ELSEVIER
Journal of Cystic Fibrosis 11 (2012) 93 – 99
Journal of Cystic Fibrosis
www.elsevier.com/locate/jcf

Original Article

CT of the paranasal sinuses is not a valid indicator for sinus surgery in CF patients

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Received 2 August 2011; received in revised form 16 September 2011; accepted 26 September 2011
Available online 20 October 2011

Abstract

Background: No guidelines comprise when or to what extent sinus surgery should be done in patients with cystic fibrosis (CF) or how a CT scan of the paranasal sinuses should influence the decision. Symptoms of rhinosinusitis and/or eradication of pathogenic bacteria from the sinuses are reasons for sinus surgery.
Methods: In this observational cross sectional study, 55 CF cases had their preoperative CT scans scored according to the Lund Mackay- and the Nair-system. Correlations between the CT scans, symptoms, surgical findings and cultures obtained during sinus surgery were made.
Results: There was no significant correlation between the CT score and detection of pus, pathogenic bacteria or symptoms. Pus and pathogenic bacteria were found in several cases without sinus opacification on the CT scan. Non pathogenic and sterile cultures were also found in sinuses with opacification.
Conclusions: A CT scan is not a valid criterion for sinus surgery in CF patients.

Keywords: Rhinosinusitis; Sinus surgery; CT scan; Nair score; Cystic fibrosis; Bacteriology

1. Introduction

Nasal and sinus mucosal disease are by definition present in patients with cystic fibrosis (CF) because of defective CFTR-channels in the sinonasal mucosa, as found in the lower CF airways [1]. Apart from viscous mucus, common findings are nasal congestion, polyposis, mucoceles, mucopurulent material, medial bulging of the maxillary walls, ostitis and aplasia of the paranasal sinuses especially of the frontal sinus [2,3] Abnormal anatomy increases the risk of complications during sinus surgery. Magnetic resonance imaging (MRI) or CT scans can visualise the anatomy, alterations in the patency and the opacification of the sinuses [3–6]. A CT scan or MRI is mandatory prior to sinus surgery in CF patients but show limitations in predicting outcome of the surgery in non-CF patients [1,7]. The Lund Mackay scoring system is commonly used when describing CT scans of the paranasal sinuses [1,8]. The Nair scoring system can also be used but differs from the Lund Mackay by including the amount of opacification in the score [9].

According to the European Position Paper on Rhinosinusitis and Nasal Polyposis (EPOS) sinus surgery is indicated in non-CF patients with chronic rhinosinusitis (CRS) after failure of medical treatment [1]. Medical treatment is the primary therapy in CF patients with symptoms of CRS as well, but no guidelines exist comprising criteria for sinus surgery in CF patients if medical treatment is unsuccessful [1,10]. In 2007 we changed our sinonasal treatment strategy for CF patients towards offering Computer-Assisted Functional Endoscopic Sinus Surgery (CAS FESS) as a supplementary tool to diagnose and attempting to eradicate putative bacterial sinus infections. This was done

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1569-1993/$ - see front matter © 2011 European Cystic Fibrosis Society. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.jcf.2011.09.009

since the influence of bacterial sinusitis on CF-lung infections was gradually recognised [11]. The preoperative CT scans were used for pre-surgical planning and guidance, but not as a criterion for FESS, which is in contrast to the role of CT in non-CF patients, in whom CT findings of the sinuses correlates with the severity of CRS [12] and represents one of the criteria in setting the CRS-diagnosis [1]. CF patients show less correlation between the radiological findings and symptoms compared with non-CF CRS patients [13].

We investigated the correlation between CT scans, CRS symptoms, surgical findings and cultured materials collected during sinus surgery in CF patients, in order to determine whether CT scans should be included as a criterion for sinus surgery in CF patients.

