



## MANAGEMENT OF MONOCHORIONIC TWIN PREGNANCY

This is the first edition of this guideline.

### 1. Purpose and scope

The purpose of this guideline is to describe and, if possible, quantify the problems associated with monochorionic placentation and to identify the best evidence to guide clinical care, including routine fetal surveillance and treatment of complications at secondary and tertiary levels.

### 2. Background and introduction

A monochorionic twin pregnancy is one in which both babies are dependent on a single, shared placenta. Around one-third of twin pregnancies in the UK have monochorionic placentas. Monochorionic placentation can also occur in higher-order multiples. There has been a recent increase in all types of multiple pregnancies with the increasing use of assisted reproductive techniques. Monochorionic (MC) and dichorionic (DC) twin pregnancies share increased risks of preterm birth, fetal growth restriction, pre-eclampsia, maternal pregnancy symptoms and postpartum haemorrhage. The particular challenges of monochorionic pregnancies arise from the vascular placental anastomoses that are almost universal and connect the umbilical circulations of both twins: twin-twin transfusion syndrome (TTTS), the consequences to the co-twin of fetal death and the management of discordant malformations. In addition, monochorionic, monoamniotic pregnancies (1% of twin pregnancies) carry a very high risk of cord entanglement.

TTTS complicates 10–15% of MC pregnancies; the placentas are more likely to have unidirectional artery-vein anastomoses and less likely to have bidirectional artery-artery anastomoses. A number of features of TTTS still elude full understanding; discordant activation of the renin-angiotensin system may be important.<sup>1</sup>

In a series of 82 consecutive MC pregnancies with blinded placental injection studies, there were similar numbers of artery-vein and vein-vein anastomoses in TTTS when compared with non-TTTS pregnancies. Fetal survival was better if artery-artery anastomoses were demonstrated after delivery.<sup>2</sup>

TTTS is found in monochorionic, monoamniotic (MCMA), as well as monochorionic, diamniotic (MCDA) pregnancies.<sup>3</sup> TTTS is more common in MCDA pregnancies than MCMA pregnancies, possibly reflecting that there are more protective artery-artery anastomoses in the latter.<sup>4</sup>

Rarely (in approximately 5% of cases), the transfusion may reverse during pregnancy, with the donor fetus demonstrating features of a recipient fetus and vice versa.<sup>5</sup> The pathophysiological basis for this is unclear. Reverse transfusion can occur following laser surgery to the placenta.

Unequal placental sharing and peripheral, ‘velamentous’ cord insertions are common in TTTS.<sup>6</sup> Significant intrauterine size discordance occurs in MC twins in the absence of TTTS in approximately 10% of pregnancies. The incidence of size discordance is as great in DC pregnancies in some series<sup>7</sup> but management of discordant growth restriction may be more difficult in MC pregnancies. Discordant fetal growth restriction may be differentiated from TTTS by the absence of polyhydramnios in one of the amniotic sacs, although the small twin may have oligohydramnios owing to placental insufficiency.

### 3. Identification and assessment of evidence

This RCOG guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines. The Cochrane Library (including the Cochrane Database of Systematic Reviews), DARE, EMBASE, TRIP, Medline and PubMed (electronic databases) were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. The search was restricted to articles published between 1966 and March 2008. The databases were searched using the relevant MeSH terms, including all subheadings, and this was combined with a keyword search. Search words included ‘monochorionic twin’, ‘TTTS’, ‘twin-twin transfusion syndrome’, ‘TRAP syndrome’, ‘amnioreduction’, ‘laser ablation’, ‘septostomy’, ‘cord occlusion’, and the search was limited to humans and to the English language. The National Library for Health and the National Guidelines Clearing House were also searched for relevant guidelines and reviews.

### 4. Diagnosis of monochorionic twin pregnancy

#### 4.1 *How is monochorionicity diagnosed prenatally and what is the accuracy of prenatal ultrasound diagnosis of monochorionicity?*

**All women with a twin pregnancy should be offered an ultrasound examination at 10–13 weeks of gestation to assess viability, chorionicity, major congenital malformation and nuchal translucency.**



**A photographic record should be retained, in the case notes, of the ultrasound appearances of the membrane attachment to the placenta.**



**If there is uncertainty about the diagnosis of chorionicity, a photographic record of the ultrasound appearance of the membrane attachment to the placenta should be retained in the case notes and a second opinion should be sought.**



**If there is doubt in the diagnosis of chorionicity, the woman should be referred to a specialist without delay, as chorionicity is best determined before 14 weeks.**



**Chorionicity is better assessed by ultrasound before 14 weeks than after 14 weeks.**



Clinicians should be aware that, although ultrasound assessment of chorionicity is very accurate, it does not have 100% sensitivity. A retrospective study reported 410 twin pregnancies with ultrasound diagnosis of chorionicity at less than 24 weeks and pathological study of fetal membranes after delivery.<sup>8</sup> Ultrasound diagnosis was based on demonstration of the ‘lambda’ or ‘twin peak’ sign (dichorionic) or ‘T-sign’ (monochorionic) at the membrane–placenta interface.<sup>9</sup> Overall, the correct diagnosis was made in 392/410 of pregnancies (96%). The sensitivity and specificity for diagnosing MC placentas were: 89.8% and 99.5% at ≤ 14 weeks of gestation and 88.0% and 94.7% over 14 weeks of gestation. Cases of TTTS have occurred after a mistaken diagnosis of DC placentation. Interestingly, the authors described four sex discordant twin pairs with MC placentas. No genetic studies were performed for zygosity. Another large series, with confirmatory histology<sup>10</sup> reported still higher sensitivity.

