

# Fetal surgery and anaesthetic implications

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Surgery to the fetus while it is still *in utero* is used to treat an increasing number of lethal and non-lethal conditions. The problems of preterm labour and premature rupture of membranes associated with open surgery have led to the development of minimal access surgical techniques. Although fetal surgery is a new and fast moving frontier of medicine, it is not one that all obstetric anaesthetists will encounter. The first successful human fetal operation was performed in 1983, but it is still only carried out in a limited number of specialist tertiary centres.

The broad challenges presented to the anaesthetist are:

- (i) those related to any anaesthetic in a pregnant woman;
- (ii) techniques used to prevent preterm labour;
- (iii) maintenance of maternal homeostasis in the face of tocolytic techniques;
- (iv) maintenance of fetal homeostasis;
- (v) provision of fetal analgesia during surgery;
- (vi) distance the mother may need to travel from home.

It is expected that the indications for fetal therapy will expand. The most frequently occurring condition operated on relatively commonly in the UK is twin-to-twin transfusion syndrome. Life-threatening conditions that have had *in utero* intervention to lessen the severity of pathology include congenital diaphragmatic hernia, obstructive uropathy, and sacrococcygeal teratoma. There is also a prospective randomized trial ongoing in the USA to determine the role and efficacy of *in utero* surgery for myelomeningocele.

Fetal surgical interventions include the following.

- (i) Minimally invasive (percutaneous insertion of shunts and *in utero*, intravascular

fetal transfusions); these are the most commonly performed procedures.

- (ii) Fetoscopic therapy.
- (iii) Open procedure, involving a hysterotomy.

Intrauterine transfusions for rhesus disease and fetal anaemia are performed by ultrasound-directed fetal vessel puncture under local anaesthesia. For other, more complex surgery, the anaesthetist is part of a multidisciplinary team which allows understanding of the pathogenesis of the fetal conditions and how the planned therapy may influence outcome. In this article, it is assumed that the anaesthetist is familiar with routine obstetric anaesthetic considerations: those relevant to the fetal surgery are highlighted.

## Twin-twin transfusion syndrome

Twin-twin transfusion syndrome (TTTS) is a serious complication of a twin pregnancy in which there is only one placenta (monochorionic twin gestation). It complicates 10–20% of monochorionic identical twin pregnancies.<sup>1</sup> It is due to unequal blood flow across vascular anastomoses between the two fetal circulations with the larger twin being at risk of cardiac overload and the smaller twin being relatively hypoperfused. In addition to the severe haemodynamic imbalance, there are discordant liquor volumes, the 'recipient' twin having severe polyhydramnios, and the 'donor' having severe oligohydramnios adhering onto the uterine wall. Both twins are therefore at risk of severe haemodynamic compromise, death, and premature delivery. TTTS is diagnosed by ultrasound. In addition to the fetal complications, parturients with severe TTTS may rarely develop 'mirror syndrome'<sup>2</sup> which is characterized by pulmonary oedema, anasarca (severe generalized oedema), albuminuria, hypertension, and a reduction in haemoglobin concentration due to haemodilution. The maternal

### Key points

Fetal surgery is performed in specialist centres and requires multidisciplinary teamwork.

In addition to obstetric anaesthetic considerations, the anaesthetist needs to be conversant with tocolytic methods.

Fetal analgesia is required for some procedures.

The use of fetoscopic procedures is increasing; however, presently, only laser ablation of placental vessels is of proven efficacy.

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manifestations generally reflect the severity of the fetal placental pathology.

