Doppler detection of arterio-arterial anastomoses in monochorionic twins: feasibility and clinical application

M.J.O. Taylor1,3, M.L. Denbow1, S. Tanawattanacharoen1, C. Gannon2, P.M. Cox2 and N.M. Fisk1

1Centre for Fetal Care, Department of Materno-Fetal Medicine and 2Department of Perinatal Pathology, Imperial College School of Medicine, Queen Charlotte’s & Chelsea Hospital, Goldhawk Road, London W6 0XG, UK

3To whom correspondence should be addressed at: Centre for Fetal Care, Department of Materno-Fetal Medicine, Imperial College School of Medicine, Queen Charlotte’s & Chelsea Hospital, Goldhawk Road, London W6 0XG, UK. E-mail: myles.taylor@ic.ac.uk

The accuracy of in-vivo detection of arterio-arterial anastomoses (AAA) in monochorionic (MC) twins and its predictive value for twin–twin transfusion syndrome (TTTS) was assessed in 105 consecutive MC twins scanned at fortnightly intervals. AAA were sought using spectral and colour energy Doppler and ultrasound findings were compared with placental injection studies. AAA were identified in vivo in 59 (56%) pregnancies and at injection study in 68 (65%). The overall sensitivity and specificity was 85% and 97.3% respectively for the detection of AAA. Detection rates were higher at later gestations, with anterior placentae and with larger diameter AAA. The median insolation time to detect an AAA was 10 min (range 1–30). Where an AAA was identified, 15% of pregnancies (nine of 59) developed TTTS compared to 61% (28 of 46) when no AAA was seen (odds ratio 8.6). We conclude that AAA can be detected in vivo with high sensitivity and specificity without undue prolongation of scanning times and have a role in risk stratification in the antenatal assessment of MC twins.

Key words: arterio-arterial anastomoses/Doppler/monochorionic twins/twin–twin transfusion

Introduction

Monochorionic (MC) twins have morbidity and mortality rates 4–5 fold greater than dichorionic twins (Bejar et al., 1990). This is in large part due to the risk, exclusive to monochorionic placentation, of twin–twin transfusion syndrome (TTTS) which affects 10–15% of MC twins and which, if untreated, is associated with a survival rate of only 20% (Saunders et al., 1992; Fisk and Taylor, 2000). Current treatments of serial amnioreduction (Mari, 1998), septostomy (Saade et al., 1998), laser ablation (Ville et al., 1998) and selective fetocide (Deprest et al., 2000) improve survival rates to 50–70% as reviewed elsewhere (Fisk and Taylor, 2000). Therefore serial ultrasonic monitoring of MC pregnancies is recommended to allow early diagnosis and treatment of this condition.

The pathophysiology of TTTS remains poorly understood but has been attributed to unbalanced intertwin transfusion mediated by deep unidirectional arterio-venous anastomoses (Fisk and Taylor, 2000). Superficial bidirectional anastomoses, either arterio-arterial anastomoses (AAA) or veno-venous anastomoses (VVA), have the capacity to compensate for any net imbalance in intertwin transfusion. Several placental injection studies have shown that TTTS is associated with a paucity of superficial anastomoses and in particular, an absence of AAA (Bajoria et al., 1995; Machin et al., 1996; Denbow et al., 2000). AAA can be identified using colour Doppler and support for this compensatory role has come from an in-vivo study which suggested that the presence of AAA protects against the development of TTTS (Denbow et al., 1998). More recently, our group has shown that such protection extends to improving survival in established disease (Taylor et al., 2000) in the few cases of TTTS that have AAA.

To date, detection of AAA has largely been performed as a part of research projects in a tertiary referral centre (Hecher et al., 1994; Denbow et al., 1998). Our hypothesis for this study was that demonstration of AAA is now sufficiently accurate that routine antenatal detection is feasible. We evaluated this prospectively in a large cohort of MC twins.

Materials and methods

In all, 105 pairs of MC twins were seen in a tertiary referral fetal medicine centre between July 1995 and July 1999. Chorionicity was assessed by established criteria (Fisk and Bennett, 1995). If monochorionic placenta was suspected, fortnightly ultrasonic surveillance was performed using an Acuson Sequoia or XP10 (Acuson Co., Mountain View, CA, USA) for fetal growth, liquor volume and Doppler studies.