2. Materials and methods

2.1. Patients

Patients from CF-centre Copenhagen, with a CF-diagnosis based on characteristic clinical features, abnormal sweat electrolytes and genotype, who underwent sinus surgery during the period of January 2007 to February 2010 were eligible to this observational, cross sectional study. Only patients with a CT scan of the paranasal sinuses performed less than 3 months prior to surgery were included. If patients had revision surgery, each surgery counted as one case. Patients were prioritised for CAS FESS based on the following three criteria ranked according to importance:

1 Intermittently lung colonised patients with a prolonged declining lung function, despite intensive antibiotic-chemotherapy, and/or increasing antibodies against Gram-negative bacteria. Especially patients with an unknown focus and increasing antibodies against *Pseudomonas aeruginosa, Achromobacter xylosoxidans* or *Burkholderia cepacia complex* were given priority.
2 Patients who have had lung transplantation were offered surgery within the first year following the transplantation.
3 Patients with severe symptoms of CRS in accordance with the EPOS guidelines.

Current treatments with corticosteroids or immunosuppressive agents (PO 6 weeks and IV 1 week prior to the CT scan) were registered since these factors are known to influence the mucosal lining in the sinuses. Treatment with topical corticosteroids was not registered. According to lung bacteriology and precipitating antibodies (normal values 0–1) [14], the patients were categorised as intermittently colonised or chronically infected with Gram-negative bacteria at the time of surgery [14,15]. The overall treatment strategy at the CF Centre Copenhagen is described in detail elsewhere [16,17].

2.2. CT scans

CT scans were performed in supine position. Slice thickness: 0.5–2.0 mm. No contrast was given. The CT scans were used for pre-surgical planning and as image guidance during surgery. The CT scans were retrospectively reviewed and assessed according to the Lund Mackay and the Nair systems [8,9].

The Lund Mackay system grades each sinus with either 0: no opacification, 1: some opacification or 2: total opacification. The Nair system grades each sinus with either 0: no opacification, 1: less than 25% opacification, 2: between 25% and 50% opacification or 3: more than 50% opacification. The Lund Mackay system also differs from the Nair system by distinguishing between the anterior and the posterior ethmoid sinuses. Both scoring systems have a range of 0–24 as the Nair system does not score the osteomeatal complex.

2.3. Surgical procedures

Patients were anaesthetised using total intravenous anaesthesia. No local disinfectants were used in the nose. Three experienced surgeons performed the operations. The purpose was to create ventilation and drainage pathways for the sinuses allowing postoperative instrumental and medical irrigations. The principle of the surgical procedure was performed as a classical FESS comprising an uncinectomy, an anterior ethmoidectomy and a medial antrostomy enlarging the natural maxillary ostium. The opened sinuses where explored and cultured leaving an enlarged ostium accessible for drainage and ventilation. The operation was finished on one side before operating on the other side, to avoid bacterial contamination from one nasal cavity to the other. Each patient was thoroughly evaluated with regards to their CT scan, symptoms, and clinical examination; based on these findings the decision regarding the extension of the surgery, covering a putative concha bulosa, the posterior ethmoids, the sphenoid and the frontal sinuses or if septum deviations were to be corrected, was made.

To optimise culture results multiple samples were prioritised including nasal secretions, pus, mucosal tissue, polyps, and bone. These samples were collected with sharp instruments or by suction. Following the surgical procedure the nasal cavities were irrigated with saline and colistin.

The surgical findings in each sinus were categorised in four groups according to the surgeons' descriptions. 1: unknown, the sinus was not opened; 2: the sinus was not developed; 3: macroscopically purulent material was described; 4: no macroscopically purulent material was described.

2.4. Microbiological samples

The material from the operation was immediately cultured in the microbiology laboratory. Gram-stained smears and aerobic cultures on selective media were performed on all samples. These media include a Sabouraud plate, a 7% NaCl plate, a *B. cepacia* plate containing colistin and gentamicin, a "blue plate" (modified Conradi Drigalski's medium) selective for Gram-negative rods and non-selective media including 5% Danish blood agar and chocolate agar (State Serum Institute, Copenhagen, Denmark). Isolated bacteria were identified as previously described [18]. Direct plating of tissue samples and pus on a 14 cm blood agar plate with discs containing

anti-pseudomonas antibiotics are used for primary susceptibility testing (Rosco® Neosensitabs) [18].

