Review Twin pregnancy: controversies in management

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Key content:
• The management of twin pregnancy poses many difficult and controversial issues; questions about management remain unanswered.
• With the rising incidence of multiple pregnancies due to greater maternal age and advances in assisted conception, the obstetrician is increasingly faced with these issues.
• This article looks at the controversies and available evidence concerning management and delivery of twin pregnancy.

Learning objectives:
• To understand the issues surrounding screening for aneuploidy in twins and the role of invasive testing.
• To understand the complex issues involved in the management of single twin demise, twins discordant for fetal anomaly and twin-to-twin transfusion syndrome.
• To be aware of the evidence available regarding the timing and mode of delivery of twins.

Ethical issues:
• An obligatory single embryo transfer policy in assisted reproduction may be an option for women at high risk of twins, but will this be in conflict with client interests and wishes?
• Complex ethical issues surround multifetal pregnancy reduction and selective feticide among twins discordant for fetal anomaly; these are matters for continuing debate.

Keywords congenital abnormality / mode of delivery / single twin demise / twin-to-twin transfusion syndrome

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Introduction
In this article we discuss the more controversial and difficult aspects of the management of twin pregnancy. These issues include the results of fertility treatment, screening for complications, indications for intervention, modes of delivery, fetal death and selective feticide.

The epidemiology of twin pregnancy and the effects of fertility treatment
Variations in rates of twin and higher order multiple pregnancies are related to assisted fertilisation and the effects of rising maternal age. The change in policy from a limit of three embryos to be transferred in women undergoing in vitro fertilisation to two is likely to result in fewer multiple pregnancies; however, projections from the UK Office for National Statistics suggest that the mean maternal age at completion of childbearing is likely to continue to rise. Hence any effect of changes in fertility rates is likely to be masked by the continuing trend related to increasing maternal age.

There are two issues to consider for women requiring fertility treatment. First, for women undergoing intrauterine insemination, withdrawal of concurrent gonadotrophin use should be considered. Second, single embryo transfer should be considered for women at high risk of twins although the default position for most women should be a double embryo transfer policy.

Early ultrasound
The Royal College of Obstetricians and Gynaecologists recommends routine early ultrasound in all pregnancies; however, there is no evidence that this improves perinatal outcome. First trimester ultrasound does, however, provide accurate dating, which is useful in growth restriction and prematurity, both of which are potential problems in twin pregnancy. Many twin pregnancies are delivered before term and accurate dating is important to avoid iatrogenic prematurity. Early scanning also allows for the determination of fetal number, amnioncity and chorionicity.

The accuracy of first trimester ultrasound in the determination of chorionicity approaches 100%. The determination of chorionicity also has implications in pregnancies where twins are discordant for anomalies (see below). However, despite the apparent advantages of early diagnosis, knowledge of chorionicity has not yet been shown in prospective clinical trials to improve outcome.

Antenatal care
It seems obvious that specialised ‘twin clinics’ would benefit women. However, although special twin management protocols may improve outcome,7 attendance at dedicated clinics per se has yet to be shown to be beneficial. Box 1 and Box 2 illustrate the scanning schedule drawn up from consensus views arising from a recent study group on multiple pregnancy.

Preterm labour
A mean cervical length of <25 mm (compared with 15 mm for singletons) is a good predictor of preterm labour before 32 weeks of twin gestation (OR 6.9; 95% CI 2.0–2.4). The use of fetal fibronectin is less predictive of preterm delivery of

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Box 1
Key events in antenatal and postnatal care to be offered for dichorionic twins. Reproduced with permission from the RCOG Press.

- Multiple pregnancy clinic: lead clinician with multidisciplinary team
- Ultrasound at 10–13 weeks: (a) viability, (b) chorionicity, (c) nuchal translucency: aneuploidy
- Structural anomaly scan at 20–22 weeks
- Serial fetal growth scans, e.g. at 24, 28 and 32 weeks and then every 2–4 weeks
- Blood pressure and urinalysis at 20, 24 and 28 weeks and then every 2 weeks
- Discussion of woman’s family’s needs relating to twins
- 34–38 weeks: discussion of mode of delivery and intrapartum care
- Elective delivery at 37–38 completed weeks
- Postnatal advice and support (hospital and community-based) to include breastfeeding and contraceptive advice

Box 2
Key events in antenatal and postnatal care to be offered for monochorionic twins. Reproduced with permission from the RCOG Press.