Evidence level 2+

3% of MC placentas have two placental masses (bipartite), so these are not necessarily dichorionic.<sup>11</sup>

## 4.2 Diagnosis of twin–twin transfusion syndrome

The diagnosis of TTTS is based on ultrasound criteria:

- the presence of a single placental mass
- concordant gender
- oligohydramnios with maximum vertical pocket [MVP] less than 2 cm in one sac and polyhydramnios in other sac (MVP  $\geq$  8 cm) (some would say  $\geq$  8 cm at  $\leq$  20 weeks and  $\geq$  10 cm over 20 weeks)<sup>12</sup>
- discordant bladder appearances – severe TTTS
- haemodynamic and cardiac compromise – severe TTTS.

## 4.3 What is the outcome of monochorionic compared to dichorionic twin pregnancies?

**Clinicians and women should be aware that MC twin pregnancies have higher fetal loss rates than DC twin pregnancies, mainly due to second trimester loss and, overall, may have a propensity to excess neurodevelopmental morbidity.**

C

A prospective Scandinavian study of 495 pregnancies diagnosed before 15 weeks found fetal loss at less than 24 weeks of gestation to be 14.2% MC compared with 2.6% DC ( $P < 0.05$ ). The number of babies alive at 8 months of age (percentage of fetuses at inclusion) was 82.4% MC compared with 96.3% DC  $p < 0.01$ .<sup>13</sup> Mean birthweight (both twins) and mean gestational age at delivery was less in MC twins ( $P < 0.01$ ). A retrospective study of 1407 twin pregnancies in Holland over a 10-year period found the perinatal mortality rate to be 11.6% in MC twins compared to 5.0% in DC twins. MC twins continued to be at greater risk even after 32 weeks.<sup>14</sup>

Evidence level 2+

## 4.4. What is the cause of the increased perinatal loss rates in MC compared with DC pregnancies?

Sebire and colleagues have suggested that the main risk of fetal death in MC pregnancies is before 24 weeks of gestation and after this time the rate of perinatal loss is only slightly higher in MC than DC pregnancies (4.9% versus 2.8%, respectively).<sup>15</sup> However, these data are from a ‘high-risk’ population often comprising ‘tertiary referrals’ with a high incidence of TTTS and other pathologies. However, recent data have indicated that, even when intensively monitored, apparently healthy MCDA pregnancies remain at a substantial risk of perinatal mortality after 24 weeks of gestation (3.3% of fetuses).<sup>16</sup> Optimal ultrasound scanning regimen is poorly defined in terms of evidence base and requires further research (see below).

## 5. Ultrasound scanning

### 5.1 What is the place of nuchal translucency measurement in monochorionic twin pregnancies?

**Nuchal translucency measurements should be offered to women with MC pregnancies who wish to have fetal aneuploidy screening.**

✓

**The place of nuchal translucency measurements in predicting TTTS is unclear, with different studies demonstrating varying sensitivity and specificity.**

C

A large, prospective, Scandinavian, five-centre study reported on 495 pregnancies diagnosed before 15 weeks.<sup>13</sup> All women were offered nuchal translucency (NT) measurements before 14 weeks of gestation, an anomaly scan at 19 weeks, fetal echocardiography by specialists at 21 weeks of gestation and a cervical scan at 23 weeks of gestation. In addition, women with MC pregnancies were scanned every 2 weeks between 12 and 23 weeks of gestation to detect TTTS. DNA testing was used to assess zygosity after delivery. TTTS was diagnosed in 23% of MC pregnancies. Unlike some other studies, NT measurements were not helpful in predicting TTTS. Two cases of TTTS had mild amniotic fluid discordance but did not develop frank TTTS until later in pregnancy (25 and 34 weeks of gestation).

A retrospective, cohort study (of 239 MC twin pregnancies) from Paris<sup>17</sup> noted that intertwin CRL discordance was defined as greater than 10% and the 95th percentile of NT thickness for CRL predicted an increased risk of perinatal death (50%). In addition, discordance in early second-trimester biometry and difference in CRL greater than 10% were associated with an increased risk of early-onset (less than 20 weeks) TTTS.

Two studies indicated that NT and CRL discordance may be useful in identifying MC twin pregnancies at risk of TTTS.<sup>17,18</sup> A study from London indicated that discordance in nuchal translucency was important in predicting fetal loss in monochorionic twins.<sup>18</sup> In 512 MC twin pregnancies scanned between 11 and 13<sup>6</sup> weeks, the study found that an NT discordance of greater than 20% was present in one in four MC pregnancies and, in this cohort, the risk of early fetal death (less than 20 weeks) was 63% and the risk of development of severe TTTS was 52% (there was a false positive rate of one in five). Discordance in fetal CRL was not a specific or sensitive screening test.

### 5.2 *Is fetal echocardiography useful in monochorionic twin pregnancy?*

**All monochorionic twins should have a detailed ultrasound scan which includes extended views of the fetal heart.**

**B**

**A fetal echocardiographic assessment should be considered in the assessment of severe TTTS.**

**D**

In the Scandinavian study,<sup>13</sup> major cardiac abnormalities had an incidence of 0.5%, of which 80% were detected antenatally: all before the echocardiographic examination. The authors concluded that the results did not justify routine formal echocardiography.