We divided the culture-results from each sinus into four groups: 1) "no culture" where no samples were obtained; 2) "pathogenic growth" containing bacteria or fungus from the sinuses that are considered pathogenic for CF patients comprising *P. aeruginosa*, *A. xylosoxidans, Burkholderia multivorans, Stenotrophomonas maltophilia, Staphylococcus aureus, Bordetella bronchiseptica, Haemophilus influenzae* and Aspergillus species; 3) "non pathogenic growth" containing organisms that are not likely to serve as a reservoir and causing CF lung infections comprising *Escherichia coli, Enterobacter cloacae, Candida albicans* and Coagulase negative staphylococci; 4) "no growth after culture".

2.5. Symptom score

From 2009, it has become standard for all CF patients to presurgical complete a validated questionnaire about symptoms and social/emotional consequences of their rhinosinusitis scoring from 0 to a maximum of 110 points (SNOT-22) [19]. No additional systemic antibiotic or steroid treatments were given in relation to surgery, which could have influenced the symptom scores.

2.6. Data and statistics

The data were processed blinded; the radiologist who staged the CT scans had no access to the patient files or to the results from the cultured samples. The laboratory technician who cultured the sinus material had no knowledge of the CT scans or the surgical findings. The physician who noted the operative findings according to the patient files had no access to the CT scans or to the results of the cultured material. After the data were processed, the findings of the CT scans were compared with the operative findings and the outcome of the cultured samples. The statistics were made in SAS 9.1.3. Since especially the Nair scoring results do not follow a normal distribution (Fig. 1A), the inter-quartile range (IQR) was used to describe the spread, although mean values were used to evaluate the correlation between CT scores and bacteriology. The correlation

