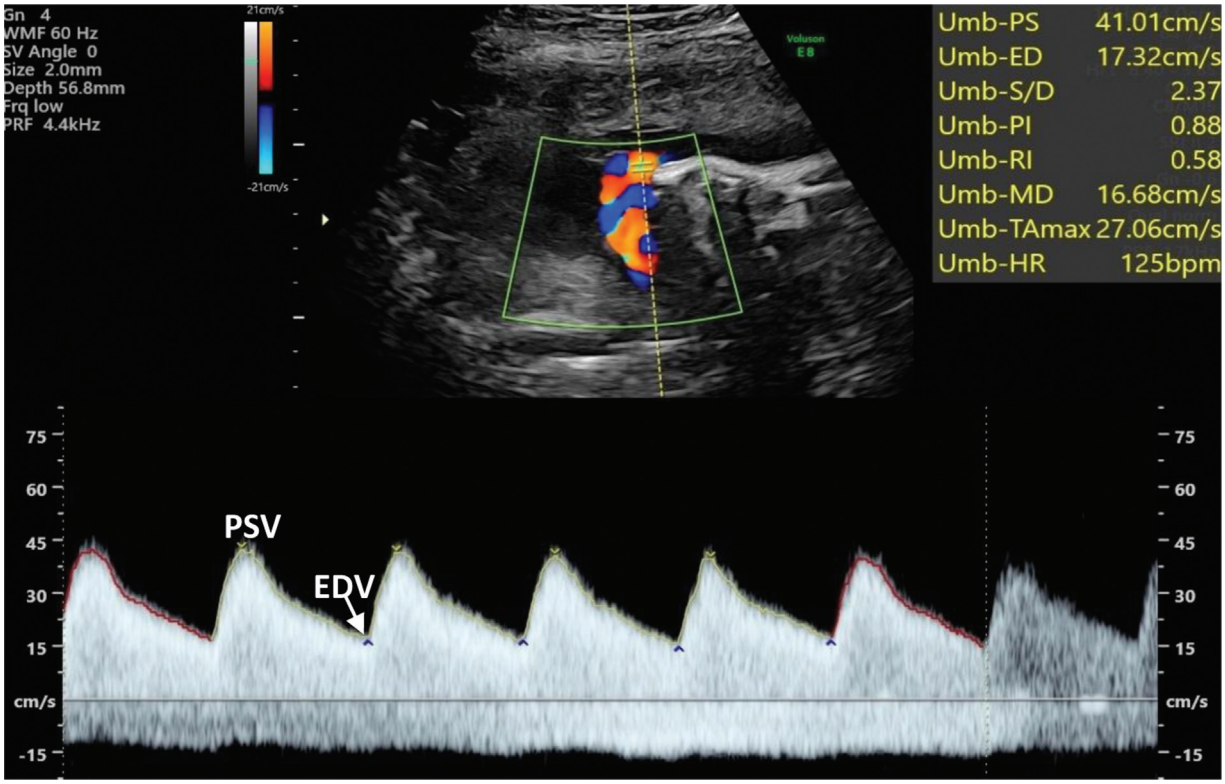

Fig. 1 Normal umbilical artery flow velocity waveform tracings obtained during the 3rd trimester. End diastolic velocities are present and are high; PSV - peak systolic velocity; EDV - end-diastolic velocity.

