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Review

The clinical application of Doppler ultrasound in obstetrics

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Key content

- Current UK guidance advocates the use of uterine artery Doppler for screening and Doppler of the umbilical artery, middle cerebral artery and ductus venosus for surveillance and timing of delivery of the growth-restricted fetus.
- This article examines available evidence concerning the clinical application of Doppler ultrasound in obstetrics, with the aim of guiding clinicians in its application.
- With increasing acceptance of the concept of 'inversion of the pyramid of antenatal care', the use of Doppler in the first trimester is also discussed.

Learning objectives

- To understand the physiological mechanisms of umbilical artery, middle cerebral artery, uterine artery, ductus venosus and tricuspid valve Doppler assessments.
- To appreciate existing clinical evidence for the use of Doppler in specific situations.
- To understand the clinical application of Doppler ultrasound in specific clinical situations.
- To appreciate the emerging clinical application of Doppler in the first trimester.

Ethical issues

- Non-tertiary centres may not have access to sonographers or equipment required to perform advanced Doppler ultrasound.

Keywords: Doppler ultrasound / ductus venosus / middle cerebral artery / tricuspid regurgitation / ultrasound / umbilical artery / uterine artery

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Introduction

Doppler ultrasonography has proven to be an invaluable obstetric tool for over 30 years.[1] It can be used to assess both the fetal and placental circulation, with the aim of facilitating the diagnosis and monitoring of important conditions, such as fetal growth restriction (FGR), fetal anaemia and twin-to-twin transfusion syndrome (TTTS).[2] More recently, Doppler has been applied to the screening for conditions such as aneuploidy and pre-eclampsia.[3] Commonly used Doppler assessment in obstetrics encompasses that of the umbilical artery (UA), middle cerebral artery (MCA), uterine artery and ductus venosus (DV). More specialised and uncommonly performed Dopplers include that of the umbilical vein (UV), aortic isthmus and atrioventricular valves.

Umbilical artery Doppler in fetal growth restriction

UA Doppler is most commonly used for the monitoring and timing of delivery of the fetus compromised by FGR.[4] UA Doppler assesses impedance within the fetoplacental circulation and the pulsatility index (PI) and resistance index serve as surrogate markers of placental vascular resistance. This is known because the number of placental arteries per high power field is lower in cases of an abnormal UA Doppler.[5] UA Doppler serves as both a prognostic and diagnostic tool in the assessment of the growth-restricted fetus.[6] An abnormal UA Doppler waveform (absent or reversed end-diastolic flow) has been demonstrated to predict fetal compromise. This pattern appears to be present 12 days preceding acute fetal deterioration.[7] Figure 1 demonstrates normal and abnormal UA Doppler waveforms.[8]

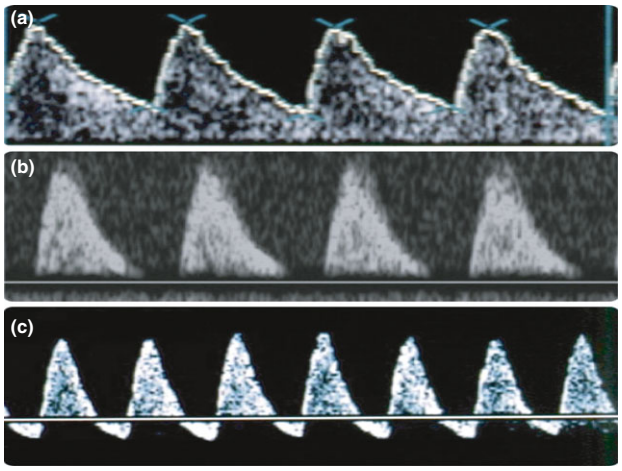

Figure 1. Umbilical artery Doppler. (a) Normal waveform; (b) absent end-diastolic flow; (c) reversed end-diastolic flow. Reproduced under the CC-BY 3.0 licence, with permission from *Cambridge Medical Journal*.[8]