Following routine biophysical assessment for evidence of TTTS (vide infra) the presence of AAA was sought as described previously (Denbow et al., 1998). Power or spectral Doppler were used to identify chorionic plate vessels crossing the vascular equator, which were then insolated by pulse wave Doppler. AAA were identified by their characteristic bidirectional interference pattern (Figure 1), whose frequency can be shown on computer modelling to occur with a periodicity reflecting the net difference between the two twins’ different fetal heart rates (Hecher et al., 1994; Taylor et al., 1999). These patterns have also been validated by observation of dynamic normalization of the waveform at the time of single fetal death (Taylor et al., 1999). Power Doppler was used initially, but by the last half of this series, it became apparent that spectral Doppler on the Acuson Sequoia was also sufficiently sensitive but had the added advantage of displaying a characteristic ‘speckled’ pattern due to the bidirectional flow which facilitated AAA detection. Power Doppler
on the other hand had the advantage of angle independence and thus the ability to detect low flow, which is particularly useful at earlier gestations. Therefore a combination of techniques was used in practice. Search for an AAA was limited to a maximum of 30 min per scanning session. Insonation was stopped when one AAA was confirmed, and the presence of multiple AAA was not sought. Thus for the purposes of this study, ultrasonic surveillance for the presence of an AAA was discontinued at subsequent visits. The actual length of insonation time was recorded in a subgroup (n = 20) with duration of scanning recorded categorically in 5 min intervals. All women gave oral consent to the additional insonation sequences for research purposes as approved by the institutional ethics committee.

The diagnosis of TTTS was based on ultrasound criteria of discordant amniotic fluid volume, i.e. polyhydramnios in one and oligohydramnios in the other defined by deepest vertical pools of >8 and <2 cm respectively (Wittmann et al., 1981; Brennan et al., 1982). The deepest pool was measured in each sac and the amniotic fluid index derived as for singletons (Phelan et al., 1987). The donor twin was recognized by the following features: smaller size, reduced liquor volume and reduced or non-visible bladder size. Characteristic features of the recipient included increased size, polyhydramnios, a chronically full bladder and on occasion evidence of cardiomegaly.

Gestational age was based on the date of the last menstrual period if certain or ultrasonography in the first trimester. Placental site was documented as anterior, posterior or fundal according to where the bulk of the placenta between the two cord insertions was situated.

Following delivery, fresh placentae were collected and, blind to the Doppler results, injection studies were performed by the perinatal pathologist (P.C.) as described previously (Denbow et al., 2000). Blinding was felt to be necessary to avoid observation bias in interpreting the results of injection studies. The presence of a single AAA/multiple AAA identified at injection study was compared with Doppler findings to calculate the sensitivities and specificities for antenatal assessment. The diameter of each AAA was documented. Data collection was incomplete for AAA diameters in 6/68 cases due to technical difficulties at injection study due to placental damage in five cases and in one case diameter was not documented.

Table 1. Relationship between AAA identification by Doppler with AAA identification at injection studies, and with the presence or absence of TTTS

<table>
<thead>
<tr>
<th></th>
<th>AAA on scan</th>
<th>No AAA on scan</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injection study</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAA&lt;sup&gt;a&lt;/sup&gt; present</td>
<td>58</td>
<td>10</td>
<td>68</td>
</tr>
<tr>
<td>No AAA present</td>
<td>1</td>
<td>36</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>46</td>
<td>105</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTTS&lt;sup&gt;b&lt;/sup&gt; absent</td>
<td>50</td>
<td>18</td>
<td>68</td>
</tr>
<tr>
<td>TTTS&lt;sup&gt;b&lt;/sup&gt; present</td>
<td>9</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td>46</td>
<td>105</td>
</tr>
</tbody>
</table>

<sup>a</sup>AAA = arterio-arterial anastomosis. <sup>b</sup>TTTS = twin–twin transfusion syndrome.

Statistical analysis was undertaken using SPSS for Windows. Data were analysed for the association between AAA findings on ultrasound with both histopathology and an absence of TTTS using sensitivities, specificities, likelihood ratios (LR) for positive and negative tests and odds ratios (OR). Categoric comparisons were evaluated by $\chi^2$ testing. A P-value <0.05 was considered significant. Data from the first 40 of these cases have been described previously (Denbow et al., 1998).

Results

In 68 pregnancies, an AAA was detected at injection study. Doppler detected an AAA in 59 of these. The mean, mode and median times to detect AAA by Doppler (n = 20) were 13.1, 5 and 10 min respectively (range 1–30).