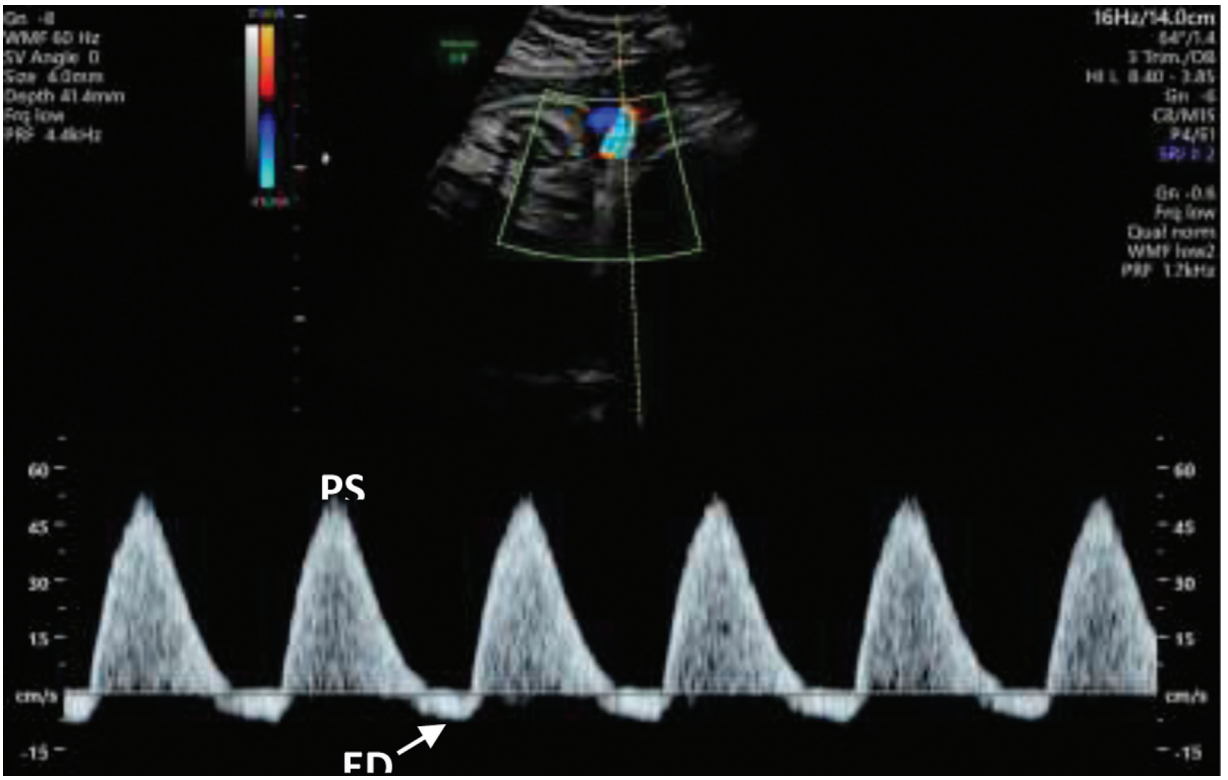

Fig. 2 Abnormal umbilical artery flow velocity waveform tracings obtained during the 2nd trimester. End diastolic velocities are absent, defining this pattern as AEDV. PSV - peak systolic velocity; EDV - end-diastolic velocity; AEDV - Absent end-diastolic velocity