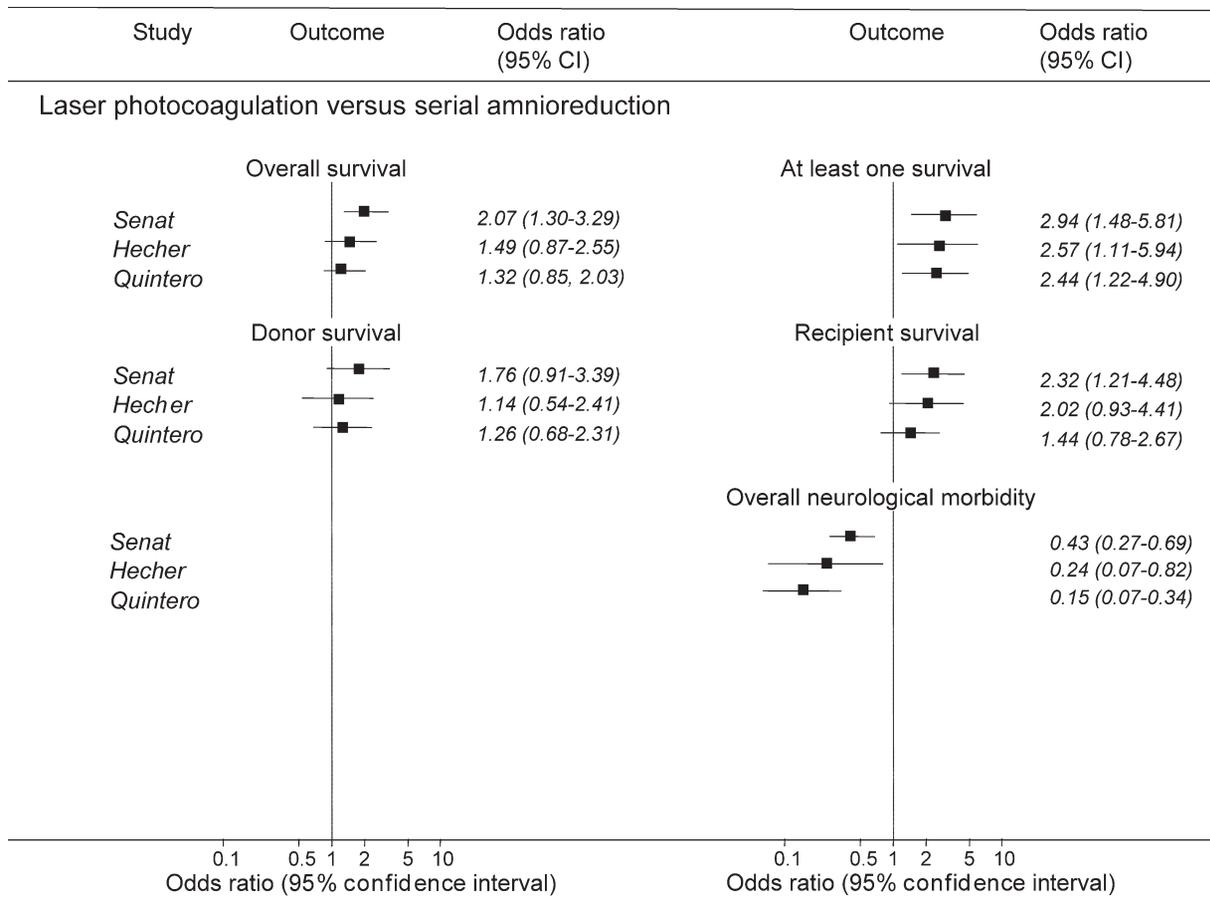
Treatment options include amnioreduction (removing 1–4 litres of amniotic fluid from around the recipient). This is often performed before 26 weeks gestation and requires serial procedures until delivery. Although this is a relatively inexpensive simple technique that can be performed with limited experience and provides potential rescue for both fetuses, it does not affect the underlying pathology. There is little improvement in the fetal condition in advanced disease and a randomized controlled trial has shown that pregnancies treated using this method have a greater likelihood of survivors with cerebral palsy.

Recently, laser ablation of placental vessels has emerged as a potential treatment for severe TTTS. It involves fetoscopic laser photocoagulation of unidirectional arteriovenous vessels on the surface of the twin placenta and attenuation of the haemodynamic consequences of this pathophysiology. This technique prolongs pregnancy compared with amnioreduction.<sup>3</sup> A recent systematic review indicated that fetoscopic laser ablation was associated with improved outcomes for fetal survival of one or both twins and

a reduced risk of long-term neurodevelopmental morbidity in survivors, see Figure 1.