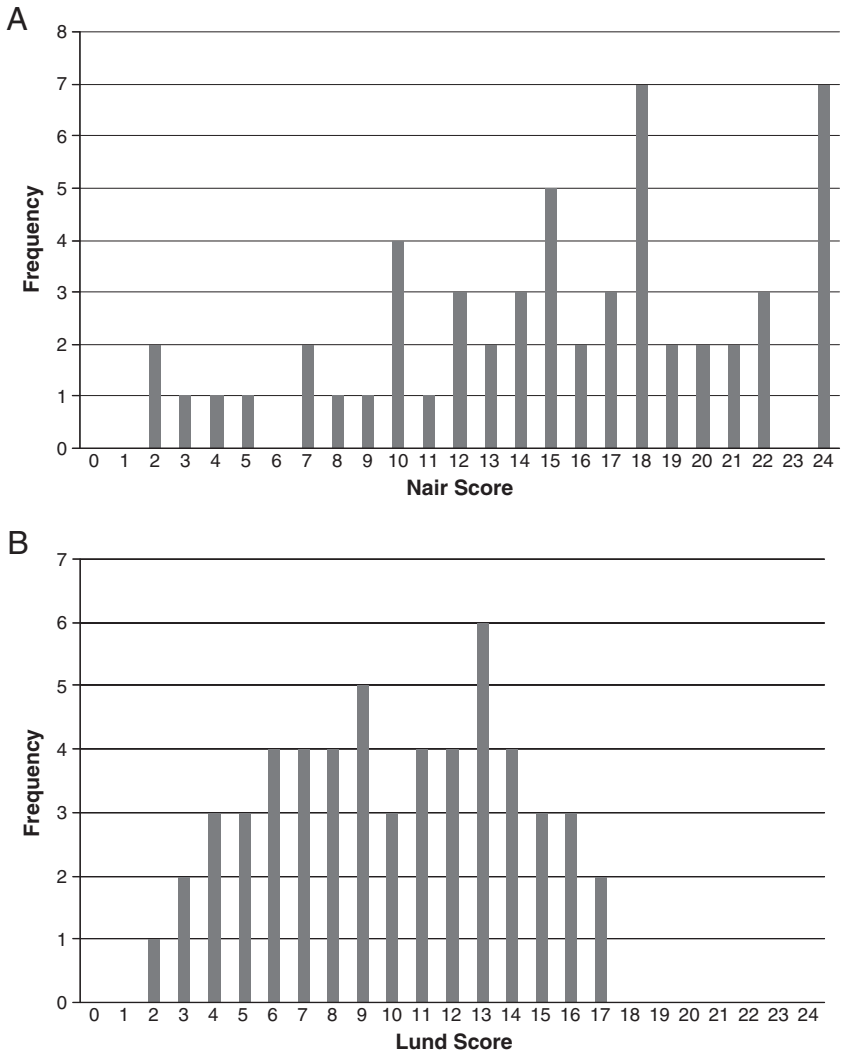

Fig. 1. A: The opacification according to the Nair staging. B: The opacification according to the Lund Mackay staging.

between the CT scores and the SNOT-22 was evaluated by simple linear regression.

3. Results

3.1. Patients

Eighty-five cases of sinus surgery on CF patients were performed. Forty-eight patients were CT scanned within 3 months prior to surgery and seven of these patients underwent surgery twice, leaving a total of 55 cases in the study. Fifteen patients were chronically lung infected (ten with *P. aeruginosa*, three with *A. xylosoxidans* and three with *B. multivorans*) and 33 patients were intermittently colonised with Gram-negative bacteria (the vast majority with *P. aeruginosa)*. Only one of the seven patients who were operated on twice was chronically infected. The male–female rate was 20/28 and 27 cases (50%) were below 18 years of age (range 6–46 years). Thirty-two patients were dF508 homozygous, 15 patients were dF508 heterozygous and one patient was homozygous for L619S.

Twelve cases received medication with potential influence on the opacification seen on the CT scan; eight cases had corticosteroids and four cases received IV treatment with corticosteroids. Two cases received immunosuppressive agents prior to the CT scan, one in addition to IV steroid treatment and one in addition to oral steroids. Forty cases underwent surgery according to the primary criterion (see above), and eight cases according to the second criterion. Overall, 38 of the 55 cases had symptoms of CRS according to the SNOT-22 score. Seven cases only had surgery due to symptoms (criterion 3) with no hope of improving their lung function (chronically lung infected or not infected with pathogenic bacteria).

3.2. CT scans

The median period of time between the CT scan and sinus surgery was 20 days (IQR: 8 to 42 days). The median Lund Mackay score was 10 (IQR: 7–13) compared with a median Nair score of 16 (IQR: 11–20). The variability of the distribution of the CT scores according to Nair and Lund Mackay are illustrated in Fig. 1.

3.3. Surgical findings

Three hundred seventy-eight out of 544 possible sinuses (69%) were opened and pus was noticed in 191 of them (51%). As seen in Table 1 the majority of the maxillary and ethmoid sinuses were explored. Polyps were found in 30 out of the 55 cases (55%). Six out of the seven revision cases had polyps. In 50% of these cases the patients were less than 18 years old. Frontal sinus aplasia was noted in 4 cases and sphenoid sinus aplasia was noted in 2 cases.

Table 1
The distribution of macroscopically pus found in the different sinuses.

	Unknown no. (%)	Pus no. (%)	No pus no. (%)	Total
Maxillaries	1 (0.9)	85 (77.3)	24 (21.8)	110
Ethmoids	28 (12.7)	80 (36.4)	112 (50.9)	220
Frontals	67 (60.9)	11 (10.0)	28 (25.5)	106
Sphenoids	70 (63.6)	15 (13.6)	23 (20.9)	108
Total	166 (30.2)	191 (34.7)	187 (34.0)	544

Table 2
The culture results distributed on the different sinuses.