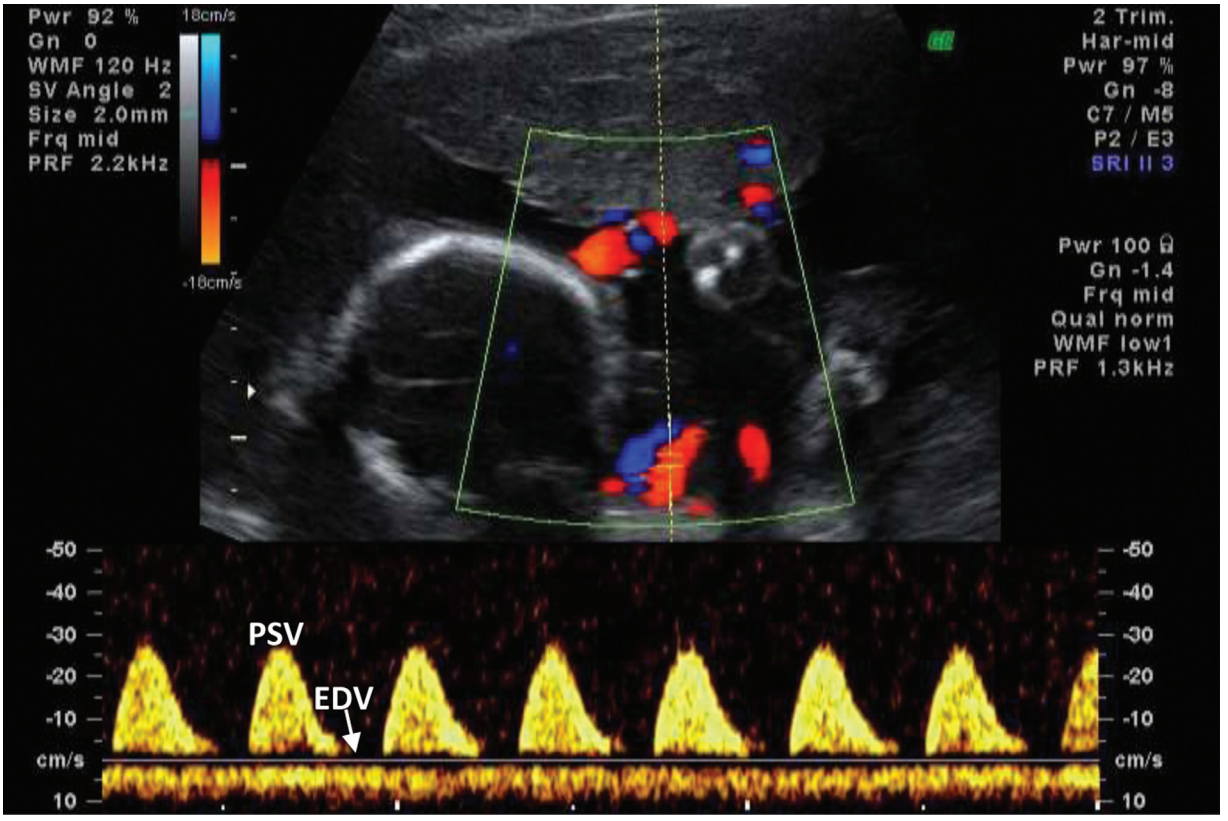

Fig. 3 Abnormal umbilical artery flow velocity waveform tracings obtained in a 3rd trimester pregnancy. End diastolic velocities are below the baseline, defining this pattern as REDV. PSV: peak systolic velocity; EDV: end-diastolic velocity; REDV: Reversed end-diastolic velocity

Absent or reversed end-diastolic velocity is frequently associated with marginal placental-end cord insertion,[1,53] which can be accurately diagnosed by Color Doppler US during the 2nd trimester.[12] Furthermore, in IUGR fetuses with AREDV, there is an increased expression of estrogen receptor-β within the fetoplacental endothelium, misbalancing the vascular tonus mediators and favoring vasoconstriction.[1,54,55] Being a vasodilator and smooth muscle relaxant,[56] the administration of intravenous or transdermal nitroglycerine causes a decrease in placental resistance to flow. This results in decreased PI, RI and S/D ratio in UA and Uterine artery (UtA) Doppler US, thus improving the outcomes.[56,57]

When compared with PEDV, AREDV fetuses have a higher incidence of low birthweight, worse Apgar scores, and oligohydramnios; greater number of labor inductions and caesarean sections due to fetal distress; admissions to neonatal intensive care unit; fetal demise; perinatal mortality and morbidity,[58–62] as well as long-term neurological impairment.[14,63–65] The lower the gestational age and fetal weight at birth, the more severe are the neonatal complications.[58] Specifically, fetuses with trisomy 21 have higher prevalence of AREDV, along with the presence of maternal malperfusion, delayed villous maturation and fetal vascular malperfusion, shortened umbilical cord, congenital cardiac anomalies, which frequently result in growth restriction, and death *in utero*.[66]

