# DUCTUS VENOSUS IN THE MANAGEMENT OF MULTIPLE PREGNANCIES

**Alexandra Matias,** MD PhD, Nuno Montenegro MD PhD
Department of Obstetrics and Gynecology, S. João Hospital, Medicine Faculty of Porto, Porto, Portugal
almatias@mail.telepac.pt

While accounting for only 2.5% of the population, twins are responsible for 12.6% of the perinatal mortality. In the particular case of monochorionic twinning the fetal loss rate is even more relevant and there is an increased risk of adverse perinatal outcome. Therefore targeted surveillance of monochorionic twins at earlier stages of gestation could anticipate and provide timely management of the pregnancies at risk of one of the most devastating type-specific complications: twin-to-twin transfusion syndrome (TTTS).

Twin-to-twin transfusion syndrome (TTTS) is the most common complication of monochorionic twin pregnancies, affecting approximately 10% of all such pregnancies (Cincotta and Fisk, 1997). With an estimated 18.000 monochorionic births per year in the United States, roughly 2000 of these patients will be affected with TTTS. By way of intertwin vascular connections, blood is transfused from the donor, who becomes growth-restricted and develops oligohydramnios, to the recipient, who develops circulatory overload and responds with polyuria resulting in polyhydramnios. Ultimately this reflects a circulatory imbalance.

The consensus is that monochorionic monoamniotic placentas and 95-98% of monochorionic diamniotic placentas have anastomoses. A paucity of vascular anastomoses, especiallly if the overall flow is unidirectional, increases the risk for the development of TTTS due to uncompensated arteriovenous flow from recipient to donor (Bajoria et al, 1995). Certain vascular patterns may be more common in monochorionic twins developing TTTS but other factors including discordant/asymmetrical chorion development must also be considered.

### √ Nuchal Tanslucency

Data gathered from the literature show that increased nuchal translucency thickness (NT) at 10-14 weeks of gestation was found twice as much as in monochorionic than in singleton pregnancies, and the likelihood ratio of developing twin-to-twin transfusion syndrome in those twins with increased NT was 3.5 (Sebire et al, 1997, 2000). Considering that monochorionic pregnancies do not show a higher prevalence of chromosomal abnormalities, the higher prevalence of increased NT in those twins could be ascribed to cardiac dysfunction. With advancing gestation, this transient heart failure eventually resolves with increased diuresis and ventricular compliance.

It would clearly be a major advance if the sequence of events could be anticipated as early as the first trimester of pregnancy based on indirect signs of haemodynamic compromise (Matias et al, 2000, 2005).

But can the characteristic circulatory imbalance of TTTS, fully expressed later in pregnancy, disclose indirect signs of cardiac dysfunction in early stages of gestation?

### √ Ductus Venosus Flowmetry

Ductus venosus (DV) is a fetal structure shunting the blood from the umbilical vein to the inferior vena cava and foramen ovale, bypassing the hepatic circulation (Montenegro et al, 1997a). This structure enables the well-oxygenated blood originating from the placenta to course almost directly to the left atrium, and thence to the left ventricle and ascending aorta, favouring flow to the fetal brain and trunk.

Alterations in the fetal venous return blood flow have been described during the second and third trimesters of pregnancy in association with hemodynamic deterioration, namely in cases of absent or reversed end-diastolic (ARED) flow in the umbilical artery (UA), end-stage fetal hypoxia or increased right ventricular afterload (Kiserud et al, 1994), or in the presence of cardiac anomalies (Kiserud et al, 1993). It is well recognised, however, that in most forms of major structural heart defect, fetal well-being is not markedly affected and overt evidence of cardiac dysfunction is not a usual finding. In hearts with markedly impaired diastolic function, atrial contraction occurs against increased impedance to forward flow. The proportion of blood ejected retrogradely into the great veins is greater than when ventricular filling is unimpaired and this explains the transient flow reversal in the ductus venosus that constitutes the negative A-wave.

The introduction of transvaginal Colour Doppler ultrasound has allowed venous return assessment in early late first- and second-trimesters of human pregnancy. Vascular haemodynamics studies from our group in fetuses with increased NT at 10-14 weeks demonstrated that abnormal flow in DV was more frequently recorded in fetuses with chromosomopathies (Montenegro et al, 1997b, Matias et al, 1998), with or without cardiac defects (Areias et al, 1998, Matias et al, 1999), probably related to heart strain. These findings are in good agreement with the overt haemodynamic alterations found in TTTS later in pregnancy (Matias et al, 2000, 2005). Therefore, strong evidence suggests that increased NT along with abnormal flow in the DV, even in the presence of a normal karyotype, may be early signs of cardiac impairment or defect (Montenegro et al, 1997b, Matias et al, 1998, 1999) (Figures 1 and 2).