	No culture no. (%)	Pathogenic growth no. (%)	Non-pathogenic growth no. (%)	No growth no. (%)	Total
Maxillaries	6 (5.5)	67 (60.9)	33 (30.0)	4 (3.6)	110
Ethmoids	84 (38.2)	90 (40.9)	32 (14.5)	14 (6.4)	220
Frontals	91 (85.8)	11 (10.0)	3 (2.7)	1 (0.9)	106
Sphenoids	97 (89.8)	7 (6.4)	3 (2.7)	1 (0.9)	108
Total	278 (51.1)	175 (31.8)	71 (12.9)	20 (3.6)	544

3.4. Microbiological samples

Material from 266 out of 544 possible sinuses (49%) was cultured and pathogenic growth was found in 175 sinuses (66%). The distribution of the cultures is shown in Table 2. Twenty sinuses in six patients were sterile. In five of these six patients other sinuses showed bacteria. Overall, 45 out of the 55 cases (82%) had growth of pathogenic bacteria from one or more of their sinuses, nine cases (16%) had only non-pathogenic cultures from their sinuses and one case had no growth in all cultured sinuses.

P. aeruginosa was cultured from 27 cases (49%) representing 60% of the pathogenic cases (Table 3). These cases had a median Nair score of 17 (IQR: 12–20) and a median Lund Mackay score of 9.5 (IQR: 7–13). The remaining 28 cases without *P. aeruginosa* had a median Nair score of 15 (IQR: 10–19) and a median Lund Mackay score of 11 (IQR: 6–13). The single case with all sterile sinuses had a Nair score of 10 and 7 by the Lund Mackay. The 10 cases without pathogenic growth had a median Nair score of 14 (IQR: 10–18) and a median Lund Mackay score of 8.5 (IQR: 6–14), whereas the 45 cases with pathogenic growth had a median Nair score of 16 (IQR: 12–20) and a median Lund Mackay score of 10 (IQR:

Table 3
A list of all pathogenic (pat.) and non-pathogenic (non-pat.) micro-organisms found at surgery and in how many, out of the 55 cases, they were found. It should be noted that 27 out of 55 cases had *P. aeruginosa* and that the data are cumulative since one case can host more than one microorganism.

Bacteria	Number of cases
Pseudomonas aeruginosa (pat.)	27
Achromobacter xylosoxidans (pat.)	7
Burkholderia multivorans (pat.)	2
Stenotrophomonas maltophilia (pat.)	8
Staphylococcus aureus (pat.)	12
Bordetella bronchiseptica (pat.)	1
Aspergillus (pat.)	2
Haemophilus influenza (pat.)	7
Escherichia coli (non-pat.)	1
Enterobacter cloacae (non-pat.)	1
Candida albicans (non-pat.)	2
Coagulase negative staphylococci (non-pat.)	39

7–13). The distribution of the Nair- and Lund Mackay scores in relation to the bacteriology is shown in Fig. 2. The CT scores are higher in the group with pathogenic growth than in the groups without pathogenic growth and sterile cultures (Nair 81% higher and Lund Mackay 19% higher). However, this was not statistical significant in either of the grading systems. Notably, several sinuses with pathogenic growth had little or no opacification.

The presence of pus in the sinuses was correlated with the Nair score. Pus was found in 20% of the sinuses with a Nair score of 0 or 1 and in 63% of the sinuses with a Nair score of 2 or 3. The relative risk (RR) of finding pus during surgery in a sinus with a Nair score of 0–1 compared to a sinus with a Nair score of 2–3 is 0.3 and the relative risk (RR) for no pus in a sinus with a Nair score of 2–3 is 0.7. No correlation was found between the presence of pus and the bacteriology (OR = 1.0 and RR = 1.0).

3.5. Symptom score

All patients who underwent surgery from June 2009 to February 2010 (28/55) completed the SNOT-22. The mean score was 22 (range 1–49). Both Nair and Lund Mackay score had a positive slope of 0.5 indicating that the grade of opacification correlates with a high symptom score but were not significant (Nair: $P = 0.37$, Lund Mackay: $P = 0.56$).

