Recalcitrant chronic rhinosinusitis. Difficulties in diagnosis and treatment
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Fever is not a symptom of chronic rhinosinusitis

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CHAPTER 2.1

ABSTRACT

Introduction
In the chronic rhinosinusitis (CRS) definition of the RhinoSinusitis Task Force (RSTF) of the American Academy of Otolaryngology-Head and Neck Surgery, fever is one of the minor symptoms. In the EP3OS definition, fever is not mentioned as a contributing factor. The main aim of this study was to evaluate the role of fever in CRS.

Patients and methods
Patients with CRS, scheduled for surgery were compared with a control group consisting of patients without CRS, suffering from esthetic complaints or obstruction of the nose. Temperature prior to surgery was measured and analysed.

Results
In both groups, hundred patients were included. In the CRS group the mean temperature was 36.94°C, with a maximum of 37.8°C. The control group revealed a mean temperature of 36.87°C. Analysis demonstrated no significant difference between the mean temperatures of the CRS patients and the controls (p=0.306). Additional analysis, correcting for possible confounders, did not reveal significant differences between both groups either.

Discussion
There have been several attempts to define CRS in the past, but an all including definition or classification system for this disorder does not currently exist. Fever is a factor under discussion. We found no significant difference between the preoperative body temperature in CRS patients and controls. These results suggest that fever is not a relevant symptom in CRS.
INTRODUCTION

Chronic RhinoSinusitis (CRS) does not seem to be one single disease, but may cover a spectrum of conditions with widely varying severities. In addition to host characteristics, including anatomical variations, allergy, ciliary dysfunction, and IgG subclass deficiencies, external factors like pollution, fungi, viruses, and bacteria all seem to play a role in the pathogenesis of CRS. This diversity of factors, make CRS hard to define. The purpose of a definition is to provide a more uniform diagnosis of CRS. This could make communication between physicians easier, improve therapy, and standardize disease for further research.1,2

To develop a working definition for CRS, the RhinoSinusitis Task Force (RSTF) of the American Academy of Otolaryngology-Head and Neck Surgery formulated a set of major and minor criteria in 1997.1 Major criteria included facial pain/pressure, facial congestion/fullness, nasal obstruction/blockage, nasal discharge/purulence, altered sense of smell, purulence in the nasal cavity on examination and fever (acute rhinosinusitis only). Minor factors were headache, (nonacute) fever, halitosis, fatigue, dental pain, cough, and ear pain/pressure/fullness. Minor criteria are not per se less troublesome to the patient than major criteria.1,3

In Europe, the most recent definition of CRS in the latest version of EP3OS included: inflammation of the nose and paranasal sinuses for more than 12 weeks with either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip) combined with facial pain/pressure and/or reduction of smell.4 In this definition fever is not mentioned as a contributing factor.

In our clinical experience, fever is not observed frequently in patients with CRS. There are, however reports that CRS could be a cause of unexplained prolonged fever.5,6 Triggered by the difference in CRS-defin itions, our clinical experience, and above all the lack of reports in literature on the role of fever in CRS, we started this evaluation.

PATIENTS AND METHODS

Patients
At the department of Otorhinolaryngology of our tertiary care institution we prospectively collected temperature data in CRS patients and control subjects. Patients with CRS according to the EP3OS-criteria, scheduled for surgery (Endoscopic Sinus Surgery (ESS), Denker procedure, Draf III procedure), were identified. Surgery was indicated in these patients because CRS symptoms and nasal endoscopic findings did not improve despite of optimal medical treatment. On the day of hospital admission, complaints like feeling of fullness and headache, as well as purulent rhinorrhea and congestive mucosa were present in the majority of patients. Exclusion criteria for the CRS group were: inverted papilloma, mucocele, or osteoma, as primary reason for surgery in the CRS patients. The control group consisted of patients without CRS, suffering from esthetic complaints or obstruction of the nose. Control subjects were also planned for nasal surgery (rhinoplasty, septoplasty, turbinectomy). Additional exclusion criteria in both groups were: use of
analgetics (Paracetamol or NSAIDs) on the day of admission; use of systemic steroids or antibiotics within 1 month before surgery.

**Temperature measurement**
Temperature was measured routinely before administration of medication by a nurse at the start of the hospital admission. Nurses were not aware of this investigation and were consequently blinded for patient grouping. Temperature was measured in both groups with the same First Temp Genius® 3000A Infrared Ear Thermometer (Sherwood Medical Netherlands B.V.). Patient characteristics like sex and age, as well as comorbidity factors, including the occurrence of asthma and allergy were extracted from the patient’s file. In most cases, asthma was diagnosed and treated by a pulmonologist. In all patients a skin prick test was performed in the past to evaluate allergy. Concurrent medication use, for example nasal and pulmonal steroid use, was also assessed.

**Statistical analysis**
Data of both groups were recorded and calculated in SPSS, version 15.0.1, and GraphPad Prism, version 4. Statistical analysis included T-tests and multivariable analysis.