In IUGR fetuses, when in the presence of PEDV, an expectant attitude and close monitoring with weekly UA assessment is suggested, while in the presence of AREDV, after an acceptable gestational age is achieved, pregnancy termination seems to be the safest option to attain a better perinatal outcome.[37,58] Based on a recent meta-analysis, the 2021 International Federation of Gynecology and Obstetrics (FIGO) initiative on fetal growth suggested the application of UA Doppler findings as relative delivery criteria from 30 weeks onward for REDV and from 32 weeks onward for AEDV.[39,67]

The analysis of FVW can alert obstetricians to other pathological entities in addition to placental disorders. A period of deceleration during a larger period of acceleration, or the opposite, is called *notching*.[68] A systolic notch in the UA FVW suggests the presence of an umbilical cord abnormality, such as an UA narrowing, an abnormal cord insertion, cord entanglement (in twin pregnancies) or a true knot. True knots, which are the major cause of notching, can impair the flow supply to the fetus and lead to adverse outcomes. The notching magnitude strongly correlates to how tight the knot is and it depends on the type of FVW being measured (envelope versus centerline), as well as on the location downstream of the constriction where the FVW is being measured.[68]

Also worth of consideration are the results of a study conducted in 2006 by Struijk et al.,[69] in which the magnitude-squared coherence function between the UtA and UA FVW was found to improve the early identification of preeclampsia during the mid-trimester. However, it has no applicability in the prediction of IUGR or of pregnancy-induced hypertension.[69]

Umbilical Artery Doppler Reference Ranges

There is a consensus that UA PI decreases linearly with advancing gestational age in uncomplicated singleton pregnancies.[15,31,35,70–75] (►**Table 1**) (►**Fig. 4**).

However, the same percentile values were not obtained for each corresponding gestational age.[15,31,35,70–75] The same could be inferred about UA RI (►**Table 2**) (►**Fig. 5**).[72–75]

Gathering values obtained in three different geographical areas, Drukker et al.[72] proposed universal charts for UA PI. They considered that uncomplicated pregnancies in excellent health, nutritional, and environmental conditions for fetal growth have similar fetoplacental function and, consequently, similar Doppler indices regardless of the country of origin and of the inherent characteristics of its population.[72] On the other hand, Ciobanu et al.[71] suggested that the *a priori* risk related to maternal characteristics and medical history should be taken into account as maternal age, body mass index, smoking, parity, and racial origin have significant impact on UA PI. Moreover, Widnes et al.[26] considered the influence of fetal gender and proposed gestational age-dependent gender reference ranges, as they found that female fetuses have a more pulsatile UA from the 20th week to the 37th week, and higher heart rates from the 26th week.

In the case of fetuses with a single umbilical artery, Contro et al.[77] found the UA PI to be 20% lower than in those with a normal 3-vessel umbilical cord. This disparity remained constant between the 23rd and 40th gestational weeks. Thus, lower reference values in such cases may allow a more accurate interpretation of Doppler measurements.[77]

Concerning twin pregnancies, Mulcahy et al.[78] described the UA PI and RI to be consistently higher, from early pregnancy, in both monochorionic (MC) and dichorionic (DC) twins in comparison with singletons. Also among twin pregnancies, MC twins tend to demonstrate slightly higher values of UA PI and RI compared with DC twins.[78] These findings are supported by Casati et al.,[79] who proposed uncomplicated MC-specific Doppler charts, which include UA PI values. Since singleton Doppler reference ranges are not suitable for interpreting findings in twin pregnancies, further studies on both complicated and uncomplicated twin gestations and their perinatal and long-term outcomes are needed.[78,79]

Maternal glucose loading[80] and fetal behavior state were found not to influence UA PI value measurements if adjusted to the fetal heart rate.[80,81] Although smoking during pregnancy is associated with an increased risk of adverse outcomes,[82–84] smoking habits seem not to influence fetal Doppler parameters.[85] A curious finding is that the left UA appears to have higher impedance to flow and as few as 2% of the pregnancies have both arteries with similar Doppler indices.[86]

