Diagnostic Study; Contrast enhanced Magnetic Resonance Imaging of the lungs in children with CF.

Gepubliceerd: 17-09-2007 Laatst bijgewerkt: 13-12-2022

We hypothesize that with Gd-MRI inhomogeneity of lung perfusion can be readily identified and that these areas match areas of trapped air as visualized by proton MRI and CT.

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21165

Bron
Nationaal Trial Register

Verkorte titel
Contrast enhanced Magnetic Resonance Imaging of the lungs in children with CF

Aandoening

1. Cystic Fibrosis in children;

2. Gd-MRI;

3. Lung hypoperfusion.

Ondersteuning

Primaire sponsor: Investigator initiated trial
Overige ondersteuning: Erasmus MC - Sophia

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The main study parameter will be the ability of the radiologist and CF-team to determine whether hypo perfusion of the lung is present in the Gd-MRI and whether this matches the area of trapped air on the proton-MRI image. And secondly whether the radiologist and CF-team can determine whether there is progression of peripheral airway disease as evaluated on Gd-MRI relative to the CT made in the previous year. This will be rated by the radiologist and the physician using a standardized evaluation form.
To evaluate whether this clinical practice is reproducible, MRI, Gd-MRI and CT scans will be scored in random order by two experienced independent observers. These observers will score independently of each other and they will be blinded as to patient characteristics. The scoring will be done using a semi-quantitative scoring system to estimate the volume% of trapped air and hypo perfusion. The volume% of trapped air on the proton-MRI will be compared to the volume% of hypo perfusion on the Gd-MRI. In addition, volume% of trapped air on the proton-MRI and hypo perfusion on the Gd-MRI will be compared to the volume% of trapped air on the chest CT made in the previous year.

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale: CF lung disease starts mostly in the first year of life. Traditionally, pulmonary function tests (PFTs) have an important place in the monitoring of CF lung disease. A major disadvantage of PFTs is that they are not very sensitive to localized structural changes. CT is the most sensitive technique to detect structural lung changes in CF. In over 50% of the patients there was discordance between longitudinal changes obtained from CT and from the PFTs. The most relevant information obtained from CT is the detection and progression of bronchiectasis. The second important early morphological change that can be observed on CT is trapped air. A major disadvantage of CT is that is exposes the patient to ionising radiation. Therefore, the use of CT in CF is restricted to one examination every two years. Proton-Magnetic Resonance imaging (proton-MRI) was introduced in the Sophia in 2006 to fill in the gap between the bi-annual CT evaluations. With proton-MRI central bronchiectasis and atelectasis can be well tracked. Unfortunately, the detection of peripheral bronchiectasis and trapped air is of relatively poor quality. Fortunately, trapped air on proton–MRI of the chest can be visualized by looking at lung perfusion since persisting hypoventilation of areas of the lung result in matched hypo perfusion. Hypo perfusion is an even more relevant finding than trapped air since it identifies areas of the lung that do not contribute to gas diffusion. Lung perfusion can be visualized by MRI using intravenously injected contrast agent Gadolinium (Gd). Gd is considered a safe contrast agent that has been used on a large scale since the early nineties. For this reason it has been introduced in the routine follow up in CF patients.

Objective:

Primary Objective:

To asses whether Gd-MRI is a feasible and sensitive technique to monitor the distribution and volume of lung hypo perfusion in patients with CF and to compare the distribution and volume of hypo perfusion on expiratory contrast enhanced Gd-MRI to the areas of trapped air on the routine proton MRI. When this is the case Gd-MRI will be added as a routine to the MRI protocol used in CF patients.

Secondary objectives:

To compare the distribution and volume of hypo perfusion on expiratory Gd-MRI with the distribution and volume of trapped air on expiratory chest CT made in the previous year.

To compare the distribution and volume of hypo perfusion on expiratory contrast enhanced Gd-MRI to PFTs parameters of peripheral airway disease (FEF75, FEF25-75, LCI).

Hypothesis: We hypothesize that with Gd-MRI inhomogeneity of lung perfusion can be readily identified and that these areas match areas of trapped air as visualized by proton-MRI and CT.

Study design: This will be a two-year cohort study. Patients who are scheduled for their routine bi-annual proton-MRI will be informed about the study at least 3 weeks before the annual examination. Informed consent will be requested. Instruction of the routine breathhold maneuvers will be exercised during the routine visit 3 months prior to the MRI. On the day of the MRI breath hold maneuvers will be shortly rehearsed. The routine annual blood withdrawal will be done after insertion of a peripheral catheter. Next the peripheral catheter will be flushed using a low strength heparin solution. Finally, the patient will have their routine proton-MRI and a Gd-MRI.

Study population: A cohort of 30 consecutive patients with CF between 6 and 18 years of age who are scheduled for their routine annual proton-MRI.

