NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of amnioreduction using septostomy with or without amniodrainage for the treatment of twin to twin transfusion syndrome

Twin to twin transfusion syndrome occurs when unborn identical twins have different sacs in the womb but share the same placenta. This may result in blood flow from one twin to the other through connections between blood vessels in the shared placenta. The volume of fluid around the twins can also become uneven. In septostomy a needle is used to make a hole in the membrane separating the twins to make the volume of the fluid surrounding the twins more even. Sometimes additional fluid may need to be removed with another needle (amniodrainage).

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2006.

Procedure name

- Amnioreduction using septostomy with or without amniodrainage for the treatment of twin to twin transfusion syndrome (also known as twin oligohydramnios-polyhydramnios sequence [TOPS])

Specialty societies

- British Maternal and Fetal Medicine Society
- Royal College of Obstetricians and Gynaecologists

Description

Indications

Approximately 70% of monozygotic twins are monochorionic/diamniotic (one placenta with two amniotic sacs).Twin to twin transfusion syndrome (TTTS) affects approximately 15% of monochorionic/diamniotic pregnancies and has has perinatal mortality of up to 80% if untreated [1]. TTTS results from shunting between the circulations of unborn twins through abnormal communications (anastomoses) in vessels of the shared placenta. Blood is transfused from the donor twin, whose growth becomes restricted and who develops oligohydramnios or anhydramnios (low or absent amniotic fluid), to the recipient, who develops circulatory overload, cardiac compromise and polyhydramnios (too much amniotic fluid). The combination of polyhydramnios in the recipient and oligo/anhydramnios in the donor squashes the donor twin against the wall of the uterus. This is referred to as a 'stuck twin'. The general disturbance of circulation and perfusion in both twins is associated with high morbidity and mortality. Morbidity among survivors includes cardiac, renal and serious neurological impairment, such as cerebral palsy. It is estimated that around 15% of survivors will have long-term neurological sequelae [2].

A staging system for TTTS has been developed by Quintero et al [3] that considers a sequence of progressive sonographic features from early (stage I) to late stage disease, ultimately ending in the demise of either fetus (stage V). Generally the earlier in gestation TTTS presents, the worse the prognosis.

Current treatment and alternatives

The options for managing TTTS include expectant medical management, amniodrainage, septostomy, laser ablation and selective fetal termination using techniques such as umbilical cord occlusion. In some cases the treatment aim is to enable one twin to survive as the chances for both surviving are extremely poor. Some women may choose to terminate the pregnancy because of the high perinatal morbidity and mortality in both twins.

Expectant management will only be appropriate in a few mild cases because of the high perinatal mortality and morbidity. Amniodrainage is a long-established procedure which aims to reduce amniotic fluid volume in the recipient polyhydramiotic twin and to prevent extremely preterm delivery. It does not treat the underlying pathophysiological cause (that is, abnormal communications between vessels in the shared placenta) nor does it allow the amniotic fluid volume to normalise around the donor twin.

What the procedure involves

Under local anaesthesia and ultrasound guidance, an amniocentesis needle is inserted in the maternal abdomen. The needle is then used to make a small hole in the intervening membrane, allowing the fluid around the recipient twin to move into the donor sac.

In some cases amnioreduction (removal of amniotic fluid via a needle passed into the uterus) may also be performed prior to and/or after the septostomy procedure.

Efficacy

The evidence on efficacy is based on two controlled trials (one randomised controlled, one non-randomised) and four case series.

Survival

In the randomised controlled trial that included 36 twin pregnancies treated with amniodrainage and 35 with septostomy with or without amniodrainage, perinatal survival of at least one twin (measured until hospital discharge) was similar in both groups (78% (28/36) versus 80% (28/35), respectively; relative risk [RR] 0.94, 95% confidence interval [CI] 0.55 to 1.61, p = 0.82). Survival of both twins was 50% (18/36) in the amniodrainage group compared with 60% (21/35) in the septostomy group (RR 0.82, 95% CI 0.52 to 1.30, p = 0.40). In the non-randomised study perinatal survival of both twins was 43% (3/7) in the amniodrainage group compared with 57% (4/7) in those who underwent septostomy with or without amniodrainage. Survival of at least one twin both with amniodrainage and with septostomy was 86% (6/7). Overall survival for amniodrainage alone was 9/14 (64.3%) versus 10/14 (71.4%) in the septostomy group. This difference was not significantly different.