Evidence level 2+

A retrospective study of a cohort of 30 pregnancies with TTTS in which echocardiographic assessment was performed (myocardial thickness, cardiomegaly, tricuspid regurgitation) failed to demonstrate that these features added to estimation of prognosis.<sup>19</sup>

In a case series of 89 survivors from 73 pregnancies treated by laser ablation for severe TTTS, 11% of fetuses had secondary, structural heart disease, primarily right-sided cardiac lesions, predominantly pulmonary stenosis.<sup>20</sup>

Evidence level 3

### 5.3 *What is the optimum ultrasound regimen for monochorionic twin pregnancies?*

**Fetal ultrasound assessment should take place every 2–3 weeks in uncomplicated monochorionic pregnancies from 16 weeks.**



Ultrasound examinations between 16 and 24 weeks focus primarily on detection of TTTS. After 24 weeks, when first presentation of TTTS is uncommon, the main purpose is to detect fetal growth restriction, which may be concordant or discordant.

Different authors report weekly or less frequent (once every 2, 3 or 4 weeks) ultrasound examinations for women with MC pregnancies. However, in the absence of clinical trials, it is not clear which schedule is most efficacious in the early detection of complications of pregnancy and the most cost-effective.

Our search has revealed no comparative studies of assessment techniques or regimens to assess fetal growth and wellbeing and to detect late-onset TTTS (after 26 weeks). Few twin pregnancies were included in the randomised trials of umbilical artery Doppler velocimetry and these were not specifically monochorionic.<sup>21</sup>

Published reports of cohorts are based on surveillance regimens that range from weekly to 4-weekly. Inevitably, most of these emanate from centres with research interests in the topic. In the absence of any clear evidence of cost-effectiveness, it is suggested that surveillance of uncomplicated MC twins should occur at intervals of every 2–3 weeks from 16 weeks, and should include, as a minimum, abdominal circumference

measurements, imaging of the fetal brains with or without head circumference measurements, measurement of maximum pool depth of both sacs and umbilical artery Doppler studies (after 24 weeks), with care taken to identify the dividing membrane and to ensure that each cord is studied separately. This may be best performed in a multiple pregnancy clinic overseen by a specialist with expertise in fetal medicine.

Umbilical artery waveforms in MC twins may show **cyclical** absent or reversed end diastolic velocities. These are more common in discordant growth restriction (45%) than uncomplicated (5%) or severe TTTS pregnancies (2%).<sup>22</sup> This condition appears to result from large artery-artery anastomoses. The significance of the Doppler findings, in terms of timing intervention, is not clear.

## 6. Grading/staging system for severity of TTTS

**Women with monochorionic twin pregnancies should be asked to report sudden increases in abdominal size or breathlessness, as this may be a manifestation of TTTS.**



*How useful are grading systems for severity of TTTS in establishing prognosis?*

The Quintero system of staging TTTS (Table 1) has some prognostic value but the course of the condition is unpredictable and may involve improvement or rapid deterioration.

Stage	Classification
I	There is a discrepancy in amniotic fluid volume with oligohydramnios of a maximum vertical pocket (MVP) $\leq 2$ cm in one sac and polyhydramnios in other sac (MVP $\geq 8$ cm). The bladder of the donor twin is visible and Doppler studies are normal
II	The bladder of the donor twin is not visible (during length of examination, usually around 1 hour) but Doppler studies are not critically abnormal
III	Doppler studies are critically abnormal in either twin and are characterised as abnormal or reversed end-diastolic velocities in the umbilical artery, reverse flow in the Ductus venosus or pulsatile umbilical venous flow
IV	Ascites, pericardial or pleural effusion, scalp oedema or overt hydrops present
V	One or both babies are dead

In a series of 173 pregnancies complicated by TTTS from three centres in the USA and Australia, where treatment was either by amnioreduction or selective laser ablation, the outcome of at least one neonatal survivor was 91% (stage I), 88% (stage II), 67% (stage III) and 50% (stage IV).<sup>24</sup> Similar findings were reported from Germany in a series of 200 TTTS pregnancies treated by laser ablation: at least one neonatal survivor: 93% (stage I), 83% (stage II), 83% (stage III) and 70% (stage IV).<sup>25</sup>

Many reports of TTTS are difficult to interpret because of referral bias. A study from Western Australia is especially valuable because it is population-based, coming from the sole perinatal tertiary service in the state.<sup>26</sup> A prospective cohort of 71 women with TTTS was treated with amnioreduction or septostomy. There was a relationship between Quintero stage at diagnosis and mean gestational age at delivery and perinatal survival: stage I, 32 weeks of gestation, 77% survival; stage II, 31 weeks of gestation, 70%; stage III, 28 weeks of gestation, 54%; stage IV, 27 weeks of gestation, 44%. However, disease progression was often unpredictable, with 28% of pregnancies improving, 35% worsening and 37% remaining in the same grade throughout gestation. Pregnancies appeared, for example, to progress from stage I to stage III without obviously passing through stage II. Very similar findings came from a smaller series in the US ( $n = 18$ ).<sup>27</sup> There were similar rates of regression and progression. Another study found a change of stage to be of greater prognostic significance than the stage itself.<sup>28</sup>

Amniotic fluid discordance (but not fulfilling 8cm/2cm criteria) together with normal umbilical artery Doppler velocimetry is associated with good outcome (93% overall survival) and uncommon progression to severe TTTS (14%).<sup>29</sup>