There is currently a wide variety of reference charts on UA Doppler indices, which could be explained, at least in part, by the heterogeneity in the methodological quality of the reports. Major methodological and statistical bias, found in some reports aiming to establish UA Doppler reference values, must be considered when examining this subject.[31] Even the studies with the highest methodological quality have significant discrepancy in cutoff values, which may signify important differences in clinical practice when using

Table 1 Values of the 95th centile for umbilical artery pulsatility index in studies reporting reference ranges

Gestational age (weeks)	Drukker et al.[72]	Acharya et al.[73]	Ciobanu et al.[71]	Srikumar et al.[75]	Ayoola et al.[74]	Baschat et al.[76]
18				1.62	1.402	
19		1.66		1.66	1.395	
20		1.62	1.553	1.55	1.388	1.31
21		1.58	1.526	1.53	1.381	1.27
22		1.54	1.499	1.54	1.375	1.28
23		1.5	1.472	1.41	1.368	1.12
24	1.38	1.47	1.446	1.42	1.361	1.21
25	1.37	1.44	1.42	1.31	1.354	1.13
26	1.35	1.41	1.395	1.24	1.348	1.11
27	1.34	1.38	1.371	1.32	1.341	1.07
28	1.32	1.35	1.346	1.33	1.334	1.05
29	1.3	1.32	1.322	1.25	1.327	1.11
30	1.28	1.29	1.299	1.08	1.321	1.04
31	1.26	1.27	1.275	1.12	1.314	0.99
32	1.24	1.25	1.252	1.1	1.307	0.93
33	1.21	1.22	1.229	1.15	1.3	0.92
34	1.19	1.2	1.207	1.2	1.294	0.89
35	1.16	1.18	1.184	1.05	1.287	0.91
36	1.14	1.16	1.162	1.05	1.28	0.93
37	1.11	1.14	1.14	1	1.273	0.95
38	1.08	1.12	1.118	1.08	1.267	0.89
39	1.06	1.1	1.097	0.95	1.26	1.01
40	1.03	1.09	1.075	0.82		0.75
41		1.07	1.053			

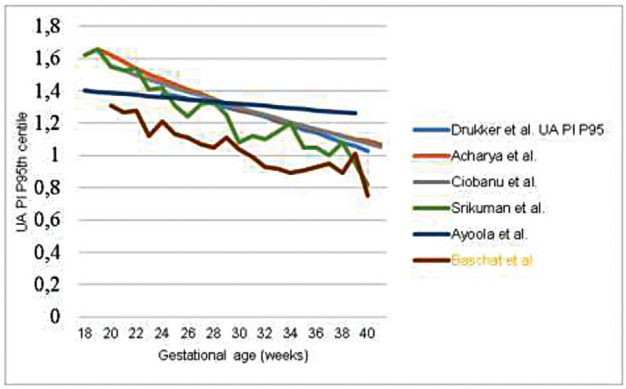

Fig. 4 Comparison of the 95th percentile of the umbilical artery pulsatility index in studies reporting reference ranges. UA: Umbilical artery; PI: Pulsatility index

one cutoff value in preference to another.[31] When evaluating the potential impact of such variability on the clinical management of small for gestational age (SGA) fetuses, Ruiz-Martinez et al.[87] found the rate of labor inductions to vary from 2.1 to 33.7%, depending on which reference chart of the UA PI was used and considering the PI cutoff > 95th percentile, as recommended in current clinical guidelines.[88] This example illustrates the magnitude of the impact that heterogeneous cutoff values have on decision-making in important clinical issues.[87] Another example is presented by Drukker et al.,[72] who found the 95th percentile values of UA PI to range between 1.28 and 1.48 at 32 weeks and between 1.03 and 1.40 at 39 weeks of pregnancy in different studies, illustrating a considerable uncertainty about what is a normal and expected cutoff value.[72]

