TTTS 1 trial: A cluster randomized controlled trial comparing a conservative management and primary laser surgery in stage 1 TTTS.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Pregnancy, labour, delivery and postpartum conditions
Study type	Interventional

Summary

ID

NL-OMON46996

Source
ToetsingOnline

Brief title
TTTS 1 trial

Condition

- Pregnancy, labour, delivery and postpartum conditions

Synonym
Twin to Twin Transfusium Syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: conervative management, Fetal therapy, laser surgery, TTTS (Twin to Twin Transfusion Syndrome)

Outcome measures

Primary outcome

This composite outcome characterizes the babies alive at 6 months without neurological sequelae. Neurological sequelae are defined as cystic periventricular leukomalacia, severe intraventricular hemorrhage (stage 3 or 4), blindness or deafness.

Secondary outcome

• 6 months and 2 year intact survival of both twins

• Perinatal, 6 months and 2 year survival of at least one twin

• Perinatal, 6 months and 2 year survival of both twins

• Complications of prematurity at 6 months and 2 years (necrotizing enterocolitis >= stage 2, bronchopulmonary dysplasia, renal failure, retinopathy of prematurity, time spent in NICU)

• Neurological morbidity at 2 years as defined by any of: cerebral palsy according to the European CP network, blindness, severe deafness requiring amplification, or abnormal scores on the Bayley's test. A Bayley's test will be considered abnormal if the mental developmental indexes (MDI) or psychomotor development indexes (PDI) are under 70.

• Maternal and obstetrical morbidity

Study description

Background summary

Giant leaps have been made in the last decades in the treatment of twin-to-twin transfusion syndrome (TTTS). Overall, the emerging best first-line treatment of severe TTTS is percutaneous laser surgery as demonstrated by the only completed randomized controlled trial (RCT) so far in the field comparing laser surgery to amnioreduction. Although these results were convincing as to the overall superiority of laser over amnioreduction, indications for invasive treatment may deserve refining.
There has been growing concerns that percutaneous laser surgery may not be indicated in early or stage 1 TTTS. This idea arose from the belief that stage 1 TTTS may not warrant immediate invasive treatment and may just be followed conservatively, thus reducing the iatrogenic complications of invasive therapy in non-progressive disease as demonstrated by small retrospective studies of early TTTS. However, advocates of immediate laser surgery would argue that postponing surgery would increase the rates of spontaneous fetal demise and secondary neurological morbidity, as well as preterm premature rupture of the membranes (PPROM) and very preterm birth. Indeed, Quintero staging is not the only potential prognostic factor after laser surgery and management should also encompass gestational age at diagnosis and cervical length.

Study objective

This study aims to compare two management strategies by an international randomized controlled trial: the first relies on the overall conclusion from the Eurofoetus trial and advocates immediate percutaneous fetoscopic surgery for all stages of TTTS including stage 1 disease; the second is a conservative strategy, in which patients are monitored weekly until delivery or until progression warranting laser surgery. The primary end-point for this comparison encompasses both survival and neurological morbidity in a composite outcome, using a cluster-designed trial allowing the use of a per-fetus outcome rather than a per-pregnancy outcome.

Study design

A multi- centre, randomized controlled trial.

Intervention

Foetscopic laser treatment (percutaneous)

Study burden and risks

The potential benefits of conservative management is that some patients may not require invasive laser- treatment. For patients randomized to primary laser, they may benefit from definitive treatment of early TTTS avoiding progression to more advanced stages of the syndrome.

The potential risks of conservative management are an increased risk of intra-uterine fetal demise (IUFD), early rupture of membranes (PPROM), miscarriage and preterm birth. The risk of progressive disease has been associated to a worsening of overall pregnancy outcome. Progression rates are estimated between 30 and 45% in pregnancies managed conservatively. For patients randomized to primary laser, the establishes risks encompass IUFD, PPROM, chorio- amnionitis, preterm birth, placental abrubtion, miscarriage and surgical failure defined as recurrence of TTTS or post- operative fetal anemia.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Eligible patients are women with monochorionic, diamniotic twin pregnancies presenting with stage 1 TTTS defined according to the Eurofoetus criteria between 16+0 and 26+6 weeks of gestation. Maternal age > 18 years.

Exclusion criteria

Patients with a cervix less than 15 mm on transvaginal scan or severe maternal discomfort are excluded as these require immediate treatment. Patients with ruptured membranes or with fetal malformations will be excluded. Also language problems for informed consent are excluded.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2013
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	20-02-2012
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	22-10-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01220011
CCMO	NL38051.058.11