**RESULTS**
In both groups, hundred patients were included. Patient characteristics are shown in Table 1. In the CRS group the mean temperature was 36.94°C (range, 36.0°C to 37.8°C; SD=0.46). The control group revealed a mean temperature of 36.87°C (range 35.9°C to 38.4°C; SD=0.50). All measured temperatures are plotted in a scatterplot (see Figure 1). No CRS patient demonstrated a body temperature above 37.8°C. An independent samples T-test was performed and confirmed that there was no significant difference in body temperature between the CRS and the control group (p=0.306).
Table 1. Patient Characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CRS</th>
<th>Control</th>
</tr>
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<tbody>
<tr>
<td>Number</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Male-female ratio</td>
<td>59:41</td>
<td>51:49</td>
</tr>
<tr>
<td>Age</td>
<td>47 years</td>
<td>37 years</td>
</tr>
<tr>
<td></td>
<td>(range, 15 to 73yr)</td>
<td>(range, 13 to 68yr)</td>
</tr>
<tr>
<td>CRS</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Nasal polyposis</td>
<td>54</td>
<td>0</td>
</tr>
<tr>
<td>Allergy</td>
<td>29</td>
<td>29</td>
</tr>
<tr>
<td>Asthma</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td>Samter’s triad</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Smoking</td>
<td>22</td>
<td>32</td>
</tr>
</tbody>
</table>

Concurrent medication:
- Nasal steroid: 51 (CRS) vs 9 (Control)
- Pulmonal steroid: 33 (CRS) vs 5 (Control)

Frequent use (not on day of admission):
- Paracetamol: 5 (CRS) vs 0 (Control)
- NSAIDs: 7 (CRS) vs 0 (Control)

Recent course (>1 month before):
- Systemic steroid: 11 (CRS) vs 0 (Control)
- Antibiotic: 13 (CRS) vs 2 (Control)

Figure 1. Temperatures of patients with CRS versus healthy controls.

![Figure 1](image-url)
Subgroup analysis on nasal polyps, asthma, allergy, and Samter’s triad, did not show any significant differences between the groups with or without the comorbidity compared to controls. Smoking did not have an impact on temperature outcome either. A factor more likely to influence body temperature was concurrent medication use. Six types of medication were evaluated: nasal and pulmonary steroid use, which was allowed during this study; Paracetamol and NSAID use (not allowed on the day of temperature measurement); regular systemic steroids and antibiotics (not allowed within 1 month before measurement). Multivariable analysis correcting for these possible confounders, did not reveal significant differences in body temperature between the CRS patients and the control group. Results are demonstrated in Table 2 showing the calculated p-values of concurrent medication use.

Table 2. Influence of concurrent medication.

<table>
<thead>
<tr>
<th>Bivariable analysis</th>
<th>coefficient</th>
<th>p-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS or control</td>
<td>0.070</td>
<td>0.306</td>
<td>-0.064</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Multivariable analysis</th>
<th>coefficient</th>
<th>p-value</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRS or control</td>
<td>0.033</td>
<td>0.686</td>
<td>-0.130</td>
</tr>
<tr>
<td>Nasal steroids</td>
<td>-0.056</td>
<td>0.543</td>
<td>-0.235</td>
</tr>
<tr>
<td>Pulmonal steroids</td>
<td>0.092</td>
<td>0.370</td>
<td>-0.109</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>0.105</td>
<td>0.645</td>
<td>-0.346</td>
</tr>
<tr>
<td>NSAID</td>
<td>0.196</td>
<td>0.314</td>
<td>-0.187</td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>0.001</td>
<td>0.994</td>
<td>-0.317</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>0.114</td>
<td>0.416</td>
<td>-0.162</td>
</tr>
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</table>

DISCUSSION

CRS is a prevalent disease with a great economic burden. There have been several attempts to define CRS in the past but an all-including definition or classification system for this disorder does not currently exist. Fever as a symptom of CRS is a factor under discussion. The prevalence of fever in patients suffering from CRS has been studied very rarely. Orlandi et al. demonstrated in their investigated cohort of patients undergoing surgery for CRS, a prevalence of 8.8%. Ling et al. reported a fever-incidence of less than 3.2% in patients scheduled for ESS. In this short evaluation we found no body temperature higher than 37.8°C in the patients requiring surgery for advanced CRS (see Figure 1). No significant difference was found between the preoperative temperature in patients with CRS and control patients. Additional analysis correcting for possible confounders (comorbidity, concurrent medication), did not reveal significant differences between both groups. Possible explanations for some of these expected findings can be given. Recorded analgetics have an estimated half time of 1-4 hours and were not administered on the day of hospital admission. This makes influence on the temperature
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measurement unlikely. Systemic steroids and antibiotics were not used within 1 month before surgery, implying no substantial impact on body temperature. Considering the number of included patients and controls, this study has the ability to detect a mean temperature difference of at least 0.17°C with 80% power (and p=0.05) between the groups. The hypothesis that CRS and control patients have a similar temperature can be confirmed without making a type II error within 0.17°C at p=0.05. A suggestion for future research could be the collection of nasal cultures to objectively prove the existence of an active paranasal inflammation or exacerbation. This could reveal interesting results and can strengthen conclusions. At our centre nasal cultures were not performed routinely.

Besides the demonstration that in the present population no difference in body temperature was found between CRS patients and controls, this article is intended to increase awareness under otorhinolaryngologists as well as primary care physicians that fever does not seem to be a relevant symptom in CRS. According to Chester et al., we suggest that the use of fever as a RSTF-criterion should perhaps be re-evaluated.

ACKNOWLEDGMENTS

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REFERENCE LIST