Umbilical Artery Doppler as a Screening Test in Low-Risk Pregnancies

According to Alfirevic et al.,[11] the methods traditionally used in low-risk pregnancies to assess fetal well-being (symphysis-fundal height measurement, fetal movements charts, and cardiotocography) have no proven ability to positively impact the low incidence and preventable adverse perinatal outcomes. Therefore, UA Doppler US was tested as a routine screening tool in low-risk pregnancies. In such pregnancies, UA Doppler US demonstrated low prognostic value concerning the risk of fetal demise, neonatal acidosis or decreased Apgar score.[89] Also, at term, an abnormal UA Doppler result in these cases can only have one consequence to improve the health of the newborn: intensified monitoring

Table 2 Values of the 95th percentile for umbilical artery resistance index in studies reporting reference ranges

Gestational age (weeks)	Drukker et al.[72]	Acharya et al.[73]	Srikumar et al.[75]	Ayoola et al.[74]
18			0.9	0.781
19		0.88	0.86	0.778
20		0.87	0.82	0.775
21		0.85	0.84	0.772
22		0.84	0.83	0.769
23		0.83	0.81	0.766
24	0.78	0.82	0.79	0.763
25	0.77	0.81	0.77	0.76
26	0.77	0.8	0.75	0.758
27	0.76	0.79	0.78	0.755
28	0.76	0.78	0.76	0.752
29	0.75	0.77	0.76	0.749
30	0.75	0.76	0.7	0.746
31	0.74	0.76	0.71	0.743
32	0.73	0.75	0.73	0.74
33	0.72	0.74	0.73	0.737
34	0.71	0.73	0.74	0.734
35	0.7	0.72	0.66	0.732
36	0.69	0.71	0.66	0.729
37	0.68	0.7	0.65	0.726
38	0.67	0.7	0.68	0.723
39	0.66	0.69	0.62	0.72
40	0.65	0.68	0.58	
41		0.67		

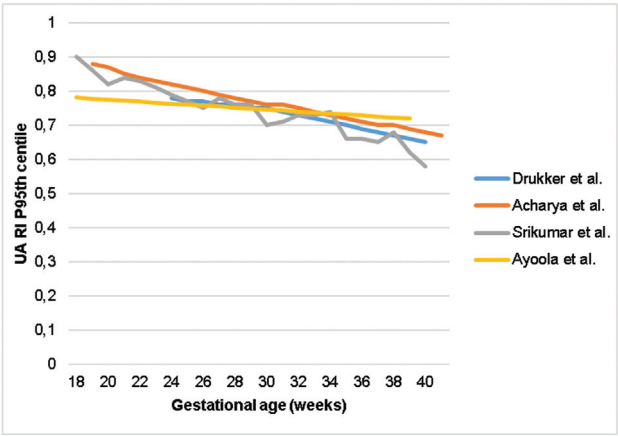

Fig. 5 Comparison of the 95th percentile of the umbilical artery resistance index in studies reporting reference ranges; UA: Umbilical artery; RI: Resistance index

with possible elective delivery in the event of deteriorating fetal distress.[90] Considering its low predictable value and its cost of time, money and considerable anxiety of the parents, nowadays the routine screening of low-risk pregnancies with UA Doppler US is not recommended.[11,15,90,91]

In contrast, according to Nkosi et al.,[92] in developing countries and small centers with less financial resources, the routine use of Umbiflow (a continuous-wave Doppler machine) to screen low-risk pregnancies from the 28th to the 32nd week is beneficial. It allowed greater recognition of increased UA RI and AREDV patterns up to 5 to 10 times more than expected.[92] The identification of these fetuses at risk, among the until then considered low-risk pregnancies, led to an adequate and active management of those pregnancies and to an improvement in perinatal outcomes, avoiding several unexplained stillbirths.[92,93]

Aiming to predict the perinatal outcome of low-risk pregnancies whose fetuses are suspected of IUGR, Gudmundsson et al.[94] proposed a new Doppler index: the placental pulsatility index. It combines the PI value of UA and UtA to evaluate the complete placental vascular impedance, and the authors suggest it has greater efficiency to predict adverse perinatal outcomes than UA and UtA alone.[94]