In the four case series, overall perinatal survival (total number of babies that were born/total number of unborn babies) ranged from 46% (12/26) to 83% (20/24). The differences in reported survival among the studies may be attributed to the severity of TTTS, with the studies with poorer results including more severe cases.

Mean gestational age at delivery

Mean gestational age at delivery ranged from 27 weeks to 31 weeks with all the studies reporting that pregnancy was prolonged following septostomy. In the non-randomised study this difference was significantly different between the two groups. However, this could again be attributed to differences in severity of TTTS between the two groups. Long-term neurological outcomes were not reported in the studies.

Specialist advisors

The specialist advisors commented that it was still unclear what the best treatment was for early-stage TTTS. They noted that results from the two comparative studies indicated no significant advantage of septostomy and amniodrainage over amniodrainage alone. Further comments were that few units perform septostomy, and that many women presenting with TTTS may undergo more than one type of procedure.

Safety

The safety evidence presented in this overview is based on one randomised controlled trial and two case series. In general ssafety data were not well reported in the studies, with only three studies reporting on safety outcomes.

In the randomised controlled trial there were two cases of disruption of the intervening membrane resulting in a monoamniotic twin gestation (one in each study arm). This complication has also been reported in two case reports. In a case series of 13 women, one woman went into spontaneous labour following septostomy and amniodrainage. This was thought to be related to placental damage.

Specialist advisors

One of the specialist advisors considered septostomy and amniodrainage to be safe procedures. It was noted by this advisor that septostomy is often unintentionally performed during the standard amniodrainage technique. All three advisors highlighted that cord entanglement is a theoretical complication of septostomy.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to amnioreduction using septostomy with or without amniodrainage. Searches were conducted via the following databases, covering the period from their commencement to 16 June 2006: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See appendix C for details of search strategy.)

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Pregnant women with twin to twin transfusion syndrome.
Intervention/test	Septostomy (with or without amniodrainage).
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on two controlled trials (one randomised controlled trial, one cohort) and four case series.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Existing reviews on this procedure

A Cochrane review has been published on interventions for the treatment of TTTS [4]. However, at the time of publication no randomised controlled trials had been published on the treatment of TTTS. The review is currently being updated.

Two other reviews have been published on treatments for TTTS [5 6]. Both reviews included limited information regarding septostomy as a treatment option for TTTS.

In the review by Robyr et al. [5] the authors state that 'a multicentre randomised controlled trial [7] has compared septostomy to amniodrainage, showing the same overall perinatal survival for both septostomy and amniodrainage. This procedure has therefore become obsolete'.

In the review by Fox et al [6] only the study by Johnson et al [8] is included (n = 14).

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

- Intrauterine laser ablation for the treatment of twin to twin transfusion syndrome (guidance in development).

Technology appraisals

- None relevant.

Clinical guidelines

- None relevant.

Public health

- None relevant.

Table 2. Summary of key efficacy and safety findings amnioreduction using septostomy with or without amniodrainage for the treatment of TTTS

Abbreviations used: GA, gestational age; IUFD, intrauterine fetal death; NND, neonatal death; PROM, premature rupture of the membranes; RR, relative risk; TTTS, twin to twin transfusion syndrome, Overall survival – total number of live births/total number of possible live births (fetuses); Two survivors – both the donor and recipient twin from one pregnancy