UA Doppler velocimetry has been shown to improve perinatal outcome in high-risk pregnancies, through a meta-analysis of randomised controlled trials. While no consistent management plan was followed, this finding is thought to be due to the avoidance of iatrogenic preterm delivery as clinicians had more information on the wellbeing of the fetus and hence were able to time delivery more optimally.[9] UA Doppler remains the most extensively studied fetal surveillance tool.[9] A publication from the Royal College of Obstetricians and Gynaecologists (RCOG) proposes an algorithm to guide clinicians on the frequency of surveillance and timing of delivery.[4] This guidance advises that in terms of surveillance, women who are at high risk of having a baby affected by fetal growth restriction (such as a previously small-for-gestational age baby, smoking, advancing maternal age) should undergo serial UA Doppler assessment fortnightly from 26–28 weeks of gestation. In terms of timing of delivery, in preterm (below 32 weeks of gestation) small-for-gestational age fetuses with absent or reversed end-diastolic flow in the UA Doppler, delivery is recommended at 32 weeks of gestation with delivery prior to this time recommended when the DV becomes abnormal or there are UV pulsations.[4] At later gestations (after 32 weeks) in the coexistence of absent or reversed end-diastolic flow in the UA Doppler, delivery is recommended no later than 37 weeks of gestation.[4]

What next after an abnormal umbilical artery Doppler?

While the value of UA Doppler is abundantly clear, what is much less clear is the value of other Dopplers such as the MCA or DV in the management of FGR.

Fundamental to knowing whether the MCA or DV Doppler should be used is knowing whether there is a temporal sequence following an abnormal UA Doppler. The classical temporal sequence of progressive Doppler abnormalities in the growth-restricted fetus is demonstrated in Figure 2. Existing research calls this temporal sequence into question and states that, although the recognised sequence of deterioration of UA to MCA to DV does exist, it does not exist more frequently than any other pattern.[10] The reason for such variance in findings is unclear. If a temporal sequence does not exist, then it calls into question

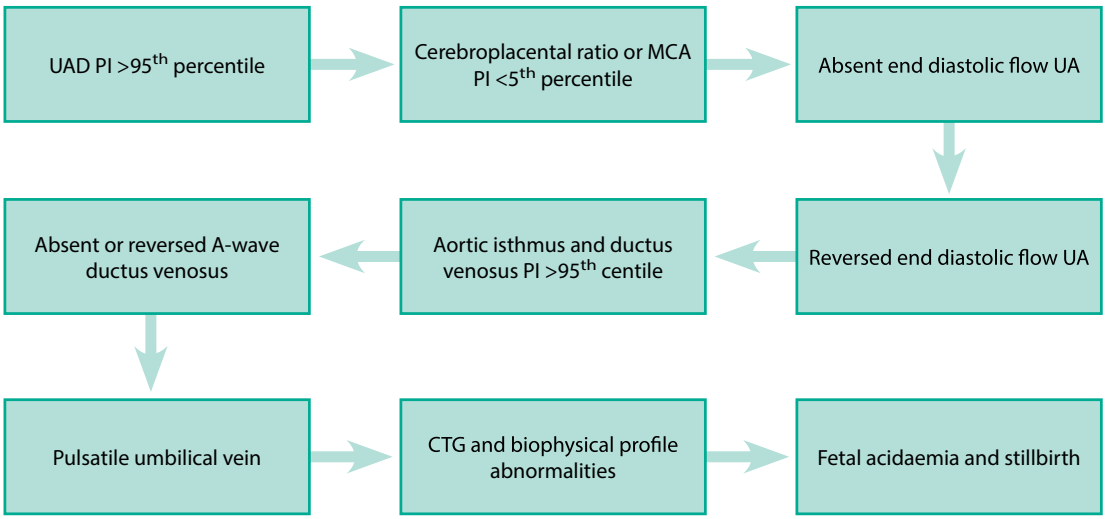

Figure 2. Apparent temporal sequence of fetal Doppler abnormalities in the growth-restricted fetus. This sequence has not been verified by other work[10] CTG = cardiotocograph; DV = ductus venosus; MCA = middle cerebral artery; PI = pulsatility index; UA = umbilical artery; UAD = umbilical artery Doppler.

the rationale for using fetal Doppler either sequentially or in combination in the management of FGR.

The conclusion of a Cochrane review states: 'Use of more sophisticated Doppler tests like assessment of blood flow in the middle cerebral artery and ductus venosus has not been subjected to the rigorous evaluation in clinical trials so far and, therefore, cannot be recommended in routine clinical practice'.[9] Guidelines from the USA echo these thoughts, stating: 'Although Doppler studies of the ductus venous, middle cerebral artery, and other vessels have some prognostic value for IUGR fetuses, currently there is a lack of randomised trials showing benefit. Thus, Doppler studies of vessels other than the umbilical artery, as part of assessment of fetal wellbeing in pregnancies complicated by IUGR, should be reserved for research protocols'.[11]