Umbilical Artery Doppler as a Screening Test in High-Risk Pregnancies

In contrast to low-risk pregnancies, the UA Doppler US is recommended as a routine surveillance method to assess

fetal well-being in high-risk pregnancies. Especially in pregnancies complicated by placental dysfunction, as in IUGR or pre-eclampsia, UA Doppler US works as a predictive test for fetal compromise.[20,22,95,96] Its applicability in other high-risk groups such as diabetes mellitus, post-term, and uncomplicated dichorionic twin pregnancy is still uncertain.[20,97–99]

The UA Doppler parameters are used to monitor fetal status and response to stress in pre-eclampsia and other hypertensive disorders related to pregnancy. However, it is the UtA PI that better predicts its future development[100,101] and anticipates adverse outcomes related to the condition.[102]

Fetuses with estimated fetal weight (EFW) $< 10^{th}$ centile are considered to be small for gestational age (SGA) and are at increased risk of fetal demise and poor perinatal outcomes when compared with non-SGA fetuses.[20,103,104] Some of these are constitutionally small healthy fetuses, whereas others are failing to reach their potential weight due to an underlying condition – IUGR fetuses.[11,20,105] Still, fetuses failing to reach their growth potential may or may not be SGA.[20,106]

The criteria for diagnosing IUGR due to placental insufficiency include UA Doppler measurements.[107] There are 2 subtypes of IUGR, depending on whether the onset is before or after the 32^{nd} week,[107] both of which have distinguishable Doppler patterns and postnatal outcomes.[10,108] The early-onset IUGR (E-IUGR) is more frequently associated with early-onset pre-eclampsia[109,110] and a classical sequence of deterioration of Doppler indices is present.[111–114] First, the UA PI increases to abnormally high values and then the middle cerebral artery PI starts decreasing as the cardiovascular redistribution occurs. As the downstream impedance to flow keeps increasing, the EDV within the UA decreases and AREDV pattern settles down. These are followed by an abnormal ductus venosus FVW and fetal heart insufficiency.[111–114] The presence of an AREDV pattern or an EFW $< 3^{rd}$ centile, before the 32^{nd} week, establishes the diagnosis of E-IUGR by itself.[107] In E-IUGR fetuses, the decision of labor induction based on fetal monitoring with non-stress test and ductus venosus Doppler seems to be associated with better results at 2 years of age.[17,38]

The late-onset IUGR (L-IUGR) is more prevalent and has a lower mortality rate than E-IUGR[108]; however, the undetected cases constitute the major cause of unexplained stillbirth.[11,103,115] In this subtype of IUGR, the UA Doppler indices remain unchanged or minimally elevated, not being reliable for diagnosis.[108] After the 32^{nd} week, the combination of biometrical parameters with Doppler measurements is more reliable than either one alone when differentiating the SGA at low-risk from those at high-risk for adverse outcomes.[108] These Doppler measurements must include the UA, the middle cerebral artery and the UtA as a multivessel screening in all pregnancies at high risk for placental dysfunction in the 3^{rd} trimester.[108,116] Finding both normal cerebroplacental ratio (CPR) and UtA Doppler indices, in fetuses presenting with an EFW $> 3^{rd}$ centile, confirms the low-risk status and the managing protocol of constitutionally small fetuses is appropriate.[108] When Doppler indices suggest placental insufficiency (UA PI $> 95^{th}$ centile or CPR $< 5^{th}$ centile), an EFW $< 10^{th}$ centile, or crossing > 2 quartiles on growth charts, has to be present to establish a high-risk status for late-SGA. However, an EFW $< 3^{rd}$ centile alone, after the 32^{nd} week, establishes the diagnosis by itself.[107]

Selective IUGR in DC twin pregnancies can also be monitored using UA Doppler US as it presents a flow progression pattern similar to that of IUGR in singleton pregnancies. In contrast, and due to the interdependent circulation, selective IUGR in MC twin pregnancies does not exhibit such pattern and the UA Doppler US is not a reliable tool to predict a possible deterioration of fetal status.[117] However, in MC pregnancies, a classification system based on the presence or absence of EDV in the UA in the affected twin guides its subsequent management.[117,118] Thus, twin pregnancies benefit from fetal well-being assessment with the UA Doppler US when there is a growth discordance, twin-to-twin transfusion syndrome, or IUGR.[119,120]