Study details	Key efficacy findings	Key safety findings	Comments
Moise (2005) [7] Multicentre (11 centres) Randomised controlled trial Study period: September 1997 – July 2002 **73 pregnant women** • **36 in the amniodrainage group** • **35 in the septostomy group** Population: Women were recruited from 11 countries. Mean maternal age was not stated. Mean gestational age at enrolment was 20.9 weeks in the amniodrainage group and 20.8 weeks in the septostomy group Indications: Women presenting between < 24 weeks' gestation with TTTS, that is recipient twin presented with polyuric polyhydramnios and the donor twin presented with oliguric oligohydramnios Technique: Amniodrainage group (additional procedures): 1 patient had cord occlusion, 1 patient had laser ablation. Septostomy group (additional procedures): 12 patients had amniodrainage, 1 patient cord occlusion, 1 patient had laser	**Outcomes measured:** perinatal survival (until hospital discharge), gestational age at delivery **Amniodrainage n = 36** / **Septostomy n = 35** / **p** **Survival** 0 Survivors: 8 (22%) / 7 (20%) 1 Survivors: 10 (28%) / 7 (20%) RR = 1.22, 95% CI 0.75 to 2.00. p = 0.44 amnio vs septostomy) 2 survivors: 18 (50%) / 21 (60%) RR = 0.82, 95% CI 0.52 to 1.30, p = 0.40 amnio vs septostomy) At least 1 survivor: 28 (78%) / 28 (80%) RR = 0.94 amnio vs septostomy, 95% CI 0.55 to 1.61 p = 0.82) **GA at delivery** Median (weeks): 29.5 / 30.7 / 0.24 Days from procedure: 59.9 / 69.2 / 0.12 **Fetal deaths** Donor: 5 (14%) / 4 (11%) / 0.76 Recipient: 4 (11%) / 5 (14%) / 0.69 **Total**: 9 (25%) / 9 (26%) **Neonatal deaths** Donor: 9 (25%) / 6 (17%) / 0.42 Recipient: 8 (22%) / 6 (17%) / 0.59 Total: 17 (47%) / 12 (34%)	**Complications** Authors noted that minimal complications were reported for both amniodrainage and septostomy. There were no cases of placental abruption or chorioamnionitis. Total disruption of the intervening membrane creating a monoamniotic twin gestation occurred in 1 case in each treatment arm.	The study was terminated after the planned interim analysis stage because the rate of survival of at least 1 twin was similar in both groups. **This resulted in the study being underpowered (sample size of 140 required).** Allocation to treatment was done using a random sequence of numbers. The trial was initiated before the Quintero staging system was developed and therefore cases were not prospectively staged. However, authors noted that 97% of gestations would have been stage I–III. 2 patients were lost to follow-up in the septostomy group (reasons stated). Perinatal survival defined as until hospital discharge (no other details given). Neurological outcomes were not assessed. Authors stated that other findings in

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<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Mean follow-up: post delivery (date not specified)

Disclosure of interest: not specified</td>
<td>
<table>
<tr><td>No of additional procedures</td><td>2 (1–12)</td><td>2 (1–9)</td><td>0.07</td></tr>
<tr><td>More than one procedure necessary</td><td>25 (69%)</td><td>16 (46%)</td><td>0.04</td></tr>
</table>
</td>
<td></td>
<td>the study indicated a slowing of the disease process in the septostomy group.</td>
</tr>
<tr>
<td>Johnson (2001) [8]
USA
Non-randomised study (cohort)

Study period: June 1998 – June 2000

n = 14 patients (pregnancies)
• 7 amniodrainage group
• 7 septostomy group

Population:
Mean maternal age was not stated
Mean gestational age at treatment was 21 weeks in the amniodrainage group and 18 weeks in the septostomy group (p = 0.01)

Indications: Women presenting with TTTS, that is recipient twin presented with polyuric polyhydramnios and the donor twin presented with oliguric oligohydramnios

Technique: 3 patients in the septostomy group also underwent amniodrainage. 2 of these 3 also underwent a second septostomy. The amniodrainage group</td>
<td>Outcomes measured: perinatal survival, gestational age at delivery

<table>
<tr><th></th><th>Amniodrainage (n = 7)</th><th>Septostomy (n = 7)</th></tr>
<tr><td>Gestational age at delivery (mean)
p = 0.08</td><td>27.5 weeks</td><td>30 weeks</td></tr>
<tr><td>Median time interval between diagnosis and delivery
p = 0.007</td><td>6.5 weeks</td><td>12 weeks</td></tr>
<tr><td>2 survivors, p = 0.4</td><td>3 (43%)</td><td>4 (57%)</td></tr>
<tr><td>1 survivor. p = 0.1</td><td>3 (43%)</td><td>2 (29%)</td></tr>
<tr><td>0 survivors</td><td>1 (14%)</td><td>1 (14%)</td></tr>
<tr><td>At least 1 survivor</td><td>6 (86%)</td><td>6 (86%)</td></tr>
<tr><td>Overall survival</td><td>64% (9/14)</td><td>71% (10/14)</td></tr>
</table>
</td>
<td>Complications
The authors did not report on complications.</td>
<td>Retrospective review.
17 women were originally eligible – 3 declined any intervention.

