# Selective fetal growth restriction in monoChOrioNic Twins - an inteRnAtional inveSTigation

Published: 13-01-2023
Last updated: 31-12-2024

Primary objective: To improve outcome prediction in sFGR by developing a prediction model at the time of sFGR diagnosis and by evaluating specific ultrasound parameters throughout the pregnancy. Secondary objectives: - To increase our knowledge of...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON51577

**Source**
ToetsingOnline

**Brief title**
CONTRAST

### Condition

- Other condition
- Foetal complications
- Mood disorders and disturbances NEC

**Synonym**
Selective fetal growth restriction (sFGR); prenatal growth restriction

**Health condition**

neurologische ontwikkeling (t/m 2 jaar) van kinderen geboren uit een sFGR zwangerschap.

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** LUMC Global financiert het eerste jaar van de PhD van Anne Noll;het 2e jaar wordt betaald door het UZ Leuven (via een bursaal);het 3e jaar door het Karolinska University Hospital (via een aanstelling van Anne Noll ter plekke)

## Intervention

**Keyword:** monozygotic, Placenta pathology, Pregnancy Complications, Selective fetal growth restriction (sFGR), Twins

## Outcome measures

### Primary outcome

Composite outcome on a pregnancy level, consisting of the occurrence of one of

the following:

- Fetal demise of one or both twins (including selective reduction), and/or:

- Iatrogenic elective birth < 32 weeks of GA because of fetal distress

Potential predictors that will be collected:

- On a twin level:

- Gestational age at time of sFGR diagnosis

- Estimated fetal weight (EFW) discordance between the twins

- Abnormal umbilical artery Doppler flow pattern

- Artery-to-artery (AA)-sharing (amount and diameter of the AA-anastomoses)

- Presence of oligohydramnios (defined as the maximum vertical pocket of less

than two cm)

- Abnormal Ductus venosus waveform

- Placental dichotomy

- Major anomalies in one or both twins - according to the EUROCAT registry

- Cord insertions

- On an individual fetal level:

- The (individual) ultrasound parameters described under 5.1.2

- On a maternal level:

- History of an uncomplicated pregnancy

- Mode of conception

**Secondary outcome**

For the full list, we kindly refer to chapter 5.1.2. and 5.1.3.

Summary:

- Ultrasound parameters (both standard and additional parameters)

- Fetal MRI (brain development)

- Antenatal characteristics

- Maternal, paternal and fetal baseline characteristics

- Analysis of sFGR (characteristics and management during pregnancy)

- Characteristics of labour

- Placental evaluation (macroscopic and microscopic)

- Neonatal variables

- Neurodevelopmental outcomes at 2 years of age

- Psychological impact on parents

# Study description

### Background summary

Optimal diagnostic management and underlying pathophysiological mechanisms of selective fetal growth restriction (sFGR) in monochorionic diamniotic (MCDA) twin pregnancies have not been fully clarified.

The current diagnostic classification system based on three different umbilical artery flow patterns has no increasing scale of severity and the predictive value is limited. Since there is no treatment available for sFGR, predicting fetal deterioration is key in preventing single or double demise. Outcome prediction is furthermore important in the selection of cases that will be offered selective reduction (to provide the larger twin with better prospects), as well as determining monitor frequency and possible hospital admission. As outcome prediction is clinically challenging, patient counselling is too, and parents often encounter a great deal of uncertainty during the pregnancy.

Furthermore, little is known about the neurological development of sFGR children (both antenatally and postpartum). Moreover, the psychological impact of an sFGR pregnancy of the future parent)s) has not been studied before. The impact of these factors should be taken into account during patient counseling, which is currently not the case.

By our knowledge, this is the first international, multicenter, prospective cohort study on sFGR.

### Study objective

Primary objective:
To improve outcome prediction in sFGR by developing a prediction model at the time of sFGR diagnosis and by evaluating specific ultrasound parameters throughout the pregnancy.

Secondary objectives:
- To increase our knowledge of the pathophysiology of sFGR in MCDA twins by performing unique histological examinations of the sFGR placentas.
- To document perinatal morbidity and mortality after sFGR.
- To examine the fetal brain development and infant neurodevelopmental outcome of until 2 years of age after a sFGR pregnancy.
- To assess the psychological impact on mental health of both parents/caregivers (if applicable) during sFGR pregnancy and postpartum.

### Study design

The design is a prospective multicenter international cohort study, in which the Leiden University Medical Centre (LUMC), the University Hospital in Leuven (UZ Leuven), the Karolinska University Hospital in Stockholm, BCNatal (Barcelona), Mount Sinai Hospital (together with the Hospital for Sick Children, both in Toronto), and the Boston Children's Hospital (Boston) collaborate.

**Study burden and risks**

MCDA twins are at substantial risk of experiencing adverse prenatal conditions, of which sFGR is one of them. The LUMC, UZ Leuven, the Karolinska University Hospital and the BCNatal are all national referral centers with extensive experience in managing complicated twin pregnancies. As sFGR is a rare condition, it can be best studies through multicenter collaboration.

Most assessments of this study will be integrated as part of clinical care for the sFGR twins. They will also be studied in our unselected cohort of MCDA twins.
Antenatal, a burden for the pregnant mother during routine ultrasound might be a prolonged examination time (+/- 10-30 minutes) for the additional measurements, which can occur a maximum of 5 times. A clinical fetal MRI will be performed between 28-32 weeks and require up to 60 minutes to complete. MRI is considered a low-risk and minimally invasive procedure.

The questionnaires filled out by the parents will cost +/- 10-20 minutes of their time (per questionnaire, per parent), with a total of 9 questionnaires (prenatally and postpartum). After birth, the placenta will be examined extensively. Neurodevelopmental evaluation at 2 years of age comprises both filling out a questionnaire by the parents (which typically takes 30 minutes per parent) and a neurodevelopmental assessment for some of the twin(s). This assessment is generally experienced as enjoyable for children and are not associated with any risk with a minimal burden (e.g. 120 minutes).

The burden for (some of) the child / children will be in the form of a neurological examination to test cognitive and motor development (Bayley-III). This is generally experiences as joyful by the children. The Bayley-III is not associated with any risks, widely used, and takes +- 120 minutes to complete. The Bayley-III is already part of standard follow-up in the Netherlands for some indications (for example birth < 30 weeks or a birth weight < 1500 grams). Not all the children will undergo the Bayley-III, for a list of indications see: chapter 5.3 (Study procedures).

# Contacts

**Public**
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
**Scientific**
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

## Inclusion criteria

- MCDA twin pregnancy
- Diagnosis of sFGR before 28+0 weeks of GA (independent of Doppler flows)
- Pregnant woman >= 18 years and able to consent
- Partner (if applicable) >= 18 years and able to consent
- Written informed consent of the pregnant woman (for the antenatal study) and of both parents (if applicable) for participation in the longitudinal follow-up)

## Exclusion criteria

- The presence of lethal anomalies (one or both fetuses)

- Multiple pregnancy higher order than twins;
- TTTS/TAPS present at moment of sFGR diagnosis.

# Study design

## Design

**Study type:** Observational non invasive

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Basic science |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 13-03-2023 |
| Enrollment: | 70 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Registration: | No |

# Ethics review

Approved WMO

| | |
|---|---|
| Date: | 13-01-2023 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

Approved WMO

| | |
|---|---|
| Date: | 24-12-2024 |
| 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 | NCT05952583 |
| CCMO | NL81805.058.22 |