In pregnancies complicated by gestational diabetes,[121] or with pre-existing diabetes mellitus without vascular disease, the non-stress test was found to be better than the UA Doppler US at predicting adverse perinatal outcomes.[98,121] Only those complicated with vasculopathy due to diabetes could benefit from periodic UA Doppler US monitoring.[98]

Discussion

The UA Doppler US has acquired an unquestionable importance as a fetal well-being surveillance method over the years and it is widely used in the clinical practice today.

In low-risk pregnancies, the placental impedance to flow is low and enables a continuous blood flow within the UA.[8,37] Placental insufficiency compromises this low-resistance system at the expense of the EDV. The higher the placental resistance, the lower the UA EDV, and the normal FVW "sawtooth" pattern progressively deteriorates into PEDV, AEDV, and ultimately into REDV patterns. These abnormal patterns are recognized as ominous and anticipatory signs of poor obstetric outcomes.[37,39,40,42,58,122] Likewise, the UA Doppler indices depend on EDV, and the PI, RI, and S/D ratio values are considered indirect measures of placental vasculature resistance to blood flow.[1,11,28–30]

Concerning low-risk pregnancies, the routine use of UA Doppler US for fetal surveillance is not recommended.[11,90,91] Nonetheless, this assumption is based on studies conducted approximately 30 years ago. Therefore, it would be paramount to replicate these investigations with more accurate methodologies to determine whether there would be changes to the current knowledge or a corroboration of past conclusions.

In high-risk pregnancies, the UA Doppler US allows an accurate risk assessment for adverse outcomes and helps in the decision-making toward minimization of perinatal mortality and morbidity.[8,11,15] Current guidelines strongly recommend the routine use of this tool in high-risk pregnancies affected by placental insufficiency, such as those with IUGR and pregnancy-related hypertensive disorders.[20,22,95,96] However, during the 3^{rd} trimester, placental insufficiency develops under normal UA Doppler indices;[108] therefore, when suspected, other methods must be used to assess fetal well-being.[10,108,116] Regarding this issue, the TRUFFLE group is currently conducting

a study (the TRUFFLE 2 study) aiming to address which monitoring methods and thresholds are ideal for determining the delivery of L-IUGR fetuses.[123] The role of UA Doppler US for fetal surveillance in high-risk pregnancies due to other precipitating factors requires further investigation.[20,31,97–99,124]

Health improvements are not due to the application of the UA Doppler US itself but, rather, the result from the decision-making based on the information provided by this technology. Also, the success of Doppler measurements depends on the efficiency to spot abnormal and suspicious findings. Reference ranges are essential to establish which values of UA Doppler parameters must be considered normal and abnormal. Surprisingly, this is the point where less consensus exists. Although all studies agree that the values decrease with advancing gestational age, their proposed cutoff values differ significantly.[15,31,35,70–75] Studies on the methodological quality of reports proposing reference ranges have shown major methodological and statistical biases.[31,87] This may explain why so many different reference ranges have already been proposed. Another factor that may contribute to this variability is the wide range of variables that may influence UA Doppler indices. These can be fetal, maternal, or pregnancy-related variables, whose impact may be different when studied individually or in interaction. Given this and considering the potential impact of such variability on clinical decisions, the lack of consensus on reference ranges should incite scientific discussion. A universal chart was recently proposed aiming to standardize UA Doppler indices globally.[72] Although it sounds promising, future studies reporting its efficacy in different populations around the globe are paramount to state a conclusion.

Conclusion

The UA Doppler US is an invaluable screening tool for high-risk pregnancies and on which important clinical decisions depend. Future investments in research are imperative to attempt to overcome the current limitations of the technique.

Conflict of Interests

The authors have no conflict of interests to declare.

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