Middle cerebral artery Doppler in fetal growth restriction

The role of the MCA Doppler in the management of FGR is less clear than its role in fetal anaemia when the peak systolic velocity (PSV) measurement can be used to assess pregnancies at risk of fetal anaemia, for example, Rhesus isoimmunisation. In this instance, a PSV value greater than 1.5 multiples of the median (MoM) is predictive of fetal anaemia.[5] A typical MCA Doppler waveform is demonstrated in Figure 3.[12]

It is believed that in FGR, there is preferential shunting to the cerebral cortex, known as the 'brain-sparing' effect, leading to an increased diastolic flow and hence reduction in PI. Another measure that is sometimes used in the assessment of FGR is the MCA PI/UA PI ratio (cerebro-placental ratio).[5] The cerebro-placental ratio has a greater sensitivity than assessing the MCA or UA Doppler PIs in isolation, with a low or abnormal result associated with adverse perinatal outcome.[13]

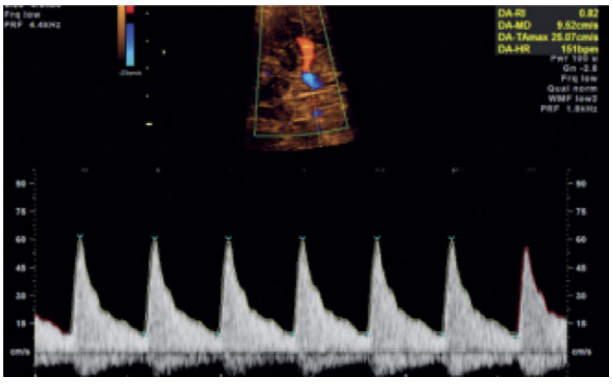

Figure 3. Normal middle cerebral artery Doppler waveform.[12] Reproduced with permission. © 2013 ISUOG.

MCA Doppler as a predictor of adverse outcome in the preterm fetus is poor.[14–16] Hence, the stance of the RCOG guideline is that MCA Doppler should not be used to time delivery in the preterm growth-restricted fetus.[4,5]

Where there does appear to be a role for MCA, however, is in the prediction of outcome in late-onset FGR. In these cases an abnormal MCA measurement has been associated with adverse perinatal outcome and neurodevelopmental abnormalities.[17–19]

Hence, RCOG guidance recommends that 'in the term SGA fetus with a normal UAD, an abnormal middle cerebral artery Doppler should be used to time delivery'.[4]

The cerebro-placental ratio has an apparent greater sensitivity in predicting adverse outcome, however, this has not been evaluated in randomised controlled trials.

Ductus venosus in fetal growth restriction

The DV Doppler acts as a marker of cardiovascular deterioration in response to FGR, specifically in cases of early-onset FGR, where the DV typically becomes abnormal after an elevation of the PI in the UA.[20]

Evidence suggests that an abnormal DV waveform (absence or reversal of the A-wave, as demonstrated in Figure 4)[12] has the potential to predict fetal acidaemia and stillbirth, and that it is the strongest single predictor of the risk of fetal death in early-onset FGR.[6] By combining the DV with other modalities, such as the UV or inferior vena cava Doppler, this effect can apparently be synergistic in the detection of a pH below 7.2, with up to a 64% specificity.[21] The predictive ability of an abnormal DV is further revealed in its correlation with reduced fetal heart rate variability on cardiotocogram and corresponding abnormalities in the fetal biophysical profile score.[6]

A 2010 systematic review of the available literature suggests that an abnormal DV Doppler has a moderate accuracy for predicting compromise of fetal and neonatal wellbeing, and of perinatal mortality in pregnancies that are affected by placental insufficiency.[22] Figure 5 demonstrates the overall predictive accuracy from this systematic review.[22]

A tool that has moderate accuracy for predicting compromise or death does not equate with a tool that should be used for surveillance in FGR. Indeed, there are no systematic reviews of effectiveness of venous Doppler as a surveillance tool.[4] This is in contrast to UA Doppler where there are randomised controlled trials and systematic reviews indicating its use as a surveillance tool.[11]

It is currently recommended by RCOG guidance that the DV Doppler should be used for the surveillance and timing of delivery of the preterm growth-restricted fetus with an abnormal UA Doppler, provided that the fetus is viable and steroids have been administered. The level of evidence for this is classified as a 'good practice point'.[4]