AAs were detected in 37/59 cases (63%) at the first scan, 13/59 (22%) at the second, 4/59 (7%) at the third, 3/59 (5%) at the fourth and 2/59 (3%) at the fifth. Only one of the 68 placentae with AAA present at injection study had more than one AAA in this case only one of the two was detected by...
Table II. Accuracy of Doppler detection of AAA pattern in predicting the presence of AAA at injection study and in predicting the absence of TTTS

<table>
<thead>
<tr>
<th>Doppler detection of AAA pattern</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LRPT</th>
<th>LRNT</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicting AAA at injection study</td>
<td>85.3 (75.4–92.3)</td>
<td>97.3 (87.4–99.9)</td>
<td>31.6 (4.6–218.7)</td>
<td>0.2 (0.1–0.3)</td>
<td>209</td>
</tr>
<tr>
<td>Predicting absence of TTTS^b</td>
<td>73.5 (62.1–83.0)</td>
<td>75.7 (60.0–87.4)</td>
<td>3.0 (1.7–5.4)</td>
<td>0.4 (0.2–0.5)</td>
<td>8.6</td>
</tr>
</tbody>
</table>

^AAA = arterio-arterial anastomosis; ^bTTTS = twin–twin transfusion syndrome; ^c95% confidence interval; ^dLRPT = likelihood ratio for positive test; ^eLRNT = likelihood ratio for negative test; ^fOR = odds ratio.

Figure 2. Influence of placental site on sensitivity of arterio-arterial anastomosis (AAA) detection by Doppler. Grey areas represent AAA detected, black areas represent AAA missed.

Doppler. Thirty-seven out of 105 pregnancies (35%) were complicated by TTTS.

Table I shows the relationship between AAA identified at scan and injection study, and between AAA identified at scan and the presence or absence of TTTS. Table II shows the accuracy of AAA detection and likelihood ratios for positive and negative tests and the ability of an AAA to predict the absence of TTTS development and corresponding likelihood ratios. The cumulative sensitivity and specificity for the detection of AAA was 85.3 and 97.3% respectively. One AAA diagnosed antenatally was not identified at injection study. However, in this pregnancy, one of the twins died in utero at 28 weeks, 2 weeks after an AAA was identified. Delivery did not occur until 38 weeks, after which placental injection showed only a VVA in the presence of considerable sclerosis of the dead fetus’s placental territory, rendering injection study problematic and the findings difficult to interpret.

The influence of placental site on sensitivity of Doppler detection is shown in Figure 2. The detection rate was higher for anterior compared with non-anterior placental sites (\( P = 0.003 \), LR = 7.8, OR = 12.5). The influence of gestational age on sensitivity of Doppler detection of AAA is shown in Figure 3. From 13–30 weeks there was a steady increase in the ratio of AAA detected to AAA not detected with relatively few additional AAA identified beyond this gestation. Detection rates were also better when the diameter of the AAA was >2 mm at injection study (\( P = 0.001 \), LR = 10.67) (Table III).

Figure 3. Gestational age and cumulative sensitivity of AAA detection by Doppler. Grey areas represent AAA detected, white areas represent AAA missed.

Figure 4 illustrates the percentage of AAA eventually detected on Doppler as a function of gestational age. Grey areas represent AAA detected, black areas represent AAA missed. Values shown within the bars are the numbers of AAA detected; values over bars are the numbers of AAA missed.

Figure 4. Percentage of eventually identified AAA detected by Doppler as a function of gestational age. Grey areas represent AAA detected, black areas represent AAA missed. Values shown within the bars are the numbers of AAA detected; values over bars are the numbers of AAA missed.
Detection of arterio-arterial anastomoses in monochorionic twins

Table III. Relationship between Doppler detection and AAA diameter at injection study

<table>
<thead>
<tr>
<th>Doppler findings</th>
<th>Diameter of AAA at injection study</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>≥2 mm</td>
</tr>
<tr>
<td>AAA positive</td>
<td>43</td>
</tr>
<tr>
<td>AAA negative</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>AAA positive</th>
<th>AAA negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter of AAA</td>
<td>43/105 (35%)</td>
<td>3/68 (84%)</td>
<td>62/173(37%)</td>
</tr>
</tbody>
</table>

Likelihood ratio = 10.67, P = 0.001.

at 20, 23 and 26 weeks when TTTS presented at 23, 30 and 34 weeks respectively. In two cases, an AAA was seen after diagnosis at 24 and 29 weeks when TTTS had presented at 23 and 25 weeks respectively. Although it is possible that detection rates might be influenced by amnioreduction, there were insufficient cases to examine this possibility. In contrast, where no AAA was identified by ultrasound, 28/46 (61%) developed TTTS (Table I). From injection studies there was a strong association between having an AAA and not developing TTTS as only 11/37 (30%) TTTS cases had an AAA present compared to 57/68 (84%) of non-TTTS cases (LR = 31.0, P = 0.001, OR = 12.3).