There has been controversy about the Quintero staging of TTTS, since stage 1 disease may not necessarily be associated with the best outcomes<sup>30</sup> To emphasise this, a recent cross-sectional study from a single centre in the USA has indicated that MC twin pregnancies complicated by TTTS as early as Quintero stages I and II had a significant proportion of recipient twins with ventricular hypertrophy (17/28, 61%), atrioventricular valve regurgitation (6/28, 21%) and objective abnormalities in either right (12/24, 50%) or left (14/24, 58%) ventricular function.<sup>31</sup> The suggestion that structural and/or functional assessment of the fetal heart (especially in the recipient) by echocardiography of MC pregnancies at risk of or with TTTS may be more useful in defining the risk of severe TTTS and treatment modalities such as fetoscopic laser ablation<sup>32</sup> is of interest and has led to calls for these criteria to be incorporated into a staging classification system.

## 7. What is (are) the optimal treatment(s) of TTTS and their outcomes?

**Twin–twin transfusion syndrome should be managed in conjunction with regional fetal medicine centres with recourse to specialist expertise.**



**Severe twin–twin transfusion syndrome presenting before 26 weeks of gestation should be treated by laser ablation rather than by amnioreduction or septostomy.**



The Eurofetus trial randomised women with TTTS to either laser ablation or amnioreduction.<sup>33</sup> The planned sample size of 172 women aimed to demonstrate a 15% difference in survival. The trial was prematurely terminated after an interim analysis of 142 pregnancies on the advice of the trial statistician. The large majority of women had Quintero stage II or III TTTS. Three women in the laser group did not undergo the procedure. Two women in the amnioreduction group did not undergo the procedure and seven underwent laser ablation, six following amnioreductions. Analysis was by intention to treat.

Evidence level 1+

Another randomised trial compared amnioreduction with septostomy (the deliberate creation of a hole in the dividing septum with the intention of improving amniotic fluid volume in the donor sac).<sup>34</sup> The trial included 73 women with TTTS (of all stages). The primary outcome was: at least one infant surviving until hospital discharge. The trial was stopped after an interim analysis because no significant differences were seen in the primary outcome.

The results of both trials have been re-analysed in a Cochrane review, adjusting where possible for clustering, recognising the non-independence of twin fetuses within a pair.<sup>35</sup> The results of a third trial (NICHD trial of amnioreduction versus laser ablation) will be added in the future. For laser ablation versus amnioreduction (Eurofetus), there were fewer deaths of both babies (RR 0.33, 95% CI 0.16–0.67), fewer neonatal deaths (RR 0.29, 95% CI 0.14–0.61, adjusted for clustering) and fewer perinatal deaths (RR 0.59, 95% CI 0.40–0.87, adjusted for clustering). More babies were alive without neurological abnormality at 6 months of age after laser ablation (RR 1.66, 95% CI 1.17–2.35, adjusted for clustering). Long-term outcomes are awaited.

Evidence level 1++

Anastomoses may be missed at laser ablation<sup>36</sup> and TTTS can recur later in up to 14% of pregnancies treated by laser ablation.<sup>37</sup> Laser ablation can be performed in mono- and dichorionic triplet pregnancies.<sup>38</sup>

Evidence level 3

Some women request termination of pregnancy when severe TTTS is diagnosed and this should be discussed as an option. Another option is to offer selective termination of pregnancy using bipolar diathermy of one of the umbilical cords; with inevitable sacrifice of that baby.<sup>39</sup> This may be

appropriate if there is severe hydrops fetalis in the recipient or evidence of cerebral damage in either twin.

Evidence  
level 3

Little information is available about maternal morbidity after laser ablation.

There are few data to inform how frequently ultrasound surveillance is required after fetoscopic laser ablation (or amnioreduction). However, some experts advocate that ultrasound examination (with brain imaging, fetal measurement and Doppler assessment) should be performed at least weekly, with consideration given to delivery of the surviving twin(s) at 34 weeks.<sup>40-42</sup> Often, the mode of delivery at this gestation is by caesarean section.

## 8. What is the optimal timing and method of delivery for otherwise uncomplicated MC pregnancies (without fetal growth restriction and TTTS)?

It is appropriate to aim for vaginal birth of monochorionic twins unless there are accepted, specific clinical indications for caesarean section, such as twin one lying breech or previous caesarean section.



Delivery should be planned for 36–37 weeks of gestation, unless there is an indication to deliver earlier.



For uncomplicated MCDC pregnancies (without TTTS or fetal growth restriction), there may be a higher risk of unexplained fetal demise despite intensive fetal surveillance.<sup>16</sup> In this cohort study, ten unexpected fetal deaths occurred in seven of the 151 uncomplicated MCDA pregnancies. The prospective risk of unexplained stillbirth after 32 weeks was 1/23 (4.35%) for MCDA twin pregnancies (95% CI 1/11–1/63).

In contrast, a series of 193 MC pregnancies from Portugal showed a low risk of fetal death after 32 weeks of gestation and did not support a policy of routine planned delivery before 37 weeks of gestation.<sup>43</sup>

Evidence  
level 3

The management of multiple pregnancies in general is controversial, as are the timing of induction and the proposed mode of delivery. It has been stated in one review<sup>44</sup> that ‘many units deliver all monochorionic diamniotic twins by caesarean section because of the 10% risk of acute transfusion in labour’, although the evidence base for this is unclear. Given the recognised hazards of caesarean section to the mother, it seems inappropriate to recommend caesarean section routinely for all monochorionic twins without proof of benefit. Our search has found no such objective evidence.