- Multiple pregnancy clinic: lead clinician with multidisciplinary team
- Ultrasound at 10–13 weeks: (a) viability, (b) chorionicity, (c) nuchal translucency: aneuploidy/TTTS
- Ultrasound surveillance for TTTS and discordant growth: at 16 weeks and then every 2 weeks
- Serial fetal growth scans: at 20–22 weeks (including fetal echocardiography)
- Serial fetal growth scans every 2 weeks until delivery
- Blood pressure and urinalysis at 20, 24 and 28 weeks and then every 2 weeks
- Discussion of woman’s family’s needs relating to twins
- 32–34 weeks: discussion of mode of delivery and intrapartum care
- Elective delivery at 36–37 completed weeks (if uncomplicated)
- Postnatal advice and support (hospital and community-based) to include breastfeeding and contraceptive advice

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twins compared with singletons, with only 50% of deliveries before 35 weeks predicted at 28 weeks of gestation. Both cervical length assessment and use of fetal fibronectin are difficult to justify in that there is no proven effective intervention. For example, paradoxically, routine admission and bed rest increase the risk of preterm delivery in twin pregnancy. Cervical cerclage also has the potential to increase the loss rate.

**Congenital anomaly among twins**

Best estimates suggest that the congenital anomaly rate of dizygotic twins is not significantly greater than that of singletons. By contrast, the congenital anomaly rate of monozygotic twins is double that of dizygotic twin or singleton pregnancies. It is likely that the congenital anomaly rate of monozygotic twins is three to four times greater than that of dichorionic twin or singleton pregnancies. In particular, among monozygotic twins there are increased risks of cardiovascular and central nervous system malformations. The majority of anomalies seen with increased frequency in twin pregnancies are related to laterality or are secondary to vascular disruptions.

**Screening for aneuploidy**

As twinning increases with maternal age, the absolute risk of chromosomal abnormality is increased in this population. Age aside, the risk of chromosomal abnormality in each twin is the same per fetus as in singleton pregnancies. In monozygotic twins both fetuses will be affected or unaffected (with rare exceptions); in dizygotic pregnancies, the risk of chromosomal abnormalities for each twin is, again, the same as for singletons. However, because there are two fetuses, the risk that one fetus would be affected in that pregnancy is double that of a singleton pregnancy.

Serum screening in the second trimester for twins is not reliable. There are several issues regarding screening for aneuploidy in twin pregnancy that differ from singleton pregnancy. First, if the test result is ‘screen positive’, the test should ideally indicate which fetuses are affected. Second, if the pregnancy is discordant for fetal anomaly, then selective feticide carries a lower loss rate in the first trimester. It is, therefore, possible that the most appropriate method of screening in twins is nuchal translucency scanning with or without serum screening and detection of the nasal bone. In some cases, increased nuchal translucency may be a reflection of cardiac compromise related to TTTS. Discordant nuchal translucency greater than the 95th centile in monozygotic twins raises the risk of TTTS four-fold.

**Invasive testing**

A recent report suggests that amniocentesis carries a loss rate of 1.8% among twins compared with 1% among singletons. However, it is generally accepted that amniocentesis and chorionic villus sampling are associated with loss rates similar to those among singleton pregnancies when carried out by experienced operators and when data are compared with the higher background loss rate among twins. Invasive testing of twins should be carried out in specialist centres capable of undertaking selective feticide. At the time of invasive testing it is imperative that the operator takes note of where and from which fetus the sample was obtained, to avoid the complication of subsequent feticide of the unaffected fetus. Each fetus should ideally be tested individually, as even genetically identical monozygotic twins can have postzygotic mutations and discordant karyotypes among monozygotic twins have been reported in the literature. Amniocentesis is usually performed between 15 and 18 weeks of gestation and, although different techniques have been described for diamniotic twins using single or double needle entry, there are no studies which have compared the two. The single needle technique requires one entry only and ensures sampling of both sacs, but there is risk of cell contamination and creation of a pseudomonamniotic twin pregnancy. Chorionic villus sampling allows for earlier testing, at 10–12 weeks of gestation, and hence earlier and potentially safer feticide. However, with chorionic villus sampling, there is a 1–5% risk of sampling error.

**Management of twin pregnancy discordant for fetal anomaly**

Effectively, the options are selective feticide or expectant management. In cases where the anomaly is non-lethal, the parents have to weigh up the risk of selective feticide against the birth of a disabled child. In cases where the anomaly is lethal, expectant management may be the preferred option. In cases where the anomaly is lethal but threatens the well-being of the normal twin (such as anencephaly, which can be associated with polyhydramnios and preterm labour), decision-making may be even more complex.

Elective delayed feticide at, for example, 32 weeks of gestation, is a recognised strategy for dichorionic twins to avoid procedure-related loss of the healthy co-twin. On the other hand, for monozygotic twins it may be preferable to resort to selective feticide soon after diagnosis to obviate the transfusional risks associated with monozygotic placentaion.