Intervention (if applicable): All patients will have an infusion of the contrast agent Gd.
Main study parameters/endpoints: The ability of the radiologist and CF team to identify areas of the lung that are hypo perfused on the Gd-MRI relative to the proton-MRI.

Secondary study parameters/endpoints.
The distribution and volume of hypo perfused lung on the expiratory Gd-MRI will be compared to the distribution of trapped air on the expiratory proton-MRI and with the expiratory chest

CT made in the previous year. This will be done using a semi-quantitative scoring system. The hypo perfusion score on expiratory contrast enhanced Gd-MRI will be correlated to the score for trapped air on the MRI, to the CT of the year before and to lung function parameters sensitive to peripheral airway disease (FEF75, FEF25-75, LCI).

In addition, the feasibility of the Gd-MRI protocol will be evaluated. Indicators will be total duration of examination time. Number of completed Gd-MRI examinations as percentage of total number of performed Gd-MRI examinations. Number of successful venous catheter insertions. Side-effects of Gd infusion in this CF patient group especially incidence of complications such as allergic reactions.

Doel van het onderzoek

We hypothesize that with Gd-MRI inhomogeneity of lung perfusion can be readily identified and that these areas match areas of trapped air as visualized by proton MRI and CT.

Onderzoeksproduct en/of interventie

After informed consent children with CF scheduled (for annual check up) for a proton MRI will also undergo a Gadolinium-MRI.

Contactpersonen

Publiek

Erasmus MC - Sophia Children’s Hospital
Room Sb2778
Wytemaweg 80

E. Wiel van der
Rotterdam 3015 CN
The Netherlands
+31(0)10 4636797

Wetenschappelijk

Erasmus MC - Sophia Children’s Hospital
Room Sb2778
Wytemaweg 80

E. Wiel van der
Rotterdam 3015 CN
The Netherlands
+31(0)10 4636797

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age between 6-18 years old;

2. Diagnosis CF confirmed;

3. Stable condition;

4. Ability to perform lung function tests and breath hold tests;

5. CT can made in the year before the MRI;

6. Signed written informed consent;

7. Able to comply with the protocol requirements.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Inability to follow instructions of the investigator;

2. Current respiratory tract infection;

3. Requiring iv antibiotics;

4. Pulmonary complications;

5. Claustrofobia;

6. History of anaphylactic reaction on contrast agent;

7. Any clinical condition which, according to the treating physician, might put the patient at risk;

8. Severe astma and/or severe allergies as determined by physician.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-11-2007
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	17-09-2007
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL1027
NTR-old	NTR1059
Ander register	: METC 2007-289
ISRCTN	ISRCTN wordt niet meer aangevraagd

Resultaten

Samenvatting resultaten

1. Armstrong, D., S. Hook, R. Carzino, G. Nixon, and K. Grimwood. 2000. Lower airway inflammation in cystic fibrosis infants. Pediatr Pulmonol:S5.3.
2. Nixon, G. M., D. S. Armstrong, R. Carzino, J. B. Carlin, A. Olinsky, C. F. Robertson, and K. Grimwood. 2002. Early airway infection, inflammation, and lung function in cystic fibrosis. Arch Dis Child 87(4):306-11.
3. Muhlebach, M. S., P. W. Stewart, M. W. Leigh, and T. L. Noah. 1999. Quantitation of inflammatory responses to bacteria in young cystic fibrosis and control patients. Am J Respir Crit Care Med 160(1):186-91.
4. Rosenfeld, M., R. L. Gibson, S. McNamara, J. Emerson, J. L. Burns, R. Castile, P. Hiatt, K. McCoy, C. B. Wilson, A. Inglis, A. Smith, T. R. Martin, and B. W. Ramsey. 2001. Early pulmonary infection, inflammation, and clinical outcomes in infants with cystic fibrosis. Pediatr Pulmonol 32(5):356-66.
5. Tiddens, H. A. W. M. 2006. Chest Computed Tomography Scans should be considered as a routine investigation in Cystic Fibrosis. Pediatric Respiratory Reviews 7:202-208.
6. Young, K., F. Aspestrand, and A. Kolbenstvedt. 1991. high resolution CT and bronchography in the asssessment of bronchiectasis. Acta Radiologica 32:439-441.
7. Hansell, D. M. 1998. Bronchiectasis. Radiologic Clinics of North America 36:107-128.
8. Munro, N. C., J. C. Cooke, D. C. Currie, B. Strickland, and P. J. Cole. 1990. Comparison of thin section computed tomography with bronchography for identifying bronchiectatic segments in patients with chronic sputum production. Thorax 45(2):135-9.
9. de Jong, P. A., Y. Nakano, M. H. Lequin, R. Woods, P. D. Pare, and H. A. W. M. Tiddens. 2004. Progressive damage on high-resolution computed tomography despite stable lung function in CF. Eur Respir J 23:93-97.
10. de Jong, P. A., A. Lindblad, L. Rubin, H. W.C., J. C. de Jongste, M. Brink, and H. A. Tiddens. 2006. Progression of lung disease on computed tomography and pulmonary function tests in children and adults with cystic fibrosis. Thorax 61:80-85.
11. Tiddens, H. A. W. M. 2002. Detecting early structural lung damage in cystic fibrosis. Pediatr Pulmonol Suppl 34:228-231.
12. Martinez, T. M., C. J. Llapur, T. H. Williams, C. Coates, R. Gunderman, M. D. Cohen, M. S. Howenstine, O. Saba, H. O. Coxson, and R. S. Tepper. 2005. High Resolution Computed Tomography Imaging of Airway Disease in Infants with Cystic Fibrosis. Am J Respir Crit Care Med.
13. Quan, J. M., H. A. W. M. Tiddens, J. Sy, S. G. mcKenzie, M. D. Montgomery, P. J. Robinson,