Allocation to groups: patients were told about the risks and benefits for both procedures. Patient choice determined the procedure used. Possibility that those with TTTS at an earlier stage were suggested to have septostomy.

All procedures were performed by a single operator (experience not documented).

Authors noted that 1 patient in the septostomy group underwent more than 1 amniodrainage procedure.

Staging information not given – this is important given that there were significant differences between the two groups in terms of timing of the first treatment. It may be that the amniodrainage group had more severe disease.

Limited demographic data were</td>
</tr>
</table>

Abbreviations used: GA, gestational age; IUFD, intrauterine fetal death; NND, neonatal death; PROM, premature rupture of the membranes; RR, relative risk; TTTS, twin to twin transfusion syndrome, Overall survival – total number of live births/total number of possible live births (fetuses); Two survivors – both the donor and recipient twin from one pregnancy

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr><td>had a mean of 4.3 amniodrainages performed (range 3–7)

Follow-up: post delivery (date not specified)
Conflict of interest: none specified</td><td></td><td></td><td>reported. Perinatal survival was not defined.
The data in the abstract and the body of the report did not reconcile. The data reported here are from the body of the report.</td></tr>
<tr><td>Saade (1998) [9]

USA

Case series (data pooled from five centres)

Study period: not stated

n = 12 patients

Population: Mean maternal age was not stated. Mean gestational age at treatment was 23.1 weeks

Indications: Pregnancies with TTTS diagnosed by ultrasonic criteria during the second or early third trimesters.

Technique: In 3 patients amniodrainage was performed at the time as septostomy

Follow-up: post delivery (date not specified)</td><td>Outcomes measured:perinatal survival, gestational age at delivery, birthweight

<table><tr><th></th><th>n = 12 (24 fetuses)</th></tr><tr><td>Gestational age at delivery (mean)</td><td>31.1 weeks</td></tr><tr><td>% discordance in birthweight (between the twins)</td><td>27.5%</td></tr><tr><td>2 survivors</td><td>9/12 (75%)</td></tr><tr><td>1 survivor</td><td>2/12 (17%)</td></tr><tr><td>0 survivors</td><td>1/12 (8%)</td></tr><tr><td>Intrauterine deaths</td><td>3</td></tr><tr><td>Neonatal death</td><td>1</td></tr><tr><td>Overall survival</td><td>83.3% (20/24)</td></tr></table></td><td>Complications
Authors reported that there were no cases of complete intra-amniotic rupture and no cases of umbilical cord entanglement in this series.</td><td>First published case series on septostomy.

Staging was not mentioned in this article.

Perinatal survival was not defined.

Limited information was reported.

This was a lack of patient standardisation as this study included data from five centres.</td></tr>
</table>

Abbreviations used: GA, gestational age; IUFD, intrauterine fetal death; NND, neonatal death; PROM, premature rupture of the membranes; RR, relative risk; TTTS, twin to twin transfusion syndrome, Overall survival – total number of live births/total number of possible live births (fetuses); Two survivors – both the donor and recipient twin from one pregnancy