This is not to imply that acute transfusion cannot occur during labour and it is one reason why continuous electronic surveillance during labour is desirable. Maternal views will also be important in reaching a conclusion about the best method of delivery.

There is no robust evidence to indicate the optimal timing of delivery in either MC or DC twin pregnancies. An RCOG Study Group<sup>41</sup> suggested that, in DC twin pregnancies, discussion should take place as to the mode of delivery and intrapartum management at 34–36 weeks. Delivery should be planned at 37–38 weeks. In MC twin pregnancies, discussion should take place as to the mode of delivery and intrapartum management at 32–34 weeks. Delivery should be planned at 36–37 weeks.

## 9. What are the consequences for the surviving twin after fetal death of the co-twin in a monochorionic pregnancy and what is optimal clinical management?

After the single fetal death in a monochorionic pregnancy, the risk to the surviving twin of death or neurological abnormality is of the order of 12% and 18%, respectively. Clinicians should be aware that the risks are much higher than in dichorionic pregnancies and that management of such pregnancies is complex.



**It should be recognised that the risks of fetal death and disability in childhood are not restricted to monochorionic pregnancies with a prior diagnosis of twin-to-twin transfusion syndrome.**



**Single fetal death in a monochorionic pregnancy should be referred and assessed in a regional fetal medicine centre.**



Damage to MC twins after the death of a co-twin is now thought to be caused by acute haemodynamic changes around the time of death, with the survivor essentially haemorrhaging part of its circulating volume into the circulation of the dying twin. This may cause transient or persistent hypotension and low perfusion, leading to the risk of ischaemic organ damage, notably but not exclusively, to the brain.

A systematic review identified 28 reports describing five or more cases of single fetal death with knowledge of chorionicity and outcome data.<sup>45</sup> Pooled estimates revealed a risk of death of the co-twin of 12% (95% CI 7–18) in monochorionic pregnancies and 4% (95% CI 2–7) in DC pregnancies. Equivalent figures for neurological abnormality in the survivor were 18% (95% CI 11–26) MC and 1% (95% CI 0–7) DC and for preterm birth 68% (95% CI 56–78) MC and 57% (95% CI 34–77) DC. Where there were comparative data within the same studies, the odds of death and neurological damage were six and four times greater, respectively, in MC than in DC survivors.

Evidence level 2++

Clinical management is complex and is best overseen by fetal medicine experts with the knowledge and experience to advise about the advantages and disadvantages of different approaches. Rapid delivery is usually unwise, unless there are significant cardiotocographic abnormalities or evidence of anaemia in the survivor, as evidenced by abnormal middle cerebral artery Doppler waveforms or if fetal death occurs late in pregnancy. Detailed counselling is essential and should be recorded in the case records. Serious compromise in the surviving fetus may be anticipated and this should be discussed with parents, including the significant risk of long-term morbidity. Evidence of fetal compromise (such as abnormal cardiotocography) could represent continuing damage to the brain and other organs, as well as already existing damage. A conservative policy is often appropriate, with brain imaging planned by 4 weeks to establish (if the baby has survived) whether serious cerebral morbidity has occurred. The appearances of such manifestations on ultrasound examination of the fetal central nervous system are variable and may take up to 4 weeks to occur. Fetal magnetic resonance imaging provides earlier and more detailed information about brain lesions in the surviving fetus than does ultrasound and its use is recommended.<sup>46</sup>

Evidence level 3

In such circumstances, termination of pregnancy would then be an option. The gestational age at the time of diagnosis will have an important influence on management options. The views of the parent or parents will be critical.

**Fetal anaemia may be assessed in the surviving twin by measurement of the fetal middle cerebral artery peak systolic velocity using Doppler sonography.**



In a prospective series of 20 MC pregnancies complicated by single fetal death, there was a strong correlation between fetal anaemia (assessed by cordocentesis) and fetal middle cerebral artery peak systolic velocity (MCA-PSV).<sup>47</sup>

In a small series ( $n = 26$ ) of pregnancies complicated by TTTS and single fetal death, the prognosis was worse for donor twins following the death of the recipient twin than vice versa. This would fit with the concept of enhanced blood loss through a unidirectional anastomosis.<sup>48</sup> There are a few reports of intrauterine transfusion of anaemic surviving co-twins but the value of this intervention is not established, in terms of preventing perinatal and long-term neurological morbidity.<sup>49,50</sup>

Evidence level 3

## 10. What are the specific problems of monochorionic, monoamniotic pregnancies and how should they be managed?

**Most monochorionic, monoamniotic twins have cord entanglement and are best delivered at 32 weeks, by caesarean section, after corticosteroids.**



It is arguable that MCMA pregnancies are ‘uncomplicated’, as most have signs of chronic cord entanglement. A retrospective study of 30 MCMA twin pairs reported a total survival of 60%.<sup>51</sup> Two pairs died after 32 weeks. Of the ten twin pairs that died in utero, cord entanglement was documented in eight. The authors recommended elective delivery at 32 weeks.

Evidence level 3

However, it merits comment that there are no comparative data available to inform objectively the timing, or method, of delivery in such pregnancies.