M. E. B. Wohl, and M. W. Konstan. 2001. A two-year randomized, placebo controlled trial of dornase alfa in young cystic fibrosis patients with mild lung function abnormalities. Journal of Pediatrics 139:813-820.
14. Robinson, T. E., M. L. Goris, H. J. Zhu, X. Chen, P. Bhise, F. Sheikh, and R. B. Moss. 2005. Dornase alfa reduces air trapping in children with mild cystic fibrosis lung disease: a quantitative analysis. Chest 128(4):2327-35.
15. de Jong, P. A., J. R. Mayo, K. Golmohammadi, Y. Nakano, M. H. Lequin, H. A. Tiddens, J. Aldrich, H. O. Coxson, and D. D. Sin. 2005. Estimation of cancer mortality associated with repetitive computed tomography scanning (CT) scanning in cystic fibrosis. Am J Respir Crit Care Med 173:199-203.
16. de Jong, P. A., Y. Nakano, M. H. Lequin, and H. A. Tiddens. 2005. Dose reduction for CT in children with cystic fibrosis: is it feasible to reduce the number of images per scan. Pediatr Radiol 36:50-53.
17. Puderbach, M., M. Eichinger, J. Gahr, S. Ley, S. Tuengerthal, A. Schmahl, C. Fink, C. Plathow, M. Wiebel, F. M. Muller, and H. U. Kauczor. 2007. Proton MRI appearance of cystic fibrosis: Comparison to CT. Eur Radiol 17(3):716-24.
18. Eichinger, M., M. Puderbach, C. Fink, J. Gahr, S. Ley, C. Plathow, S. Tuengerthal, I. Zuna, F. M. Muller, and H. U. Kauczor. 2006. Contrast-enhanced 3D MRI of lung perfusion in children with cystic fibrosis-initial results. Eur Radiol.
19. Failo, R., P. A. Wielopolski, H. A. W. M. Tiddens, W. C. J. Hop, G. P. Krestin, R. Pozzi Mucelli, and M. H. Lequin. 2007. Lung morphology assessment using Magnetic Resonance Imaging (MRI): a robust ultra-short TR/TE 2D Steady State Free Precession (SSFP) sequence in cystic fibrosis (CF) routine follow up. Submitted.
20. Molinari, F., C. Fink, F. Risse, S. Tuengerthal, L. Bonomo, and H. U. Kauczor. 2006. Assessment of differential pulmonary blood flow using perfusion magnetic resonance imaging: comparison with radionuclide perfusion scintigraphy. Invest Radiol 41(8):624-30.
21. Vonk-Noordegraaf, A., S. A. van Wolferen, J. T. Marcus, A. Boonstra, P. E. Postmus, J. W. Peeters, and A. J. Peacock. 2005. Noninvasive assessment and monitoring of the pulmonary circulation. Eur Respir J 25(4):758-66.
22. Bellin, M. F. 2006. MR contrast agents, the old and the new. Eur J Radiol 60(3):314-23.
23. Niendorf, H. P., J. Haustein, I. Cornelius, A. Alhassan, and W. Clauss. 1991. Safety of gadolinium-DTPA: extended clinical experience. Magn Reson Med 22(2):222-8; discussion 229-32.
24. Wang, T., G. Schultz, H. Hebestreit, A. Hebestreit, D. Hahn, and P. M. Jakob. 2003. Quantitative perfusion mapping of the human lung using 1H spin labeling. J Magn Reson Imaging 18(2):260-5.
25. Shellock, F. G., and E. Kanal. 1999. Safety of magnetic resonance imaging contrast agents. J Magn Reson Imaging 10(3):477-84.
26. Bellin, M. F., M. Vasile, and S. Morel-Precetti. 2003. Currently used non-specific extracellular MR contrast media. Eur Radiol 13(12):2688-98.
27. ACR guidance Document for Safe MR Practices:2007.ARJ:188,June 2007.