During a four-year period 55 monochorionic diamniotic pregnancies were identified in our Ultrasound Unit during routine ultrasonographic assessment at 11-14 weeks of gestation. Nuchal translucency and Doppler blood flow waveforms in the DV were recorded in both twins between 11-14 weeks of gestation. TTTS was recorded in those fetuses which combined increased NT and abnormal flow in the DV. Until now, in all cases with both discrepant NT and abnormal blood flow in the DV, TTTS eventually developed. Whenever NTs were discrepant but with normal flow in the DV, no cases of TTTS were found (Figures 1 and 2).

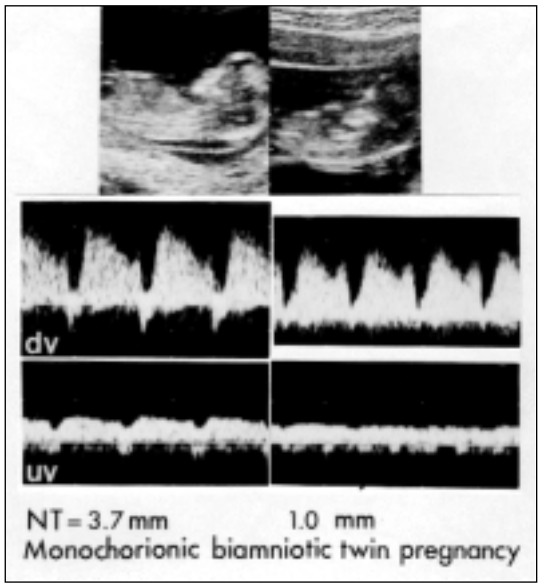


**Figure 1.** *A monochorionic biamniotic twin pregnancy was established at 12 weeks of gestation (case 3). Doppler blood flow waveforms in both fetuses were obtained in the umbilical vein (UV) and ductus venosus (DV) in the same scan. A nuchal translucency (NT) discrepancy was noted (NT=3.7/1.0 mm). The fetus with increased nuchal translucency shows an inverted A-wave in the DV and dicrote pulsatility in the UV. TTTS developed at 17 weeks and the patient was referred for laser ablation of anastomosis (with permission from Twin Research).*

Acute polyhydramnios/oligohydramnios sequence in the second trimester of pregnancy occurred in four out of 55 cases of monochorionic twin pregnancies. Three cases shared two characteristics: increased NT thickness in at least one of the fetuses and abnormal DV flow. In the fourth case, though NTs were similar, there was abnormal flow in the ductus venosus of one fetus. In the other 15 cases, in which one of the fetuses presented

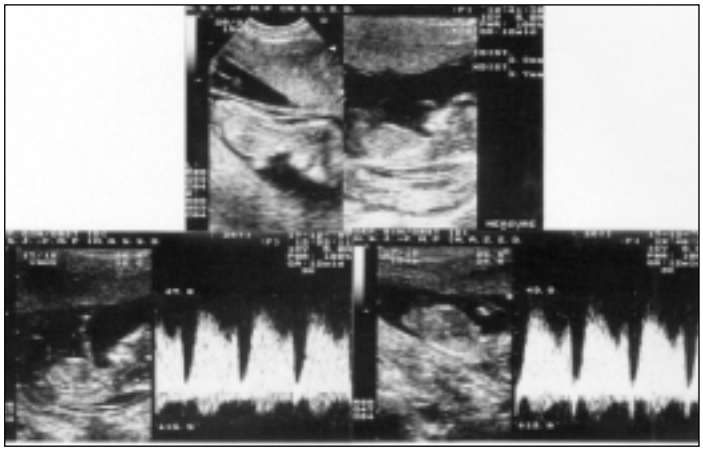

**Figure 2.** *A monochorionic biamniotic twin pregnancy was established at 12 weeks of gestation (case 1). Doppler blood flow waveforms in both fetuses were obtained in the ductus venosus (DV). A discrete nuchal translucency (NT) discrepancy was noted (NT=3.3/3.7 mm). The fetus with the highest nuchal translucency shows an inverted A-wave in the DV and later developed signs of TTTS at 18 weeks of gestation.*

increased NT thickness but normal flow in the DV, no signs of TTTS were recorded throughout pregnancy. The remaining cases with normal NT and normal findings in the DV were uneventful. In one case, NTs were discrepant and DV flow was abnormal in one of the fetuses, but only growth discordance >20% was detected at birth.