Real-time ultrasound allows location of the placenta, umbilical cord, and amniotic membranes. Technically, an anterior placental site may be more surgically demanding. However, modification of surgical instruments, positioning of the patient, and the creation of an adequate ‘operating window’ using amnioinfusion all aid adequate visualization of the chorionic plate and inter-twin membrane. Risks of the procedure include: amniorrhexis (pre-labour ruptured amniotic membranes) 5%; subchorionic bleed (<1%); preterm delivery; neuromorbidity; and double or single fetal death. Follow-up is required as there is a 5% recurrence rate.

In many centres, maternal spinal, epidural, or combined spinal/epidural anaesthesia is used. Alternatively, local infiltration of the skin and subcutaneous tissues with lidocaine 1% (down to the myometrium) and maternal sedation is used. In addition to maternal sedation, pharmacotherapy also causes fetal immobilization. In a randomized controlled trial, Missant and colleagues<sup>4</sup> demonstrated that remifentanyl was a safer option than diazepam.



**Fig. 1** A systematic review of the RCT and two comparative controlled trials assessing the efficacy of fetoscopic laser ablation in the treatment of severe TTTS

## Congenital diaphragmatic hernia

The incidence of congenital diaphragmatic hernia is 1:2400 live births.<sup>1</sup> It causes pulmonary hypoplasia by compression of lung tissue from the herniated organs and arguably abnormal development of the pulmonary vasculature. Until recently, the possibilities available to expectant parents of a fetus diagnosed with congenital diaphragmatic hernia were termination of pregnancy or continuation of the pregnancy until term with postnatal surgical correction. A series of case cohort studies using modern fetoscopic procedures have indicated that potentially severe congenital diaphragmatic hernia with a high predicted risk of fatal pulmonary hypoplasia may have improved overall survival with *in utero* therapy.

Recent studies have focused on '*in utero* triage' of the fetus emphasizing the exclusion of co-existent structural and chromosomal anomalies which carry a corresponding poor prognosis. In addition, poor lung development can be prospectively identified by ultrasound; liver in the fetal chest; and a lung-head ratio of <1 are relatively sensitive and specific for identifying fetuses developing pulmonary hypoplasia. Such triage has allowed the possibility of fetal therapeutic intervention. Animal studies have indicated that transient tracheal occlusion may prevent or lessen the structural and physiological effects of pulmonary hypoplasia.<sup>5</sup> To date, two studies have utilized lung-head ratio to establish the prospective high risk of pulmonary hypoplasia within groups of fetuses and compared outcome after treatment by fetoscopic tracheal occlusion with conservative management.

In such fetoscopic procedures, combined spinal anaesthesia or local anaesthesia is required and immobilization of the fetus is essential.

## Ex utero intrapartum treatment procedure

The *ex utero* intrapartum treatment (EXIT) procedure is now used to establish a patent airway in the management of fetuses with potential airway obstruction.<sup>6</sup> It allows the continuing placental perfusion of the partially exteriorized fetus until a formal airway has been established. Some common indications include:

- (i) mass obstructing the upper airway, e.g. cystic hygroma, thyroid goitre;
- (ii) congenital high airway obstruction syndrome (CHAOS). This spectrum of anomalies includes laryngeal web, atresia, or cyst, and tracheal atresia or stenosis. It is characterized by enlarged lungs, dilated distal airways, everted diaphragm, ascites, and ultimately non-immune hydrops fetalis;
- (iii) thoracic abnormalities, e.g. hydrothorax, tumours.

The EXIT procedure allows intubation, tracheostomy, or even resection of the lesion while the infant is still on placental support. Management requires obstetricians, anaesthetists, otolaryngologists, and paediatric surgeons. EXIT procedures are performed during caesarean section before clamping of the umbilical cord. When performing a hysterotomy, only the fetal head and shoulders

are delivered to preserve umbilical blood flow and to prevent evaporative heat and fluid loss. This allows time to secure the neonatal airway. Continued uteroplacental circulation has been maintained for up to 1 h without fetal compromise.<sup>7</sup> A potential complication is antepartum haemorrhage at the time in which the fetal airway is being secured due to the need for uterine relaxation.