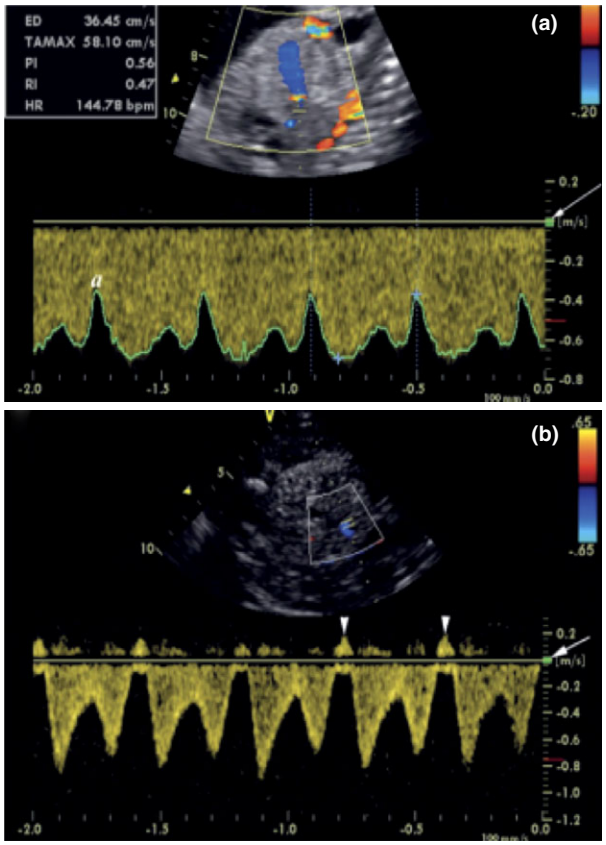

Figure 4. (a) Normal ductus venosus in the third trimester; (b) an abnormal waveform with a wave inversion (arrow).[12] Reproduced with permission. © 2013 ISUOG.

With regard to the use of DV and the timing of delivery, there are neither data nor consensus among clinicians. This is the subject of the 'trial of randomized umbilical and fetal flow in Europe',[23] which aims to inform clinicians if delivery is best performed when early DV changes are seen or if delivery is best postponed until late venous changes are encountered.

Uterine artery Doppler in the prediction of fetal growth restriction

Uterine artery Doppler can be used to help distinguish placental causes of growth restriction from other causes of growth restriction. Its role, however, is increasingly thought to be in screening for pre-eclampsia and FGR. Typically, such a screening test is undertaken at 20 to 24 weeks of gestation and a raised PI, raised resistance index or notching is considered an abnormal test.[24] Normal and abnormal uterine artery Doppler waveforms are demonstrated in Figure 6.[12]

In a low-risk population, uterine artery Doppler has limited accuracy in predicting a small-for-gestational-age

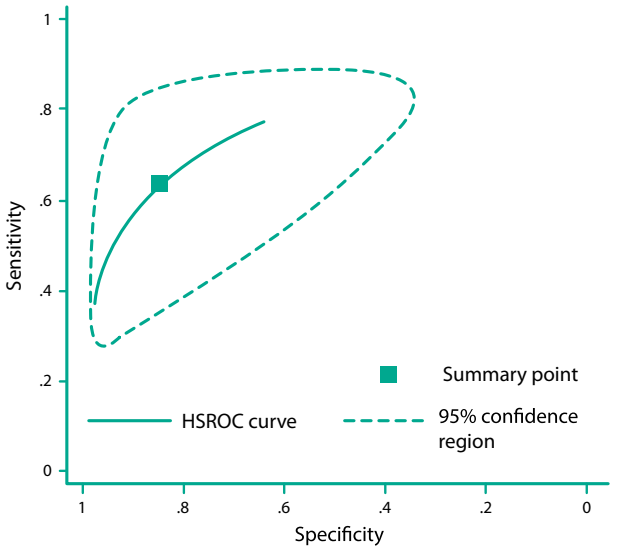

Figure 5. Graph demonstrating that ductus venosus has moderate predictive accuracy for perinatal death. The closer the index values are to the upper left-hand corner, the greater the accuracy of the test. Reproduced from Morris et al.[22] © 2010, with permission from Elsevier.

neonate and hence the RCOG guideline suggests that it should not be used in this population.[4]

In high-risk women, however, uterine artery Doppler has a moderate predictive value for a small-for-gestational-age neonate and hence the RCOG guideline recommends its use in this population.[4] However, the specificity of the test is such that even in the presence of a normal uterine artery Doppler, the clinician is likely to continue with serial ultrasound measurements in later gestation.