It is widely accepted that alterations in cardiac hemodynamics leading to cardiac failure are accurately described by alterations in venous blood flow waveform patterns: the abnormal pulsatility pattern consists of increased velocity of blood flow away from the heart during atrial contraction and has been reported in the fetus with heart failure (Montenegro et al, 1997b, Matias et al, 1998, 1999). Further transmission of the venous pulsations into the portal and umbilical circulations correlates with increasing cardiac compromise. The most striking feature is the reduced or reversed velocity during atrial contraction in the DV. In fetuses with congenital heart defects, growth restriction and TTTS as well as in our series this particular haemodynamic alteration seems to reflect impaired cardiac performance and appears as a sign of ominous prognosis.

Hecher and coworkers (1995 a, b) found highly pulsatile venous waveforms in the recipient with fully established TTTS. Umbilical vein pulsations correlated to atrial contraction and absent or reversed flow during atrial contraction in the DV are signs of congestive heart failure due to hypervolemia and increased preload from placental vascular anastomotic transfusion. Zosmer et al proposed that cardiac dysfunction may be induced in utero by sustained strain upon the heart by TTTS, predominantly affecting the right ventricle, and, in fact, some surviving twins of TTTS show a persistent right ventricular tract obstruction (functional pulmonary stenosis) and pulmonary hypertension in the neonatal period, which may be aggravated by systolic right ventricular dysfunction. Diastolic abnormalities were also described in the right ventricle, with abnormal filling patterns, prolonged isovolumic relaxation time and abnormal flow patterns in the inferior vena cava and ductus venosus.

Our results are in good agreement with the evidence that increased NT thickness along with abnormal flow in the DV, even in the presence of a normal karyotype, may be early signs of cardiac impairment or defect. Following the same rationale, the underlying haemodynamic changes associated with TTTS may manifest as increased NT thickness in the recipient between 10 and 14 weeks of gestation (Matias et al, 2000, 2005) as a consequence of heart failure due to hypervolemia. With advancing gestation, this transient heart failure may resolve due to increased diuresis and ventricular compliance. This is not surprising with the sphincter-like ductus venosus being known as a crucial distributor of well-oxygenated umbilical venous blood to the coronary and cerebral circulations. In fact, DV appreciation as a regulatory shunt can add valuable information to fetal venous haemodynamic evaluation. Blood flow in the ductus venosus is characterised by high velocity during ventricular systole (S-wave) and diastole (D-wave) and the presence of forward flow throughout the cardiac cycle. Only in the presence of cardiac failure, with or without cardiac defects, when end-diastolic pressure becomes elevated, does atrial systole produce large atrial pressure waves and cause reversal in the atrial waveform of ductus venosus.[5,7,9]

The issue of safety at such a vulnerable gestational period as the first trimester of pregnancy should be mentioned. The Pulsed Doppler mode has the highest energy output, but combining it with much lower energy output modes, such as Colour Doppler and Power Doppler, the identification of vascular structures is easier and the time of fetal exposure to the ultrasound beam will be shorter. As bone ossification is incipient at this stage of pregnancy, the danger of aggressive thermal effects is reduced.

Until now we could only been able to diagnose TTTS in monochorionic pregnancies when fully established by identifying the disparity in fetal size and amniotic fluid volume between donor and recipient. However obstetrical management might be more efficacious if TTTS could be screened in earlier stages of pregnancy. It may well be that the combination of discrepant NT and abnormal venous return at 11-14 weeks of gestation in monochorionic twins represents the warning sign predictive of the subsequent development of TTTS. The usefulness of both first trimester clues should be further investigated in a large multicenter collaborative study. Only then, assessment of both NT and DV flow would turn out to be clinically significant and motivate the ultrasonographer to undertake a closer surveillance of these twins highly prone to develop TTTS. Therefore, positive screening could facilitate timely therapeutic strategies and thus improve outcome of these high risk pregnancies.

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