## 11. Higher order multiple pregnancies

*What is the outcome of dichorionic compared to trichorionic triplet pregnancies?*

**Clinicians and women should be aware that triplet pregnancies that include a monochorionic pair have higher fetal loss rates than trichorionic triplet pregnancies. They may also be complicated by twin–twin transfusion syndrome. Therefore, increased ultrasound surveillance is warranted.**



A retrospective study of naturally conceived triplet pregnancies managed in three tertiary referral units in the UK found a 5.5-fold increased risk of adverse perinatal outcome in dichorionic, triamniotic pregnancies (that is, containing monochorionic twins) than trichorionic, triamniotic pregnancies. Referral bias may have influenced the findings. A similar retrospective study from two tertiary centres in Germany described 84% survival in fetuses of mono- and dichorionic triplet pregnancies combined, compared with 92% in fetuses of trichorionic triplet pregnancies.<sup>53</sup> This difference did not reach statistical significance.

Evidence level 2

## 12. What is the incidence of and the therapeutic options for discordant abnormalities in monochorionic pregnancies, including twin reversed arterial perfusion sequence?

**Monochorionic twins that are discordant for fetal anomaly must be referred at an early gestation for assessment and counselling in a regional fetal medicine centre.**



Selective feticide by intracardiac injection of potassium chloride is not an option in MC pregnancies because of the presence of anastomoses. A series of 80 MC pregnancies (twin and triplet) with severe discordant abnormalities, twin reversed arterial perfusion (TRAP) sequence or severe TTTS, underwent cord coagulation by bipolar diathermy or intrafetal laser ablation.<sup>54</sup> Overall, 74% of co-twins survived (95% CI 64–83). One pregnancy had to be terminated because of chorioamnionitis.

Not all pregnancies with TRAP sequence require invasive treatment and this appears to be dependent on:

- i) the relative size of the ‘acardiac’ twin to the pump twin and
- ii) the presence of any cardiovascular impairment in the ‘pump’ twin.<sup>55</sup> Careful monitoring and ultrasound surveillance is required.

## 13. How are conjoined twins diagnosed and what are the outcomes?

Conjoined twins are very rare, occurring in around one in 90 000–100 000 pregnancies worldwide. The underlying pathogenic mechanism remains uncertain, with theories including incomplete separation of the

developing embryo, development of co-dominant axes and embryonic fusion. In one recent series of 14 cases of prenatally diagnosed conjoined twins at a single referral centre, 20% of parents opted for termination of pregnancy, 10% of fetuses died in utero and the overall individual survival rate to discharge of those attempting pregnancy continuation was about 25%.<sup>56</sup> Most cases are now prenatally diagnosed and delivered by elective caesarean section but vaginal deliveries of conjoined twins are reported. Risk of dystocia and uterine rupture has been reported in association with prenatally undiagnosed cases.

Prenatal diagnosis of conjoined twins is now well-reported from the mid first-trimester, using B-mode ultrasound, Doppler, colour Doppler and three-dimensional imaging techniques, with detailed assessment of cardiovascular anatomy important for determining prognosis and planning management.

## 14. Training

All sonographers who undertake routine ultrasound scans during pregnancy must be trained to establish chorionicity by inspection of the dividing membrane.

All sonographers who undertake growth scans of MC twins should be made aware of the features of TTTS, and the need to refer if such features present.

Ideally, training should be delivered within the framework of a multidisciplinary multiple pregnancy clinic that provides holistic care to the pregnant woman and her babies.

## 15. Auditable standards

1. Correct prenatal diagnosis of chorionicity greater than 95%.
2. Prospective outcome (primary outcomes perinatal mortality and long-term paediatric morbidity) after fetoscopic laser ablation for TTTS corrected for stage and severity.

## References

1. Kilby MD, Platt C, Whittle MJ, Oxley J, Lindop GB. Renin gene expression in fetal kidneys of pregnancies complicated by twin-twin transfusion syndrome. *Pediatr Dev Pathol* 2001;4:175-9.
2. Denbow ML, Cox P, Taylor M, Hammal DM, Fisk NM. Placental angioarchitecture in monochorionic twin pregnancies: relationship to fetal growth, fetofetal transfusion syndrome, and pregnancy outcome. *Am J Obstet Gynecol* 2006;182:417-26.
3. Gallot D. Ultrasonographic signs of twin-twin transfusion syndrome in a monoamniotic twin pregnancy. *Ultrasound Obstet Gynecol* 2005;25:308-9.
4. Umur A. Monoamniotic-versus diamniotic-mono chorionic twin placentas: Anastomoses and twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2003;189:1325-9.
5. Wee LY, Taylor MJ, Vanderheyden T, Wimalasundera R, Gardiner HM, Fisk NM. Reversal of twin-twin transfusion syndrome: frequency, vascular anatomy, associated anomalies and outcome. *Prenatal Diagnosis* 2004;24:104-10.
6. Fick ALM. Unequal placental sharing and birth weight discordance in monochorionic diamniotic twins. *Am J Obstet Gynecol* 2006;195:178-83.
7. Sebire NJ, D'Ercole C, Soares W, Nayar R, Nicolaides KH. Intertwin disparity in fetal size in monochorionic and dichorionic pregnancies. *Obstet Gynecol* 1998;91:82-5.
8. Lee YM, Cleary-Goldman J, Thaker HM, Simpson LL. Antenatal sonographic prediction of twin chorionicity. *Am J Obstet Gynecol* 2006;195:863-7.
9. Sepulveda W, Sebire NJ, Hughes K, Odibo A, Nicolaides KH. The lambda sign at 10-14 weeks of gestation as a predictor of chorionicity in twin pregnancies. *Ultrasound Obstet Gynecol* 1996;7:421-3.
10. Menon DK. A retrospective study of the accuracy of sonographic chorionicity determination in twin pregnancies. *Twin Res Hum Genet* 2005;8:259-61.
11. Lopriore E. Twin pregnancies with two separate placental masses can still be monochorionic and have vascular anastomoses. *Am J Obstet Gynecol* 2006;194:804-8.
12. Moise KJ. Neurodevelopmental outcome after laser therapy for twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2006;194:1208-10.
13. Sperling L. Detection of chromosomal abnormalities, congenital abnormalities and transfusion syndrome in twins. *Ultrasound Obstet Gynecol* 2007;29:517-26.
14. Hack KE, Derks JB, Elias SG, Franx A, Roos EJ, Voerman SK, et al. Increased perinatal mortality and morbidity in monochorionic versus dichorionic twin pregnancies: clinical implications of a large Dutch cohort study. *BJOG* 2008;115:58-67.
15. Sebire NJ, Snijders RJ, Hughes K, Sepulveda W, Nicolaides KH. The hidden mortality of monochorionic twin pregnancies. *Br J Obstet Gynaecol* 1997;104:1203-7.
16. Barigye O, Pasquini L, Galea P, Chambers H, Chappell L, Fisk NM. High risk of unexpected late fetal death in monochorionic twins despite intensive ultrasound surveillance: A cohort study. *PLoS Med* 2005;2:e172.
17. El Kateb A, Nasr B, Nassar M, Bernard JP, Ville Y. First-trimester discordance in crown-rump length predicts timing of development of twin-twin transfusion syndrome: OP05.02. *Prenat Diagn* 2007;27:922-5.
18. Kagan KO, Gazzoni A, Sepulveda G, Sotiriadis A, Nicolaides KH. Discordance in nuchal translucency thickness in the prediction of severe twin-to-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2007;29:527-32.