Study details	Key efficacy findings	Key safety findings	Comments
Disclosure of interests: none specified			
Adegbite (2003) [10] UK Case series Study period: 1997-1999 **n = 13 patients** Population: Mean maternal age was not stated. Mean gestational age at treatment was 21 weeks (range 18–25.5 weeks) Indications: Pregnancies diagnosed with TTTS, that is recipient twin presented with polyuric polyhydramnios and the donor twin presented with oliguric oligohydramnios Technique: All women were treated with a combined septostomy and amniodrainage procedure. In 2 patients amniodrainage was also performed prior to septostomy	**Outcomes measured**: survival, gestational age at delivery, birthweight N = 13 (26 fetuses) Gestational age at delivery (mean): 27 weeks (20–34 weeks) % discordance in birth weight between twins: 22% Median interval between treatment and delivery: 4 weeks (3 days to 13.6 weeks) 2 survivors: 6 (46%) 1 survivor: 2 (15%) 0 survivors: 6 (46%) Intrauterine deaths: 10 Neonatal death: 4 Overall survival: 46% (12/26)	**Complications** Authors reported that 1 woman went into spontaneous labour within 72 hours of the procedure – appeared to be due to procedure related placental damage.	Consecutive patients which means that all patients presenting in the study period were treated with the combined septostomy/amniodrainage method. No statement is made of alternative treatments such as laser, cord coagulation. Staging was not mentioned in this article. Perinatal survival was not defined However, authors suggested that the higher survival rate in the Saade series is due to the inclusion of milder cases. Authors were interested in the role of placental angioarchitercture in relation to TTTS.

Abbreviations used: GA, gestational age; IUFD, intrauterine fetal death; NND, neonatal death; PROM, premature rupture of the membranes; RR, relative risk; TTTS, twin to twin transfusion syndrome, Overall survival – total number of live births/total number of possible live births (fetuses); Two survivors – both the donor and recipient twin from one pregnancy

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr><td>Follow-up: post delivery (date not specified)

Disclosure of interests: none specified</td><td></td><td></td><td></td></tr>
<tr><td>Lim (2005) [11]

Singapore

Case series

Study period: January 2002 – September 2003

n = 7
• 4 patients had amniodrainage and septostomy
• 1 patient cord occlusion
• 2 patients expectant management

Population: Median maternal age was 31 years (range 22–44 years) (based on 11 patients). Median gestation at diagnosis was 17.4 weeks (range 16.4–26 weeks)

Indication:
5 patients were stage I(including 1 septostomy patient)
2 patients were stage II (both had septostomy)
3 patients were stage III (including 1</td><td>Outcomes measured: perinatal survival (survival up until 4 weeks), gestational age at delivery, birthweight

<table><tr><td></td><td>Amniodrainage/ septostomy n = 4</td><td>Other procedures n = 3</td></tr><tr><td>Gestational age at delivery</td><td>28.1–34.7 weeks</td><td>20.1–36.9 weeks</td></tr><tr><td>2 survivors</td><td>4</td><td>1</td></tr><tr><td>1 survivor</td><td>0</td><td>1</td></tr><tr><td>0 survivors</td><td>0</td><td>1</td></tr><tr><td>Survival (28 days)</td><td>100%</td><td>50%</td></tr><tr><td>Overall survival</td><td colspan="2">11/14 (78.6%)</td></tr><tr><td colspan="3">There was 1 neonatal death at 55 days</td></tr></table></td><td>Complications

Complications following the procedure were not mentioned.

However, the authors reported on postnatal morbidity including: neonatal jaundice, respiratory distress syndrome, hyperglycaemia.</td><td>The study population consisted of 11 patients – 3 patients opted for elective termination of the pregnancy, 1 was lost to follow-up.

Other procedures included cord occlusion and expectant management.

Unclear whether amniodrainage was offered before or after septostomy.

Study did not seek to compare treatments.

Authors noted that compared with an earlier series in the same hospital (listed in appendix A), TTTS had been detected at earlier gestations and in earlier stages, and management had resulted in a longer diagnosis–delivery interval.</td></tr>
</table>

Abbreviations used: GA, gestational age; IUFD, intrauterine fetal death; NND, neonatal death; PROM, premature rupture of the membranes; RR, relative risk; TTTS, twin to twin transfusion syndrome, Overall survival – total number of live births/total number of possible live births (fetuses); Two survivors – both the donor and recipient twin from one pregnancy