Uterine artery Doppler in the first trimester

The concept of the 'inverted pyramid of care' has received increasing attention.[3] This proposes that disorders such as pre-eclampsia and FGR can be screened for in early gestation by a combination of history, placental biomarkers, mean arterial blood pressure and uterine artery Doppler measurements. The benefit of performing such an assessment is that it allows the provision of aspirin prior to 16 weeks of gestation. Low dose Aspirin has been demonstrated to reduce the risk of pre-eclampsia by 17% in at-risk pregnancies.[25]

In the first trimester, uterine artery Doppler can apparently predict 81% of women with early-onset pre-eclampsia, 45% with late-onset pre-eclampsia and 50% with gestational hypertension, with a false positive rate of 10%.[26] This detection rate increases to 96% for early pre-eclampsia and to 54% for all pre-eclampsia, with a false positive rate of 10% with the addition of biomarkers, mean arterial blood pressure and maternal history.[27]

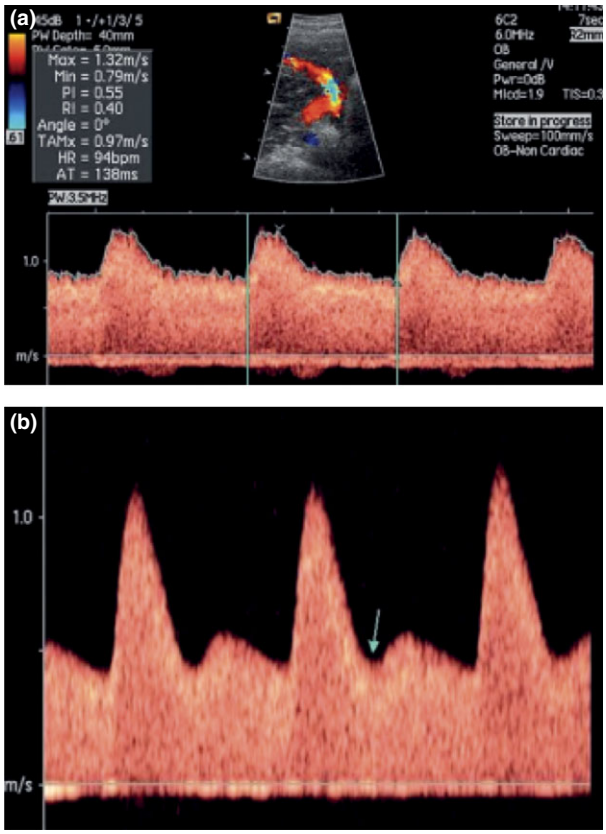

Figure 6. Second trimester uterine artery Doppler waveforms. (a) Normal; (b) abnormal.[12] Reproduced with permission. © 2013 ISUOG.

This concept is the subject of intense investigation by a number of research groups such as the Fetal Medicine Foundation.[28]

Aortic isthmus Doppler in fetal growth restriction

The aortic isthmus is a section of the aorta located between the origin of the left subclavian artery and the connection of the ductus arteriosus to the descending aorta.[29] Anatomically, it demonstrates the balance between the impedance of the brain and systemic circulation. Elevation or reversal of flow precedes abnormalities in the DV, often by approximately one week.[6] An abnormal aortic isthmus recording is associated with adverse perinatal outcome and similar to DV, is a measure of subclinical cardiac dysfunction.[30] Its true value in clinical practice is uncertain at present.

Umbilical vein Doppler in fetal growth restriction

Beyond the second trimester, the UV has a continuous blood flow and end-diastolic flow can become pulsatile in pregnancies affected by FGR.[5] Similar to the DV, the UV serves as a measure of the fetal venous circulation, which is the circulation that deteriorates towards the end of the temporal sequence (if such a sequence exists). End-diastolic pulsations within the UV are a marker of increased venous pressure; relaying fetal decompensation with inevitable right-sided heart failure and myocardial hypoxia.[2] Emerging evidence suggests that an abnormal DV PI for veins must coexist with UV pulsations to accurately predict adverse perinatal outcome.[31] Further research is required.