General anaesthesia is indicated. The mother is prepared for the eventuality of major haemorrhage with monitoring instituted before surgery, i.e. two large bore i.v. cannulae, arterial line, central venous line, and availability of cross-matched blood. A rapid sequence induction with left uterine displacement (reducing aorto-caval compression) is carried out with the administration of high concentrations of volatile anaesthetic agent (e.g. isoflurane 2–3%) to maintain uterine relaxation. Other tocolytics (Table 1) may be needed if there is inadequate uterine relaxation. Vasopressor agents are required for the consequent maternal hypotension in order to maintain uterine blood flow and maternal well-being. Fetal anaesthesia is obtained via placental transfer of volatile agents, but occasionally muscular paralysis may be necessary to ensure fetal immobility.<sup>7</sup> Once the fetal airway has been secured, the uterus is made to contract with an infusion of oxytocin.

Close monitoring of uterine contraction, cardiovascular parameters, and any haemorrhage is essential after the operation. Thus, mother and baby will both require high dependency care. In the absence of contraindications (e.g. coagulopathy), epidural analgesia can be considered for the mother.

**Table 1** Tocolytic agents

Agent	Advantages	Caution
β-adrenergic agents, e.g. terbutaline, ritodrine		Maternal tachycardia, hypotension, myocardial ischaemia, decreased glucose tolerance, pulmonary oedema
Magnesium sulphate		In high concentration fetal side-effects include decreased heart rate variability, reduced muscular activity at birth
Halogenated volatile agents, e.g. isoflurane	Used to provide intraoperative relaxation	Prolonged use can cause fetal acidosis
Glyceryl trinitrate	Rapid onset of action	
Non-steroidal anti-inflammatory drugs, e.g. indomethacin		Limited to short-term use for 48 h, and before gestational age of 32 weeks, due to risk of premature closure of ductus arteriosus in the fetus, decreased renal function resulting in oligohydramnios, increased risks of necrotising enterocolitis and intraventricular haemorrhage
Calcium antagonists		Maternal hypotension

## Obstructive uropathy

Obstructive uropathy occurs in one in 1000 live births.<sup>5</sup> Upper urinary tract obstruction is associated with less morbidity and mortality than lower obstruction which is usually caused by posterior urethral valves.

The obstruction increases bladder pressure, resulting in changes in bladder structure and function, vesicoureteric reflux, hydronephrosis, and a risk of chronic renal failure later in life.<sup>1</sup> The resulting oligohydramnios and pulmonary hypoplasia increases neonatal mortality. Fetal surgery aims to prevent this from occurring.

Open surgery (nephrostomy) carries a high mortality, a risk of amniorrhexis and preterm labour, and a third of those treated still require transplantation at a later stage. It requires maternal hysterectomy and has largely been abandoned. Fetal vesicoamniotic shunting is the placement of a catheter, using a percutaneous needle under continuous ultrasound guidance, into the fetal bladder. The distal end of the catheter traverses the fetal anterior abdominal wall and drains into the amniotic cavity. This procedure is usually performed under local anaesthesia with lidocaine.

## Myelomeningocele

The diagnosis of myelomeningocele is possible in early pregnancy. It causes progressive neurological impairment and carries a poor prognosis. Prenatal diagnosis and treatment may allow prevention of the neurological deficit and preserve spinal cord cryoarchitecture.

## Tocolysis

Tocolysis is essential during fetal surgery and after operation as fetal interventions are associated with preterm labour. Impaired uterine blood flow or partial placental separation can occur due to uterine manipulation or incisions, hence jeopardizing umbilical-placental blood flow. Even minor interventions (e.g. needle insertion for intrauterine transfusion) can result in strong uterine contractions, and hence may cause unintentional puncture of other structures. Tocolysis is also important after operation as preterm uterine contractions can still occur. Table 1 gives examples of the tocolytic agents which can be used and the main points about their use. The choice of agent is determined by maternal side-effects.<sup>6</sup> Drugs acting on the uterus have been reviewed elsewhere.<sup>8</sup>

## Fetal stress

There is considerable evidence that the fetus may experience pain. Not only is there a moral obligation to provide fetal anaesthesia and analgesia, but it has also been shown that pain and stress may affect fetal survival and neurodevelopment.<sup>7</sup> Factors suggesting that the fetus experiences pain include the following.