Study details	Key efficacy findings	Key safety findings	Comments
septostomy patients) 1 patient was stage IV Technique: amniodrainage/septostomy was offered to all patients with TTTS when severe polyhydramnios was diagnosed and when severe polyhydramnios recurred **Follow-up: until 6 months (although date not specified)** Disclosure of interests: none specified			
Hubinot (2000) [12] Belgium Case series Study period: not stated **n = 7** Population: not specified Indications: Pregnancies diagnosed with TTTS (no other details given) Technique: septostomy (unclear if with or without amniodrainage) **Follow-up: post birth (period not specified)** Disclosure of interests: not stated	**Outcomes measured**: perinatal survival **n = 7** Number of second trimester pregnancies: 7 Number of IUFD: 5 Number of NND: 1 Number of children alive and well: 8 Survival rate: 57%	**Complications** The authors did not report on complications.	Very limited information was provided. Review paper but included some survival data. The review paper referenced another in terms of survival data. However, this was a study of 3 case reports [13]. In the discussion section the authors noted that procedure-related risks were similar to those of serial amniodrainage.

Validity and generalisability of the studies

- TTTS is a rare condition, and accordingly the number of fetuses included in the literature is overall small.
- The one randomised controlled trial on this procedure was stopped early as it was shown that there was no difference in survival between the treatment arms.
- Only a few centres in the world undertake and publish results on this procedure. Therefore it is likely that there is some overlap in terms of patients in the published papers.
- The women included in the studies underwent septostomy as well as septostomy and amniodrainage.
- In general safety outcomes have not been well reported.
- None of the studies reported on maternal outcomes.
- There is a lack of long-term data.
- There have been no published studies looking at neurological outcomes following septostomy.
- Very few studies defined perinatal survivals and in most studies length of follow-up was unclear.
- There is now some evidence to show that TTTS stage is important in terms of treatment.[13] However, in several studies it was difficult to determine the severity of the condition as many of the studies were performed before the Quintero staging system[14] was devised. Differences in severity of the condition may account for some of the reported differences among the studies in terms of survival.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Professor Nick Fisk, Professor M Kilby, Mr M Denbow and Mr Myles Taylor

- Optimal therapy for early stage I and possible stage II TTTS at presentation remains unclear.

- It is unclear whether laser should be used for all cases of TTTS, or instead amniodrainage with/without septostomy should be used in early-stage TTTS.

- The published randomised trial (amniodrainage vs septostomy [7]) suggested fewer procedures were required if septostomy was done concomitantly. However, this study did not include early-stage TTTS in which progression would indicate subsequent endoscopic laser.
- There are some concerns that prior septostomy may not allow subsequent laser treatment.
- The results from the two comparative studies indicate no significant advantage of septostomy and amniodrainage compared with amniodrainage alone, in terms of fetal outcome. So it is still unclear whether septostomy alone should be used instead of amniodrainage.
- Most tertiary referral fetal medicine units perform laser therapy or amniodrainage or both in the management of TTTS. Few units perform septostomy. Inadvertent septostomy during either laser or amniodrainage is common.
- Few units would consider amniodrainage alone as the alternative treatment.
- Tertiary referral fetal medicine centres will be the main area where this amnioreduction/septostomy will be performed. However, more and more doctors trained in fetal medicine are based in district general hospitals and would be able to perform this procedure.

Audit criteria

- Perinatal survival
- Greater than or equal to one survival
- Double survival
- Gestational age at delivery
- Number of procedures required
- Birthweight of donor and recipient twin
- Amniorrhexis

- Delivery within 48 hours to 1 week of the procedure
- Delivery prior to 28 weeks
- Periventricular leucomalacia
- Long-term neural developmental disability

Issues for consideration by IPAC

- This overview does not included evidence on amniodrainage alone.
- The title of this procedure was originally *Amnioreduction with or without septostomy for monochrorionic twin to twin transfusion* (as per Specialist Advice) however following further clinical advice it was changed to *amnioreduction using septostomy with or without amniodrainage* as the new or uncertain procedure is septostomy rather than amniodrainage.

References

1 De Lia J, Fisk N, Hecher K et al. (2000) Twin-to-twin transfusion syndrome - Debates on the etiology, natural history and management. Ultrasound in Obstetrics & Gynecology Vol. 16: 213.