4. Discussion

We present the largest published case series of CF patients who underwent sinus surgery with focus on eradicating pathogen bacteria. They all fulfilled a suggested Lund Mackay score [12] and the EPOS criteria for having CRS [1], which do not deal with the matter of bacteria in the sinuses. The high CT scores reflect that most CF patients have a significant

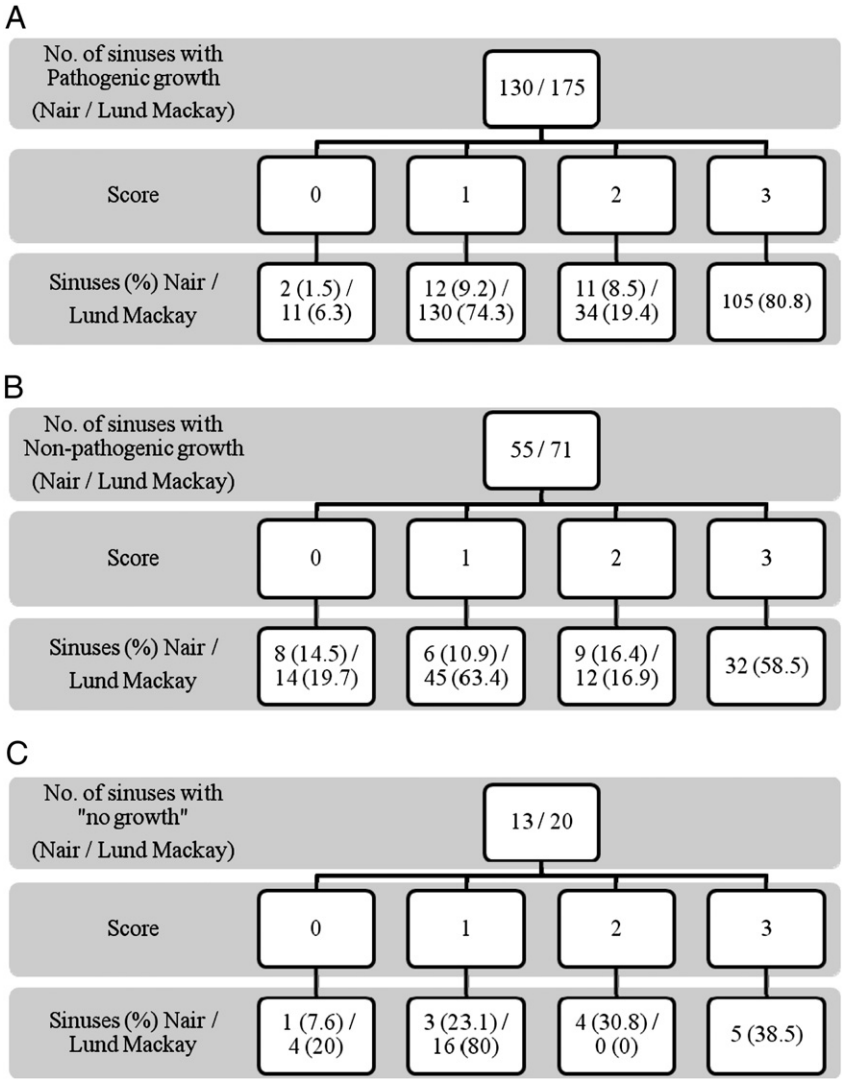

Fig. 2. A: Nair and Lund Mackay staging of the sinuses correlated to the pathogenic growth. Nair staging cumulates the anterior and posterior ethmoids and does not comprise the osteomeatal complex which is why this system operates with fewer sinuses. B: Nair and Lund Mackay staging of the sinuses correlated to the nonpathogenic growth. C: Nair and Lund Mackay staging of the sinuses correlated to no growth after culture.