Discussion

This study demonstrates that high sensitivity and specificity rates for in-vivo detection of AAA can be achieved without excessive increases in scanning times.

The predictive value of detecting AAA in vivo is highlighted by the 9-fold reduction in risk of developing TTTS when one is found. While not eliminating this risk entirely, patients may well derive some reassurance from this information. Indeed, since the perinatal mortality is reduced in MC pregnancies with an AAA present whether or not TTTS develops (Denbow et al., 2000), the whole pregnancy can be regarded as being at lesser risk of this complication. Moreover, should TTTS develop, the presence of an AAA is associated with substantially increased chances of both twins surviving (Taylor et al., 2000). Clinically, the demonstration of an AAA in MC twins goes some way to reassuring parents that a favourable outcome can be anticipated and that the excess risks associated with TTTS do not apply in their case.

The detection of an AAA also serves to confirm monochorionic placenta. If chorionicity has not been determined in early pregnancy, the standard techniques used become less reliable after the first trimester (Stagiannis et al., 1995), whereas demonstration of an AAA establishes this with 100% reliability. This information is highly relevant to genetic counselling, the management of imminent single fetal demise, discordant growth restriction or fetal anomaly, and is of great importance in selecting the appropriate technique for karyotype determination or selective feticide. We acknowledge, however, that absence of AAA on Doppler does not definitively indicate dichorionicity. Indeed, 37/105 (35%) MC pregnancies did not have an AAA at injection study. Although an AAA appears to protect against TTTS, AAA may increase the chances of co-twin death after single intrauterine death and/or neurological morbidity (Bejar et al., 1990; Bajoria et al., 1999).

There are three potential obstacles to uptake of this technique: poor equipment, lack of necessary operator skill and insufficient time. High resolution ultrasound equipment with the necessary colour Doppler facilities is now readily available in most obstetric ultrasound units and will become increasingly so as costs fall. This study was performed by two research fellows (M.T. and M.D.) with little prior scanning experience, both of whom acquired the necessary skills within a 2–3 month period, suggesting that learning this technique lies within the grasp of all ultrasonographers. Finally, the average time to detect an AAA was only 10 min and this may fall further with increasing experience.

There are several limitations to this test. The test is a positive outcome predictor, in that its identification confers a lower complication risk on that pregnancy. Absence of an AAA on Doppler, however, could be either because an AAA is genuinely absent and hence a negative predictor, or simply because it has not yet been detected. The likelihood ratio of 0.2 for a negative test suggests that there is five times less chance of not detecting an AAA that is present than correctly identifying absence of an AAA. In this study, the percentage of AAA detected at a particular gestation which are eventually detected ranges from 78% at 16 weeks to 100% at >28 weeks (Figure 4). Thus, this implies firstly that AAA can be identified with a high degree of reliability in the mid-trimester and secondly that the sensitivity at a particular gestation does not differ substantially from the overall cumulative sensitivity of 85%. Ideally, AAA need to be identified at a stage before the average time that TTTS develops, which in our unit is at ~22 weeks (Taylor et al., 2000). We expect detection in future to occur at earlier gestations because of increasing experience with the technique and because of earlier referrals of MC twins for assessment. Future ultrasound developments such as three-dimensional Doppler (Pretorius et al., 1998) may also enable earlier detection especially of the smaller vessels which proved elusive in the current study.

Notwithstanding the above limitations, this study shows detection of AAA to be the first accurate and clinically useful example of in-vivo mapping of chorionic plate vessels in MC twins. TTTS accounts for a substantial proportion of the increased perinatal mortality and morbidity of MC twins. Detection of an AAA gives a risk of TTTS 9-fold lower than if one is not detected. We suggest that antenatal detection of AAA by colour Doppler is a clinically valuable tool in the assessment of MC twins.

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References


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