2 Jain V and Fisk NM. (2004) The Twin-Twin Transfusion Syndrome. Clinical Obstetrics & Gynecology 47: 181-202.

3 Quintero RA, Morales WJ, Allen MH et al. (1999) Staging of twin-twin transfusion syndrome. Journal of Perinatology 19: 550-555.

4 Roberts D, Neilson JP, and Weindling AM. (2001) Interventions for the treatment of twin-twin transfusion syndrome. Cochrane Database of Systematic Reviews

5 Robyr R, Quarello E, and Ville Y. (2005) Management of fetofetal transfusion syndrome. Prenatal Diagnosis 25: 786-795.

6 Fox C, Kilby MD, and Khan KS. (105) Contemporary treatments for twin-twin transfusion syndrome. Obstetrics & Gynecology 1469-77, 2005.

7 Moise KJ, Jr., Dorman K, Lamvu G et al. (2005) A randomized trial of amnioreduction versus septostomy in the treatment of twin-twin transfusion syndrome. American Journal of Obstetrics and Gynecology 193: 701-707.

8 Johnson JR, Rossi KQ, and O'shaughnessy RW. (2001) Amnioreduction versus septostomy in twin-twin transfusion syndrome. American Journal of Obstetrics and Gynecology 185: 1044-1047.

9 Saade GR, Belfort MA, Berry DL et al. (1988) Amniotic septostomy for the treatment of twin oligohydramnios-polyhydramnios sequence. Fetal Diagnosis & Therapy 86-93, 1998.

10 Adegbite AL, Ward SB, and Bajoria R. (1923) Perinatal outcome following amniotic septostomy in chronic TTTS is independent of placental angioarchitecture. Journal of Perinatology 498-503, 2003.

11 Lim YK, Tan TYT, Zuzarte R et al. (2005) Outcomes of twin-twin transfusion syndrome managed by a specialised twin clinic. Singapore Medical Journal 46: 401-406.

12 Hubinont C, Bernard P, Pirot N et al. (1992) Twin-to-twin transfusion syndrome: treatment by amniodrainage and septostomy. [Review] [50 refs]. European Journal of Obstetrics, Gynecology, & Reproductive Biology 141-4, 2000.

13 Hubinont C, Bernard J-P, mwebesa W et al. (1996) Nd:YAG laser and needle disruption of the interfeal septum: a possible therapy in severe twin to twin transfusion syndrome. Journal of Gynecologic Surgery 12: 183-189.

Appendix A: Additional papers on amnioreduction using septostomy with or without amniodrainage not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Dickinson JE, Evans SF. (2004) The progression of disease stage in twin-twin transfusion syndrome. *Journal of Maternal-Fetal and Neonatal Medicine* 16: 95–101.	= 71 patients (n = 6 with septostomy).	Pregnancy outcomes for TTTS are correlated with stage at diagnosis.	Those patients who had septostomy have been included in the RCT.[5] Primary interest of the study is in relation to staging.
Taylor MJ, Govender L, Jolly M et al. (2002) Validation of the Quintero staging system for twin-twin transfusion syndrome. *Obstetrics and Gynaecology* 100: 1257–65	52 patients (n = 3 had septostomy alone, n = 4 had septostomy with additional procedures).	Staging system would be used within caution.	Those patients who had septostomy have been included in the RCT.[5] Primary interest of the study is in relation to staging.
Taylor MJ, Denbow ML, Duncan KR et al. Antenatal factors at diagnosis that predict outcome in twin-twin transfusion syndrome. *American Journal of Obstetrics and Gynaecology* 183: 1023–8.	23 patients (n = 3 had septostomy alone, n = 1 had septostomy with additional procedures).	Study identified three factors that predict poor outcomes in TTTS.	Those patients who had septostomy have been included in the RCT.[5] Primary interest of the study is in relation to staging.
Pistorius LR, Howarth GR. (1999) Failure of amniotic septostomy in the management of 3 subsequent cases of severe previable twin-twin transfusion syndrome. *Fetal Diagnosis and Therapy* 14: 337–40.	3 patients.	All 3 showed initial improvement. However, all 3 pregnancies were lost within 5 days of procedure due to PROM and premature labour	Small cases series.
Hubinont C, Bernard J-P, Mwebesa W et al. (1996) Nd:YAG laser and needle disruption of the interfeal septum: a possible therapy in severe twin to twin transfusion syndrome. *Journal of Gynaecologic Surgery* 12: 183–9.	3 patients.	All 3 cases were associated with a significant improvement in the condition and delayed delivery.	Limited information.
Szuki S, Ishikawa G, Sawa R et al. (1999) Iatrogenic monoamniotic twin gestation with progressive twin twin transfusion syndrome. *Fetal Diagnosis and Therapy* 14: 98–101.	1 patient.	Case report of a specific complication.	Case report.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Cook TL, O'Shaughnessy R. (1997) Iatrogenic creation of a monoamniotic twin gestation in severe twin-twin transfusion syndrome. *Journal of Ultrasound in Medicine* 16: 853–5.	1 patient.	Case report of a specific complication.	Case report.
Wee HY, Tan TY, Khoo PC et al. (2003) A case series of pre-viable severe twin-twin transfusion syndrome. *Annals of the Academy of Medicine, Singapore*. 32: 645–8.	1 patient.	Case report of a specific complication.	Case report.

