LEMON: The Long-term Effects of selective fetal growth restriction in MOnochorionic twins

Published: 05-11-2020
Last updated: 08-04-2024

The main objective is to assess long-term neurodevelopmental, cardiovascular, pulmonary, and growth outcomes in a cohort of MC twins with sFGR and to compare outcomes within sFGR twin pairs.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Observational non invasive

Summary

ID

NL-OMON55047

Source
ToetsingOnline

Brief title
LEMON

Condition

- Myocardial disorders
- Foetal complications
- Cognitive and attention disorders and disturbances

Synonym
Selective intrauterine growth restriction (sIUGR); prenatal growth restriction

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: Dutch Hart Foundation

Intervention

Keyword: cardiovascular outcome, monochorionic twins, neurodevelopment, selective fetal growth restriction

Outcome measures

Primary outcome

To assess long-term neurodevelopmental outcome, cognitive and motor development will be evaluated using standardized psychometric age-appropriate tests and a neurological examination. Echocardiography will be used to assess differences in structural cardiac measures and cardiac function, including aortic pulse-wave velocity (aPWV) and carotid intima-media thickness (cIMT). Spirometry will be recorded in children >= 4 years old to quantify lung function, including forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and forced mid-expiratory flow rate (FEF(25%-75%). Growth will be assessed using available childhood growth curves from the primary care system and by detailed anthropometric measurements.

Secondary outcome

The project addresses multiple secondary objectives that can be grouped into the same five categories as the primary objectives:

I. Neurodevelopmental outcome

a) To describe the incidence of mild and severe NDI.

b) To identify potential risk factors within the sFGR population for low cognitive test scores.

c) To evaluate long-term behavioral outcome, attachment, quality of life and school functioning including academic performance.

II. Cardiovascular outcome

a) To assess within-pair differences in blood pressure.

III. Pulmonary outcome

a) To document within-pair differences in atopic constitution.

IV. Growth

a) To assess pubertal development.

b) To assess intra-twin growth patterns in the sFGR population.

V. (Epi)genetics

a) To describe epigenetic differences in peripheral tissue (buccal swabs) as a possible underlying mechanism for the mediation of the long-term effects of FGR. The specific DNA methylation patterns found in the Twinlife study will be examined in the population of the current study as well to examine their link with long-term outcomes.

Study description

Background summary

Selective fetal growth restriction (sFGR) in monochorionic (MC) twin pregnancies is characterized by a large intertwin growth discrepancy due to

unequal placental sharing.
Neonatal morbidity and mortality associated with sFGR have been thoroughly described, but data on long-term outcomes is lacking although we know that fetal growth restriction (FGR) in singletons has been associated with an increased risk of neurodevelopmental impairment (NDI), cardiovascular disease (CVD), impaired lung function and suboptimal growth later in life.
Knowledge of long-term outcomes is essential both for adequate counselling of parents of these vulnerable patients and for early identification of children who will benefit from additional postnatal monitoring. Moreover, a better understanding of long-term outcome might aid in devising feasible management options in the future.
Therefore, insight into long-term outcomes is crucial in providing the highest standard of care for MC twins with sFGR. The results of this study will be complementary to the Twinlife study (NL67331.058.18) which is already ongoing at the LUMC.

Study objective

The main objective is to assess long-term neurodevelopmental, cardiovascular, pulmonary, and growth outcomes in a cohort of MC twins with sFGR and to compare outcomes within sFGR twin pairs.

Study design

An observational cohort study.

Study burden and risks

The total duration of the participation for each child is approximately * day, including the questionnaires and the assessments. The neurodevelopmental assessment comprises approximately 2-3 hours of examination time and is generally experienced as enjoyable for children. The echocardiography, blood pressure measurement, aPWV measurement using the arteriograph constitutes 30-45 minutes per child. The growth measurements and buccal swabs will generally be completed within 10 minutes per child. The spirometry will be performed in approximately 30-45 minutes per child. Thus, the total burden is considered minimal. Parents will be asked to fill in a total of six questionnaires regarding background, health, school functioning, behaviour, attachment and quality of life prior to and during the follow-up examination. Children >= 8 years of age will fill in a self-assessment on pubertal development stage. No risk is associated with study participation. Participation does not result in individual benefits.

Contacts

Public
Leids Universitair Medisch Centrum

albinusdreef 2
leiden 2333za
NL
Scientific
Leids Universitair Medisch Centrum

albinusdreef 2
leiden 2333za
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

To be eligible to participate in this study, a subject must meet all the following criteria:
• MC twins with sFGR born in the LUMC.
• Children aged 2 to 17 years at time of inclusion.
• Children currently living in the Netherlands.

The parents of a potential subject must meet the following criteria:
• Parent(s) aged >= 18 years, who are able to consent.
• Written informed consent from both parents to participate, form being approved by the Ethic Committee.
When one of the parents has passed away, the surviving parent with parental

authority can provide informed consent. When both parents have passed, guardians or caretakers with parental authority can provide informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• MC twins with TTTS or TAPS.
• Twin Reversed Arterial Perfusion (TRAP).
• Monoamniotic twin pregnancies.
• Children passed away before inclusion.
• Single survivors.
• Children born with congenital/chromosomal abnormalities.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-01-2021
Enrollment:	154
Type:	Actual

Ethics review

Approved WMO

Date:	05-11-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

	metc-ldd@lumc.nl
Approved WMO Date:	23-08-2021
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
CCMO	NL75027.058.20