Atrioventricular valves in fetal growth restriction

Assessment for tricuspid regurgitation has been reported to have prognostic value in predicting perinatal outcome in FGR.[32] When assessing the atrioventricular valves, the Doppler waveform for both mitral and tricuspid valves has a characteristic dual-peak pattern: an E-wave corresponding to ventricular filling and an A-wave corresponding with atrial contraction. The A-wave is typically taller than the E-wave in normal fetuses. However, in those affected by FGR, the E/A ratio increases and in more severe cases there is mitral or tricuspid regurgitation where a reversed jet can be seen within the right atrium on colour flow Doppler.[5]

Middle cerebral artery Doppler in fetal anaemia

The MCA Doppler is currently the main tool for surveillance for fetal anaemia in cases of red cell alloimmunisation disease. The MCA has revolutionised the management of fetal anaemia and is as good if not better than the Delta OD 450 from amniotic fluid, which was once the traditional method of surveillance.[5] The MCA PSV can predict the existence of moderate-to-severe fetal anaemia with a sensitivity of 100% and a false positive rate of 12%.[33] The velocity of blood flow within the fetal arterial circulation is inversely proportional to the degree of anaemia due to increased fetal cardiac output, which is secondary to reduced blood viscosity.[2] An MCA PSV greater than 1.5 MoM may prompt the optimum time to perform cordocentesis and intrauterine transfusion.[34] Figure 7 demonstrates how MCA PSV can be plotted against gestational age to determine if the PSV is within the normal range.[5]

Other uses of Doppler

Aneuploidy screening

A further role for tricuspid regurgitation and DV is in first trimester screening with a significant association between the presence of tricuspid regurgitation and of a reversed A-wave in the DV between 11 and 13+6 weeks of gestation and the

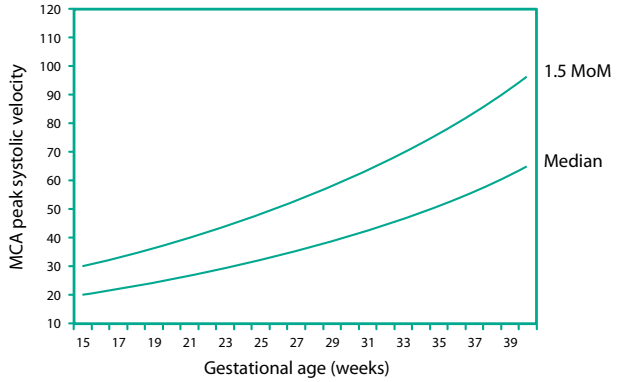

Figure 7. Peak velocity of systolic blood flow in the middle cerebral artery with advancing gestation. Curves demonstrate the median peak systolic velocity in the middle cerebral artery, and 1.5 multiples of the median, respectively. Reprinted from Mari et al.[5] © 2008, with permission from Elsevier.

presence of fetal aneuploidy or congenital cardiac defects. The use of Doppler screening in the first trimester can be combined with other investigations such as nuchal translucency, maternal age and serum biomarker such as pregnancy-associated plasma protein A to optimise the sensitivity and specificity of first-trimester fetal aneuploidy screening.[35,36] This is likely to be replaced by other methods of screening such as testing fetal cells from the maternal circulation.[37]

Doppler application in twin-to-twin-transfusion syndrome

The Quintero system is a staging classification system used in monochorionic twin pregnancies affected by TTTS. Stage III Quintero incorporates the absence or reversal of end-diastolic flow within the UA Doppler, pulsatile flow within the UV and/or a reversal of flow within the DV Doppler in one or both twins.[38] Doppler status is an important prognostic marker in fetuses affected by TTTS and forms part of the fetal cardiovascular profile score, a ten-point scale that incorporates various assessments inclusive of the presence of hydrops, abnormal venous and arterial Doppler, cardiomegaly, atrioventricular valve regurgitation and cardiac dysfunction.[39] Hence, Doppler status can guide clinicians in the management and counselling of patients affected by this serious condition.[5] Additionally, the MCA PSV can be used post-laser ablation for TTTS to assess for the complication of twin anaemia-polycythaemia sequence.[5,34,40] It is important in TTTS to assess fetal cardiac function in both the recipient and donor twins, including assessment for tricuspid regurgitation, notably in the recipient. The coexistence of TTTS with tricuspid regurgitation is a marker of severe TTTS, which may not necessarily be reflected in the Quintero stage.[41]

Conclusion

In fetal growth restriction, Doppler of the UA remains the most extensively investigated tool. There is less evidence available for the use of MCA and DV Dopplers. Current RCOG guidance recommends the use of these Dopplers in the surveillance and timing of delivery. MCA Doppler is the technique of choice for the monitoring of red cell alloimmunisation disease and for fetal anaemia.

Disclosure of interests

The authors report no conflict of interest.

Contribution of authorship

FM was the principal developer of this article and CPD question set through critical appraisal of current research in this field in addition to the consulting of relevant experts. SO and FMcA subsequently edited the article and revised it critically for intellectual content and hence provided final approval.

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