The COllaborative Neonatal NEtwork for the first CPAM Trial, the CONNECT

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Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory disorders congenital
Study type	Interventional

Summary

ID

NL-OMON51712

Source
ToetsingOnline

Brief title
CONNECT trial

Condition

- Respiratory disorders congenital

Synonym
Congenital lung abnormality, lung abnormality

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Congenital, Cystic Adenomatoid Malformation of Lung, Patient Outcome Assessment, Thoracic Surgery

Outcome measures

Primary outcome

The primary outcome is the difference in maximal endurance using the BRUCE treadmill test at five years of age between the surgical and conservative group, measured in minutes and SDS.

Secondary outcome

o Pulmonary morbidity during follow-up (occurrence of infections, cough, dyspnoea, respiratory insufficiency and other pulmonary symptoms).

o Frequency of surgical intervention due to pulmonary morbidity during follow-up period

o CPAM characteristics on prenatal ultrasound images, reported according to structured report, see Appendix D (35)

o CPAM characteristics on CT-scan at 3-9 months of age, reported according to structured report form Appendix C (34)

o CPAM development / post-surgical appearance on repeated CT imaging, reported according to structured report form (34)

o Parental anxiety, pre-operative and at all follow-up visits by means of the Visual Analogue Scale for Anxiety (VAS-A) (38, 39)

o Quality of life analysis by means of the Infant Toddler Quality of Life Questionnaire (ITQOL) (40)

o Pathological characteristics of resected material (macroscopic, microscopic,

immunohistochemistry, molecular diagnostics) as assessed by local

pathologist of participating centre according to Appendix B (23)

o Abnormal anthropometric measurements during follow-up, measured with help of

local SD-score computation

o Analysis of the cost-effectiveness of both management strategies and

comparison between them, see chapter 10-c

Study description

Background summary

Congenital Pulmonary Airway Malformation (CPAM), formerly known as Congenital Cystic Adenomatoid Malformation (CCAM), is the most common congenital lung abnormality (CLA), comprising approximately 30% of all CLA. A CPAM is a congenital cystic lung lesion with an abnormal connection to the tracheobronchial tree and normal pulmonary vascularization. Advances in prenatal ultrasound have led to increased incidence figures, momentarily estimating the incidence to be approximately 4 in 10,000 births. Despite the increasing incidence, much is still unknown about the developmental causes, best treatment options, and natural course of CPAM. When CPAM patients present with symptoms, surgical resection is usually recommended. However, the majority of CPAM patients are asymptomatic at birth and remain so during childhood. In this case, a conservative wait-and-see management is propagated by some for this originally benign, possibly regressive disease while others believe in an operative approach. Arguments for early surgical resection include the risk of symptom development, possibly indicating emergency surgery leading to an increased risk of complications. Other arguments include the possible malignant degeneration of these lesions, parental anxiety, and hypothetical compensatory lung growth following early resection. Arguments in favour of expectant management include the risk of postoperative complications, the fact that the majority of patients will remain asymptomatic, and the evidence in literature that surgical resection does not rule out the development of malignancy in the lesion region. All abovementioned arguments are based on retrospective studies, expert opinion or empiricism, but hard evidence is lacking. We hypothesize that asymptomatic patients can be managed expectantly but must be structurally monitored. As most patients remain asymptomatic, and to date no postnatal predictors have been identified for the quality of life and daily activities in this patient group, focus on functional outcome measures such as pulmonary

morbidity and endurance of physical activity is desirable.

Study objective

The main objective is to identify the optimal management for patients with an asymptomatic CPAM, based on functional outcome measures. Furthermore, the primary objective is to stratify asymptomatic CPAM patients into a low and high risk group for developing symptoms, infection and malignant degeneration and to hereby introduce a personalised medicine approach towards management. Secondary objectives include the detection of predictive prenatal and postnatal features and the assessment during follow up of: physical growth, psychomotor development and pulmonary morbidity, parental anxiety, quality of life, and the effectiveness of quantitative imaging in predicting outcome.

Study design

Randomised, controlled, multicentre superiority trial. Randomisation will take place as centre specific block randomisation with 1:1 allocation.
One hundred and sixty-six patients will be recruited within a multinational European consortium (the CONNECT consortium).

Intervention

Children assigned to the intervention group will undergo surgical resection of the CPAM between 6 and 9 months of age. Children assigned to the control group will be monitored conservatively. The follow-up scheme will be uniform for both treatment groups and last for 5 years.

Study burden and risks

The risk and burden of pulmonary resection in asymptomatic CPAM patients is low. It is currently the standard care for this patient group in the majority of centres globally (67-77%). On the other hand, a conservative follow-up is considered a safe and viable alternative (standard of care in 23-33% of centres), as only a fraction (3-9%) of initially asymptomatic CPAM patients goes on to develop symptoms during the first years of life. The burden of the follow-up scheme in this trial is considered low and is also standard of care in participating centres. The added knowledge gained by analysing the longitudinal information attained by the second CT-scan & the questionnaires outweighs the burden of this procedure and the radiation exposure.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

- Lesion detected during routine prenatal ultrasound screening
- Delivery at term: gestational age >=37 weeks
- Birthweight > -2SD or >P10
- Asymptomatic at birth defined as no prolonged respiratory distress or oxygen support (< 24 hours)
- Asymptomatic up to the moment of inclusion
- Confirmation of CPAM on postnatal chest CT-scan at 3-9 months of age, according to structured report form
- Unilateral lesion occupying no more than one lung lobe as assessed on chest CT-scan at 3-9 months of age

Exclusion criteria

- Bilateral lesion
- Development of symptoms before randomization, considered by treating

physician as caused by CPAM with reasonable certainty
- Complicated pregnancy defined as (pre-)eclampsia, pregnancy diabetes in mother, foetal hydrops or severe polyhydramnios on prenatal ultrasound
- Syndrome associated anomalies on genetic analysis confirmed by genetic expert
- Major associated malformations. Anomalies include cardiac malformations requiring surgical correction or follow-up by a paediatric cardiologist, congenital malformations requiring major surgical intervention, and anomalies that affect normal lung growth and development.
- Suspicion of malignancy on chest CT scan evaluation at the age of 3-9 months
- Participation in another randomised controlled trial

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:	Pending
Start date (anticipated):	01-10-2022
Enrollment:	70
Type:	Anticipated

Ethics review

Approved WMO Date:	13-12-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL81003.078.22