PROM, premature rupture of the membranes; RCT, randomised controlled trial; TTTS, twin to twin transfusion syndrome.

Appendix B: Related published NICE guidance for amnioreduction using septostomy with or without amniodrainage for the treatment of TTTS

Guidance	Recommendation
Interventional procedures	None relevant.
Technology appraisals	None relevant.
Clinical guidelines	None relevant.
Public health	None relevant.

Appendix C: Literature search for amnioreduction using septostomy with or without amniodrainage

Database	Version searched	Date searched
Cochrane Library	Issue 2, 2006	22/05/2006
CRD databases	Issue 2, 2006	22/05/2006
Embase	1996 to 2006 Week 18 1980 to 2006 Week 23	15/05/2006 14/06/2006
Medline	1966 to 2006 April Week 4 1966 to 2006 May Week 5	10/05/2006 14/06/2006 (additional refs)
Premedline	5 May 2006 13 June 2006	10/05/2006 14/06/2006 (additional refs)
CINAHL	1982 to 2006 April Week 4 1982 to 2006 June Week 2	15/05/2006 14/06/2006 (additional refs)
British Library Inside Conferences		30/05/2006
NRR	Issue 2, 2006	30/05/2006
Controlled Trials Registry	Issue 2, 2006	22/05/2006

Search strategy used in Medline

The search was adapted for use in the databases above.

1 exp Fetofetal Transfusion/ (887)
2 Fetofetal Transfuison$.tw. (0)
3 Fetofetal Transfusion$.tw. (49)
4 TwinTwin Transfusion.tw. (0)
5 Twin to Twin Transfusion$.tw. (251)
6 TTTS.tw. (173)
7 Monochorion$.tw. (785)
8 Twins, Monozygotic/ (6624)
9 or/1-8 (7639)
10 Amniocentesis/ (6303)
11 Amniocentes$.tw. (5151)
12 (Amnio$ adj3 (reduc$ or less$ or Diminish or shrink or condense or cut or trim or drain$)).tw. (393)
13 (amnio$ adj3 surg$).tw. (65)
14 Amnioreduct$.tw. (96)
15 amniodrain$.tw. (26)
16 or/10-15 (8983)
17 septostom$.tw. (477)
18 9 and (16 or 17) (224)
19 Fetofetal Transfusion/ (887)
20 twintwin transfusion$.tw. (0)

21 TTTS.tw. (173)
22 twin to twin transfusion$.tw. (251)
23 monochorion$.tw. (785)
24 Twins, Monozygotic/ (6624)
25 or/19-24 (7638)
26 (amnio$ adj3 (reduc$ or less$ or diminish or shrink or condense or cut or trim or drain$)).tw. (393)
27 Amniocentesis/ (6303)
28 Amniocentes$.tw. (5151)
29 (amnio$ adj3 surg$).tw. (65)
30 or/26-29 (8905)
31 25 and 30 (167)
32 from 31 keep 1-167 (167)
33 18 not 32 (57)
34 from 33 keep 1-57 (57)