opacification of their sinuses compared with non CF patients. This is explained by their diffuse inflammatory sinus disease with mucosal oedema [13], secretions captured in the sinuses, sinus polyps and pus from pathogenic or non-pathogenic bacteria. Diagnostic imaging is mandatory prior to surgery because of the varying anatomy in CF patients, and our results show that the Nair scoring system offers a better and more nuanced evaluation of this by grading the opacification. As expected, CT scans with highly opacified sinuses were associated with clinical signs of infection (pus), presence of pathogenic bacteria and CRS symptoms but far from significant because of the variability of the data, thus giving CT scans low specificity. Interestingly, we found that nearly all CF patients had bacteria in their sinuses and several sinuses with pathogenic bacteria without radiological or clinical signs of inflammation. We suspect that this percentage is actually higher since sinuses with pus are more likely to be explored and cultured. As in the lungs, it is difficult to distinguish between thick CF mucus and pus, which could be the reason for the cases with negative cultures in spite of described pus.

In non CF patients it is known that opacified sinuses do not necessarily reflect sinus disease [20], but it is unknown, especially in CF patients, whether sinus disease can be present despite a normal CT scan. The immune response in the CF-sinuses is reduced and they can thereby serve as a reservoir for pathogenic bacteria, promote their adaptation, and maintain the deleterious lung infections [11]. Consequently, we believe that sinus surgery in the future will be more focused on eradicating bacteria from the sinuses [2,11,21–27]. Thus, the decision of setting CF-patients up for sinus surgery should be a collaboration between physicians specialised in CF, microbiologists and ENT specialists. Our results indicate that this decision should be made without placing great emphasis on the CT scan, making repeated CT scans redundant. An endoscopic guided culture from the middle meatus can be taken being in concordance with sinus aspirates in 86% of adults with CRS [21] and 83% among children with acute rhinosinusitis [28].

Similarly, the surgeons should create drainage and culture thoroughly from the sinuses unaffected by the CT scan, since these results influence the post-operative antibiotic treatment. A CT scan is the most commonly used tool for pre-surgical planning. MRI does not use ionising radiation and can differentiate between infectious material and thickened mucosa and should therefore be kept in mind as an alternative tool to CT scans [6].

We used the SNOT-22 questionnaire, which is the most common way to objectively quantify CRS symptoms, being aware that some symptoms (e.g. cough) are influenced by other conditions than CRS and that CF patients are known to underreport symptoms of CRS [21].

The guidelines [1] do not recommend a maximum period between the CT scan of the paranasal sinuses and sinus surgery in CF or non-CF patients with CRS. Optimally, the CT scan should have been performed just prior to surgery. Especially the fluctuation of the antibiotic therapy and the corticosteroid treatment alters the clinical and radiological findings over time. We accepted to include patients who were scanned less than 3 months prior to surgery comprising a median period of time of 20 days between the CT scan and the surgery reflecting our present waiting period for a non-acute CT-scan.

The paranasal sinuses are normally sterile, but a review study estimated that only 2.9–23.5% of CF patients have sterile sinuses [1]. Compared with these studies our data are based on a larger case series and we had a thorough method of collecting samples identifying bacteria which is why our results of bacterial sinusitis contribute to the literature.

Guidelines describing how or when to eradicate *P. aeruginosa* from CF-sinuses are non-existing, neither with surgery nor with medical treatment [1,10]. We encourage, that such guidelines are established and included in the EPOS and that the role of CT and MRI should be addressed.

5. Conclusion

No significant correlation between CT scans and CRS-symptoms, clinical findings or bacteria could be shown in a large CF-cohort because of the large variability of these data. CT scans with low scores do not exclude pathogenic bacteria; thus CT is only required for pre-surgical planning because of the low specificity.

Acknowledgements

We would like to thank the nurses at the CF centre (especially Majbritt Presfeldt) and the laboratory technicians at the Department of Clinical Microbiology (Katja Bloksted and Ulla Jacobsen) for their dedication to this project. The work was thankfully supported by The Candys Foundation.

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