Selective feticide among monozygotic twins using intracardiac potassium chloride (or another agent) was previously not considered possible because of the risk of transplacental passage of the lethal agent as well as the risk of agonal twin transfusion at the time of fetal demise and its co-twin sequelae. Since the development of...
Cord-occlusive techniques, selective feticide among monochorionic twins is now possible. A variety of occlusive techniques have been described. In the first trimester, interstitial laser application is the method of choice. In mid pregnancy (17–25 weeks of gestation), bipolar cord occlusion is used. In late pregnancy (after 26 weeks of gestation), ultrasound-guided cord ligation is the method of choice.

Single twin demise

A recent systematic review of observational data suggested that, following the death of one twin, the risk of monochorionic and dichorionic co-twin demise was 12% (95% CI 7–11) and 4% (95% CI 2–7), respectively. The risk of neurological abnormality of the surviving co-twin was 18% and 1% for monochorionic and dichorionic twins, respectively.

If intrauterine death occurs in a viable pregnancy, most clinicians would counsel a conservative approach for both monochorionic and dichorionic twins. In the case of monochorionic pregnancies, the exact timing of multiorgan injury or multicystic encephalomalacia is unknown but is thought to be at death and to be caused by massive blood loss from the survivor into the low-pressure circulation of the dead twin. This would result in systemic hypotension and cerebral hypoperfusion in the survivor and is consistent with the fact that immediate delivery of the surviving co-twin does not confer a better outcome.

Although ultrasound could suggest a diagnosis of multicystic encephalomalacia, most units would seek the support of magnetic resonance imaging (MRI). Cavitating lesions appear 2 weeks after the initial insult and brain atrophy appears weeks later. Hence, in some units MRI is scheduled 3 weeks or more after single twin demise.

In their recent study of single twin death in monochorionic pregnancies, O’Donoghue et al.

concluded that co-twin death after vascular occlusion techniques was associated with less neurological injury to the surviving co-twin than spontaneous co-twin demise. This finding would be consistent with the experience in many units in the UK, that single twin demise following laser ablation in cases of TTTS appears to have a lower risk of multicystic encephalomalacia for the surviving co-twin than spontaneous demise of one monochorionic twin.

In terms of timing of delivery of the surviving co-twin, most authors would recommend delivery by 38 weeks of gestation. However, others have suggested delivery as early as 34 weeks of gestation. The evidence base for this is lacking for monochorionic and dichorionic twins. Vaginal delivery of the surviving co-twin is considered a reasonable option; there is no evidence base for delivery by caesarean section.

If single twin demise occurs in a monochorionic pregnancy before viability, the risk pertaining to multicystic encephalomalacia, coupled with the lack of specificity of predictive investigations immediately available, means that some mothers may opt to terminate the pregnancy.

In monochorionic placentaion, the gradual understanding that co-twin demise may be a consequence of acute haemodynamic changes has led some clinicians to suggest a role for fetal blood sampling and intrauterine transfusion. These attempts have had mixed outcomes. Although the numbers of cases are small, the combined data from studies by Tanawattanacharoen and Senat suggest that a good outcome may be achieved in 6 out of 13 anemic fetuses. It may be that this method of management deserves greater consideration.

Twin-to-twin transfusion syndrome

The gold standard for the diagnosis of TTTS is the presence of a polyhydramnios/oligohydramnios sequence by ultrasound. Although Quintero et al.

introduced ultrasound staging of TTTS, these stages do not reflect different steps in the natural progression of the disease and the prognosis is not dependent on the initial stage of diagnosis.

The treatment of choice before 26 weeks of gestation is laser ablation of the intercommunicating vessels. The Eurofetus randomised trial showed that, when compared with serial amnioreduction, laser photocoagulation resulted in a higher likelihood of survival of at least one twin (76% versus 56%; 95% CI 0.25–0.93; P = 0.009). A systematic review by Fox et al.

and a recent Cochrane review similarly found a better perinatal outcome for laser ablation compared with amnioreduction, with more babies alive without neurological abnormality at 6 months after laser ablation. There has been some debate as to the role of laser ablation in early-stage disease, but the limited evidence available would favour laser ablation over amnioreduction (although the study included in this review was not powered to test this hypothesis). Selective feticide has been proposed as an attempt to salvage one twin when the outcome of the co-twin appears hopeless. This approach has not been thoroughly investigated but would seem intuitively inferior, as selective feticide has a maximum survival rate of 50% and laser ablation has the potential to salvage both fetuses at all stages of the disease. Whether selective laser ablation of the intercommunicating vessels is more effective than non-selective laser ablation is also unclear. However, some authors have reported better outcomes with the former approach.

