Primary Spontaneous Pneumothorax and Renal Cell Carcinoma

Published: 26-09-2019
Last updated: 06-05-2024

By performing a low-dose CT of the thorax in patients with primary spontaneous pneumothorax (PSP) the typical pulmonary abnormalities are detected related to the mutation in the folliculine gene. In this way the Birt-Hogg-Dube syndrome can be...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54609

Source
ToetsingOnline

Brief title
PSP-RCC

Condition

- Other condition
- Congenital and hereditary disorders NEC
- Renal disorders (excl nephropathies)

Synonym
lung collaps by air in the pleural cavity, pneumothorax

Health condition

longaandoening: pneumothorax

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: SFOH (stichting fonds oncologie holland)

Intervention

Keyword: -birt-hogg-dube-syndrome, -pneumothorax, -renal cell carcinoma

Outcome measures

Primary outcome

The prevalence of pulmonary parenchyma abnormalities which can be found by performing low-dose CT scan of the chest and which are probably related to Birt-Hogg-Dube syndrome in patients presenting with primary spontaneous pneumothorax.

Secondary outcome

The prevalence of Birt-Hogg-Dube syndrome based on finding the folliculin gene mutation in a cohort of patients with primary spontaneous pneumothorax.

Other abnormalities in the pulmonary parenchyma found by performing low-dose CT of the chest and probably related to the primary spontaneous pneumothorax.

Study description

Background summary

More than 15% of all kidney tumors are related to germline mutations (1). Part of this is caused by the autosomal dominant mutation in the folliculin (FLCN) gene on chromosome 17p11.2 (OMIM # 135150). This mutation is responsible for a number of phenomena that are all, or in part, present in the carriers of the mutation and are associated with the names of 3 Canadian researchers, resulting in Birt-Hogg-Dubé syndrome (BHD). Although this was later corrected in Hornstein-Birt-Hogg-Dubé (2), the most commonly used indication is still BHD.

This hereditary syndrome is characterized by fibrofolliculomas in the face and upper part of the thorax, usually numerous lung cysts that occur both subpleural and in the lung parenchyma, and a high frequency of renal cell cancer (RCC). Characteristic of the thin-walled lung cysts is the often varying size from a few millimeters to several centimeters in diameter and the presence in all lung lobes (3). Pathological examination of resection material shows that the cysts are usually not connected to the bronchial tree (4). The genetic defect is responsible for the strongly limited possibility of the covering epithelium of the cysts to stretch (5), so that the thin-walled cysts can easily rupture and a pneumothorax can develop. This is particularly evident in situations with external pressure changes (6). Research has shown that 5-10% of SP patients have a mutation in the FLCN gen 7,8
Standard diagnostics for PSP is chest X-ray, CT is only performed on indication (9). SP has a relapse frequency of about 50%, with relapse, pleurodesis is performed. In SP by BHD, the risk of recurrence is about 75% (10). Research into factors that give a high risk of recurrence is cost-effective as far as the prevention of recurrence is concerned (11). Nevertheless, this is not (yet) part of the existing guidelines. The characteristic lung cysts of BHD are only clearly visible on CT and are so specific that the diagnosis can often be made with CT chest (12). After this, confirmation by determining the mutation is indicated.
Approximately 35% (13) of the BHD carriers develop one or more kidney tumors (RCC), chromophobic or oncocytic type. Determining carrier status offers opportunities for identification of family members who, in the presence of the mutation, are also at risk for developing RCC. For the detection of new BHD carriers there is no standard research, patients are found by symptoms, and through them family members with this mutation. A potentially effective alternative way of detecting a large proportion of the BHD patients may be the standard examination of SP patients with CT and NGS (14). This is still supported by the high frequency of pneumothorax as the first symptom of BHD syndrome, up to 65% of the BHD population (15).
The VUMC database shows that in a cohort of 115 carriers (16) with 5 years of follow-up, 2 new RCCs were found, the frequency being 0.3 / 100 man-years, and moreover, per discovered carrier 3.6 family members found with the same mutation (17).

Study objective

By performing a low-dose CT of the thorax in patients with primary spontaneous pneumothorax (PSP) the typical pulmonary abnormalities are detected related to the mutation in the folliculine gene. In this way the Birt-Hogg-Dube syndrome can be diagnosed and the prevalence of the syndrome in patients with pneumothorax can be determined. Also other abnormalities as probable cause for the pneumothorax could be found.

Study design

After treatment for primary spontaneous pneumothorax at first policlinic check a low-dose CT of the chest will be performed and a blood sample by which pulmonary abnormalities in the lung parenchyma and an eventual present mutation of the folliculin gene can be detected.

Study burden and risks

There will be a minimal burden for the patient when participating in this study. After treatment for the pneumothorax a tube of blood and a low-dose CT is performed in an outpatient setting at first outpatient regular check. The patient included in the study will have to spend one extra visit to the hospital to have the CT scan and blood sample being performed. We estimate that the visit to the hospital for the CT scan and blood sampling will take about 1.5 hour. There will be a minimal risk for the patient in perspective of the irradiation exposure by performing a low-dose CT scan of the thorax. In fact, the current guidelines do not recommend CT chest with a primary spontaneous pneumothorax, usually no CT scan is performed with a pneumothorax. However, the risk of the radiation load is very small for the patient.

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 (16-17 years)
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
-Able to give written informed consent prior to participation in the study. Subjects must be able to read, comprehend and write at a level sufficient to complete study related materials.
-Subjects must have a diagnosis of spontaneous pneumothorax (this might be a 2nd PSP if not proven to be related to a known disease or first contralateral pneumothorax)
-Age: at least 16 years of age at visit 1
-Gender: male or female

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
-Age < 16 years old
-Subjects with claustrophobia making it impossible to perform a CT scan
-Has a history or current evidence of any condition, therapy, or laboratory abnormality that might confound the results of the trial, interfere with the subject*s participation for the full duration of the trial, or it is not in the best interest of the subject to participate, in the opinion of the treating investigator.
-A CT scan of the thorax is already been performed for this subject within a year before the PSP
-lung carcinoma
-lung metastases
-Iatrogenic pneumothorax
-secondary spontaneous pneumothorax

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-09-2020
Enrollment:	350
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	26-09-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	17-02-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	22-04-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-10-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	12-07-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-09-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	05-06-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-03-2024
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
CCMO	NL68125.058.19
Other	NL7953