19. Anderson BL, Sherman FS, Mancini F, Simhan HN. Fetal echocardiographic findings are not predictive of death in twin-twin transfusion syndrome. *J Ultrasound Med* 2006;25:455-9.
20. Herberg U, Gross W, Bartmann P, Banek CS, Hecher K, Breuer J. Long term cardiac follow up of severe twin to twin transfusion syndrome after intrauterine laser coagulation. *Heart* 2006;92:95-100.
21. Giles WB. Doppler ultrasound in multiple pregnancies. *Baillieres Clin Obstet Gynaecol* 1998;12:77-89.
22. Gratacos E. Incidence and characteristics of umbilical artery intermittent absent and/or reversed end-diastolic flow in complicated and uncomplicated monochorionic twin pregnancies. *Ultrasound Obstet Gynecol* 2004;23:456-60.
23. Quintero RA, Morales WJ, Allen MH, Bornick PW, Johnson PK, Kruger M. Staging of twin-twin transfusion syndrome. *J Perinatol* 1999;19:550-5.
24. Quintero RAM. Stage-based treatment of twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2003;188:1333-40.
25. Huber A, Diehl W, Bregenzner T, Hackeloer BJ, Hecher K. Stage-related outcome in twin-twin transfusion syndrome treated by fetoscopic laser coagulation. *Obstet Gynecol* 2006;108:333-7.
26. Dickinson JE, Evans SF, Dickinson JE, Evans SF. The progression of disease stage in twin-twin transfusion syndrome. *J Matern Fetal Neonatal Med* 2004;16:95-101.
27. Luks FI, Carr SR, Plevyak M, Craig SD, Athanassiou A, Ralston SJ, et al. Limited prognostic value of a staging system for twin-to-twin transfusion syndrome. *Fetal Diagn Ther* 2004;19:301-4.
28. Taylor MJ, Govender L, Jolly M, Wee L, Fisk NM. Validation of the Quintero staging system for twin-twin transfusion syndrome. *Obstet Gynecol* 2002;100:1257-65.
29. Huber A. Perinatal outcome in monochorionic twin pregnancies complicated by amniotic fluid discordance without severe twin-twin transfusion syndrome. *Ultrasound Obstet Gynecol* 2006;27:48-52.
30. Ville Y. Twin-to-twin transfusion syndrome: time to forget the Quintero staging system? *Ultrasound Obstet Gynecol* 2007;30:924-7.
31. Michelfelder E, Gottliebson W, Border W, Kinsel M, Polzin W, Livingston J, et al. Early manifestations and spectrum of recipient twin cardiomyopathy in twin-twin transfusion syndrome: relation to Quintero stage. *Ultrasound Obstet Gynecol* 2007;30:965-71.
32. Raboisson MJ, Fouron JC, Lamoureux J, Leduc L, Grignon A, Proulx F, et al. Early intertwin differences in myocardial performance during the twin-to-twin transfusion syndrome. *Circulation* 2004;110:3043-8.
33. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. *N Engl J Med* 2006;354:136-44.
34. Moise KJJ. A randomized trial of amnioreduction versus septostomy in the treatment of twin-twin transfusion syndrome. *Am J Obstet Gynecol* 2005;193:701-7.
35. Roberts D, Neilson JP, Kilby MD, Gates S. Interventions for the treatment of twin-twin transfusion syndrome. *Cochrane Database Sys Rev* 2008;CD002073.
36. Lewi L, Jani J, Cannie M, Robyr R, Ville Y, Hecher K, et al. Intertwin anastomoses in monochorionic placentas after fetoscopic laser coagulation for twin-to-twin transfusion syndrome: is there more than meets the eye? *Am J Obstet Gynecol* 2006;194:790-5.
37. Robyr R. Prevalence and management of late fetal complications following successful selective laser coagulation of chorionic plate anastomoses in twin-to-twin transfusion syndrome. *Am J Obstet Gynecol* 2006;194:796-803.
38. Van Schoubroeck D, Lewi L, Ryan G, Carreras E, Jani J, Higuera T, et al. Fetoscopic surgery in triplet pregnancies: a multicenter case series. *Am J Obstet Gynecol* 2004;191:1529-32.
39. Taylor MJ, Shalev E, Tanawattanacharoen S, Jolly M, Kumar S, Weiner E, et al. Ultrasound-guided umbilical cord occlusion using bipolar diathermy for Stage III/IV twin-twin transfusion syndrome. *Prenat Diagn* 2002;22:70-6.
40. Cavicchioni O, Yamamoto M, Robyr R, Takahashi Y, Ville Y. Intrauterine fetal demise following laser treatment in twin-to-twin transfusion syndrome. *BJOG* 2006;113:590-4.
41. Consensus views arising from the 50th Study Group: Multiple Pregnancy. In: Kilby M, Baker P, Critchley H, Field D, editors. *Multiple pregnancy*. London: RCOG Press; 2006. p. 283-6.