- (i) *Neural development.* Peripheral nerve receptors develop between 7 and 20 weeks gestation, and afferent C fibres begin development at 8 weeks and are complete by 30 weeks gestation. Spinothalamic fibres (responsible for transmission of pain) develop between 16 and 20 weeks gestation, and thalamocortical fibres between 17 and 24 weeks gestation.
- (ii) *Behavioural responses.* Movement of the fetus in response to external stimuli occurs as early as 8 weeks gestation, and there is reaction to sound from 20 weeks gestation. Response to painful stimuli occurs from 22 weeks gestation.
- (iii) *Fetal stress response.* Fetal stress in response to painful stimuli is shown by increased cortisol and  $\beta$ -endorphin concentrations, and vigorous movements and breathing efforts.<sup>7,9</sup> There is no correlation between maternal and fetal norepinephrine levels, suggesting a lack of placental transfer of norepinephrine. This independent stress response in the fetus occurs from 18 weeks gestation.<sup>10</sup> There may be long-term implications of not providing adequate fetal analgesia such as hyperalgesia, and possibly increased morbidity and mortality.

## Fetal analgesia

As with any procedure, the provision of analgesia depends on the likely severity of pain associated with the intervention. However, analgesia is recommended for:

- (i) endoscopic, intrauterine surgery on placenta, cord, and membranes;
- (ii) late termination of pregnancy;
- (iii) direct surgical trauma to the fetus.

For open surgery, where a general anaesthetic technique (with or without an epidural) is used, the fetus obtains anaesthesia via the placenta, although direct administration from i.m. injections can also be used.

For fetoscopic fetal surgery, maternal anaesthesia is most usually by local anaesthetic infiltration or a regional block. A combined spinal/epidural minimizes haemodynamic changes.

These techniques can be supplemented with sedation or remifentanyl. Local or regional techniques are sometimes difficult because of maternal anxiety; in addition, they may not adequately immobilize the fetus. A mobile fetus can displace the endoscope resulting in bleeding, fetal trauma, or compromised umbilical circulation resulting in fetal death. The short-acting opioid remifentanyl is easy to titrate and crosses the placenta readily immobilizing the fetus. Using a continuous infusion rate of remifentanyl  $0.1 \mu\text{g kg}^{-1} \text{min}^{-1}$ , fetal immobilization and maternal sedation are achieved.<sup>4</sup> Mild respiratory acidosis occurs but maternal apnoea can be avoided and good operating conditions obtained. This technique is recommended for TTTS.<sup>4</sup>

Fetal anaesthesia, homeostasis, and immobility can be provided by direct fetal injections (i.m. or into the umbilical cord) with the use of opioids, atropine, and neuromuscular blocking agents. Fetal

**Table 2** Complications of minimal access fetal surgery

Complication	How it can be minimized
Bleeding	Avoid placenta on entering uterus
Preterm labour	Use of tocolytics. Many theories used to describe why this occurs (e.g. rapid changes in uterine volume, infection, hormonal changes, fetomaternal stress, and membrane rupture)
Chorioamniotic membrane separation	Surgical technique
Premature rupture of membranes	Most common problem associated with fetal surgery. Research is ongoing into sealing ruptured membranes with collagen plugs

i.m. opioids reduces the stress response.<sup>5</sup> Suitable anaesthetic techniques for fetoscopic surgery on membranes, cord, and the placenta are as discussed above.

## Complications

The complications of minimal access fetal surgery are summarized in Table 2.

## Social factors

As minimal access fetal surgery is only carried out in specialist centres, patients frequently have to travel long distances. Organization needs to include social support for the families where necessary. This is an important factor when considering discharge from hospital. Good communication between the tertiary centre and referring hospital is vital.

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Please see multiple choice questions 25–28