The best method of treatment of TTTS after 26 weeks of gestation is uncertain. In their
Twin reversed arterial perfusion (TRAP)

This is a rare complication unique to monochorionic placentation. It occurs when, because of an apparent lack of well-formed cardiac structure, an acardiac twin is abnormally perfused by a structurally normal co-twin (pump twin) via a single superficial artery-to-artery anastomosis through which arterial blood flows in a retrograde fashion. The anatomical structure of the acardiac twin is variable, ranging from relatively normal morphology to an apparently amorphous structure with no recognisable normal anatomy.

Overall, with conservative management, intrauterine death of the pump twin occurs in 25%, polyhydramnios in 50% and preterm birth in 80% of cases. The overall pump twin survival rate with no intervention is 60%. Several authors have attempted to provide parameters to aid prognosis. Postmortem measurements suggest that in cases where the acardiac twin:pump twin weight ratio is >70%, the outcome is worse, and an antenatal estimation of >50% of this weight ratio seems to be associated with a worse outcome; however, some authors disagree. High resistance and low flow to the acardiac fetus, as measured by umbilical artery Doppler assessment, appear to convey a better outcome for the pump twin. The available data suggest that conservative management should be contemplated in cases of TRAP sequence where there is an abdominal circumference ratio of <50% with no evidence of compromise of the pump twin. If in utero interventions are considered, there are essentially two approaches: cord occlusion or intrafetal ablation. Both procedures can be performed with the aid of ultrasound or fetoscopy, but optimal timing is unknown. Both procedures are equivalent in outcome for the surviving pump twin. Lee et al. reported in 2007 that radiofrequency ablation of acardiac twins resulted in >90% survival of pump twins.

Timing and mode of delivery

There are few absolute indications for elective caesarean section in twin pregnancy. Conjoined twins should be delivered by caesarean section and monoamniotic twins should be delivered by elective caesarean section but the exact timing of delivery remains uncertain. Consideration should be given to elective delivery of uncomplicated monoamniotic twins not later than 34 weeks of gestation, to avoid the complication of cord entanglement. Caesarean section is also the recommended route of delivery when twin A is presenting non-vertex. In cases of complicated monochorionic twins, such as those previously treated by laser for TTTS, delivery is generally contemplated at not later than 34 weeks of gestation, by caesarean section.

In cases of uncomplicated monochorionic and dichorionic twins, the issue of timing and mode of delivery is more contentious. There is evidence of increasing stillbirth among twins after 37–38 weeks of gestation compared with singletons. Consensus views arising from a twins study group commissioned by the Royal College of Obstetricians and Gynaecologists recommend delivery by 37–38 weeks of gestation for dichorionic twins and by 36–37 weeks in uncomplicated monochorionic pregnancies.

Some units deliver all monochorionic diamniotic twins by caesarean section because of the perceived risk of acute transfusion in labour. That this can occur is not contentious; certainly, the literature is studded with case reports describing this event. What is contentious is the incidence of the event and hence the justification for universal delivery by caesarean section. Not surprisingly, an accurate estimate of acute transfusion in labour is not available. One often-quoted risk estimate of 10% comes from a review article in which the author does not provide any evidence to support this figure. Another figure of 7.5% is sometimes quoted, derived from a series of three cases in a unit that delivered 180 monochorionic and dichorionic sets of twins. Bhide et al. attempted to correlate inter-twin haemoglobin values and length of time between deliveries. This report was based on 20 sets of monochorionic twins and no statistically significant correlation was found. A strategic alternative to universal delivery by caesarean section involves close monitoring and a short inter-twin delivery time. This advice is without any evidence base and, furthermore, is not always feasible. A recent RCOG guideline states: ‘It is appropriate to aim for vaginal birth of monochorionic twins unless there are accepted, specific clinical indications for caesarean section.’

The optimal mode of delivery of vertex/non-vertex twins is a subject of continuing debate. Recent studies have shown that planned caesarean section may achieve a 75% reduction in the risk of perinatal death compared with attempted vaginal delivery, by reducing the risk of anoxia to the
second twin. In their retrospective study of 15,000 vertex/non-vertex twins Yang et al. concluded that the risk of neonatal morbidity and death of the second twin was higher if both twins were delivered vaginally or if the second twin was delivered by caesarean section after vaginal delivery of the first, compared with caesarean delivery of both twins. However, a Cochrane review on caesarean delivery of the second twin not presenting cephalically found an increased risk of maternal febrile morbidity and no identified improvement in neonatal outcome. The Twin Birth Study is an ongoing multicentre randomised controlled trial aimed at answering this question.

References