42. Blickstein I, Arabin B, Chervenak FA, Kavak ZN, Keith LG, Shinwell, et al. The Istanbul international consensus statement on the perinatal care of multiple pregnancy. *J Perinat Med* 2007;35:465-7.
43. Simoes T. Prospective risk of intrauterine death of monochorionic-diamniotic twins. *Am J Obstet Gynecol* 2006;195:134-9.
44. Duncan KR. Twin-to-twin transfusion: update on management options and outcomes. *Curr Opin Obstet Gynecol* 2005;17:618-22.
45. Ong SSC, Zamora J, Khan KS, Kilby MD. Prognosis for the co-twin following single-twin death: a systematic review. *BJOG* 2006;113:992-8.
46. Righini A, Salmona S, Bianchini E, Zirpoli S, Moschetta M, Kustermann A, et al. Prenatal magnetic resonance imaging evaluation of ischemic brain lesions in the survivors of monochorionic twin pregnancies: report of 3 Cases. *J Comput Assist Tomogr* 2004;28:87-92.
47. Senat MV, Couderc S, Bernard J, Ville Y. The value of middle cerebral artery peak systolic velocity in the diagnosis of fetal anemia after intrauterine death of one monochorionic twin. *Am J Obstet Gynecol* 2003;189:1320-4.
48. Bajoria R, Wee LY, Anwar S, Ward S. Outcome of twin pregnancies complicated by single intrauterine death in relation to vascular anatomy of the monochorionic placenta. *Human Reprod* 1999;14:2124-30.
49. Senat MV, Bernard JP, Loizeau S, Ville Y. Management of single fetal death in twin-to-twin transfusion syndrome: a role for fetal blood sampling. *Ultrasound Obstet Gynecol* 2002;20:360-3.
50. Nakata M, Sumie M, Murata S, Miwa I, Kusaka E, Sugino N. A case of monochorionic twin pregnancy complicated with intrauterine single fetal death with successful treatment of intrauterine blood transfusion in the surviving fetus. *Fetal Diagn Ther* 2007;22:7-9.
51. Ezra Y, Shveiky D, Ophir E, Nadjari M, Eisenberg VH, Samueloff A, et al. Intensive management and early delivery reduce antenatal mortality in monoamniotic twin pregnancies. *Acta Obstet Gynecol Scand* 2005;84:432-5.
52. Adegbite AL, Ward SB, Bajoria R. Perinatal outcome of spontaneously conceived triplet pregnancies in relation to chorionicity. *Am J Obstet Gynecol* 2005;193:1463-71.
53. Geipel A, Berg C, Katalinic A, Plath H, Hansmann M, Germer U, et al. Prenatal diagnosis and obstetric outcomes in triplet pregnancies in relation to chorionicity. *BJOG* 2005;112:554-8.
54. Lewi L, Gratacos E, Ortibus E, Van Schoubroeck D, Carreras E, Higuera T, et al. Pregnancy and infant outcome of 80 consecutive cord coagulations in complicated monochorionic multiple pregnancies. *Am J Obstet Gynecol* 2006;194:782-9.
55. Weisz B. Tailored management of twin reversed arterial perfusion (TRAP) sequence. *Ultrasound Obstet Gynecol* 2004;23:451-5.
56. Agarwal U, Dahiya P, Khosla A. Vaginal birth of conjoined thoracopagus: a rare event. *Arch Gynecol Obstet* 2003;269:66-7.

## APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: *Development of RCOG Green-top Guidelines* (available on the RCOG website at [www.rcog.org.uk/index.asp?PageID=75](http://www.rcog.org.uk/index.asp?PageID=75)). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels	Grades of recommendations
1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias	<b>A</b> At least one meta-analysis, systematic reviews or randomised controlled trial rated as 1++ and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias	<b>B</b> A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
1- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias	<b>C</b> A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal	<b>D</b> Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal	<b>Good practice point</b>
2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal	 Recommended best practice based on the clinical experience of the guideline development group
3 Non-analytical studies; e.g. case reports, case series	
4 Expert opinion	

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The final version is the responsibility of the Guidelines Committee of the RCOG.

The guideline review process will commence in December 2011  
unless otherwise indicated

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The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken.