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Functional Endoscopic Sinus Surgery Improves Sinus-Related Symptoms and Quality of Life in Children With Chronic Rhinosinusitis: A Systematic Analysis and Meta-Analysis of Published Interventional Studies

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Abstract

Aim. To assess the current knowledge and evaluate the quality of evidence in the use of FESS for the treatment of chronic rhinosinusitis in children, regarding the respective changes in the quality-of-their-life (QoL) and the outcome that follows the operation. *Materials/Methods.* Systematic literature review in Medline and other database sources and meta-analysis of pooled data. *Results*. 15 studies were systematically analyzed. Four represented Level II, five Level III, and six Level IV evidence. The total number of treated patients was 1301. Thirteen research groups reported that pediatric FESS is an effective treatment for chronic rhinosinusitis; the respective positive outcome ranged between 71 and 100% of operated children. Five studies concluded that this treatment modality is associated with significant improvement in the children's postoperative QoL. Systemic diseases and environmental factors may have unfavourable prognostic effects; cystic fibrosis is associated with at least 50% recurrence rate. The rate of major complications following pediatric FESS is 0.6%, and the respective rate of minor complications 2%. *Conclusion*. The surgical management in children with chronic rhinosinusitis, despite the reservations expressed by many clinicians, is effective when optimal medical treatment proves unsuccessful (grade B strength of recommendation), and is associated with improvement in the children's QoL (grade B strength of recommendation). FESS also improves the sinusitis-associated symptoms and QoL in children with cystic fibrosis (grade C strength of recommendation. Most complications of pediatric FESS reported in the literature are minor, and associated with difficulties in the postoperative assessment and care of pediatric patients.

Keywords

chronic rhinosinusitis, rhinitis, nasal polyposis, cystic fibrosis, children, FESS, quality of life

Introduction

Acute and subacute rhinitis in young children and rhinosinusitis in older children are common diseases in childhood, with symptoms and signs that may vary significantly from child to child. These conditions are usually easily curable, sometimes even without treatment, although relapses are frequent. On the contrary, chronic rhinosinusitis may cause significant morbidity to children, and affect their everyday quality of life.

The European Position Paper on Rhinosinusitis and Nasal Polyps has defined chronic rhinosinusitis in children as the presence of 2 or more symptoms, one of which should be either nasal blockage/obstruction/congestion or nasal discharge (anterior/posterior nasal drip), with or without facial pain/pressure, or cough for at least 12 weeks, in an effort to achieve a wider consensus regarding this condition.[1] We should also take into account that chronic rhinosinusitis is usually considered as a single disease entity, irrespective of the presence of nasal polyps.

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Table 1. Levels of Evidence Regarding the Primary Research Question in Studies That Investigate the Results of a Treatment (http://www.cebm.net/index.aspx?o=1025).

Category of Evidence	Study Design
Level I	• High-quality randomized trial with statistically significant difference, or no statistically significant difference but narrow confidence intervals
	• Systematic review of Level I randomized control trials (and study results were homogenous)
Level II	• Lesser quality randomized control trial (eg, <80% follow-up, no blinding, or improper randomization)
	• Prospective comparative study
	• Systematic review of Level II studies or Level I studies with inconsistent results
Level III	• Case–control study
	• Retrospective comparative study
	• Systematic review of Level III studies
Level IV	• Case series
Level V	• Expert opinion

Table 2. Strength of Recommendation by Category of Evidence for Guideline Development[13].

Strength of Recommendation	Category of Evidence
A	Directly based on Category I evidence
B	Directly based on Category II evidence or extrapolated recommendation from Category I evidence
C	Directly based on Category III evidence or extrapolated recommendation from Category I or II evidence
D	Directly based on Category IV evidence or extrapolated recommendation from Category I, II or III evidence

With regard to nasal polyposis, it is less frequent in children compared to adults, with the exception of cystic fibrosis–related polyposis.[2] In addition, 52% of children with nasal polyps have a positive family history indicating the implication of hereditary and genetic factors.[3] Other conditions that may have a relation with chronic rhinosinusitis in children are allergy,[4-8] immune deficiency,[4,6] primary ciliary dyskinesia,[4,6] and gastroesophageal reflux.[9]

Medical therapy is the mainstay of treatment in pediatric rhinosinusitis, taking also into account the aforementioned parameters. However, the outcome has a wide variation and chronic rhinosinusitis may have a serious impact on children's quality of life, and their respective health status. Hence, many assessment tools have been developed in an effort to estimate the burden of pediatric chronic rhinosinusitis from a public health perspective.[10-12]

In cases resistant to medical treatment, surgery has been proposed as an alternative method of management. However, and despite the wide use of functional endoscopic sinus surgery (FESS) in adults, pediatric FESS is not routinely performed, and most ENT surgeons are very cautious in recommending such treatment.

The aim of the present study was to review the current knowledge and assess the quality of evidence on the use of FESS for the treatment of chronic rhinosinusitis with or without nasal polyposis in children, with regard to the respective changes in the quality of their life and the outcome that follows the operation.

Materials and Methods

An extensive search of the literature was performed in Medline and other available database sources until December 2012, having the following as primary endpoints: (*a*) to assess the clinical effectiveness of FESS in the treatment of pediatric chronic rhinosinusitis and (*b*) to determine the impact of FESS in the children's quality of life.

During the search the keywords "FESS," "pediatric," "children," "nasal," "sinus," "rhinosinusitis," "polyp," "cystic fibrosis," and "quality-of-life" were used. The keywords "FESS," "pediatric," and "rhinosinusitis" were considered primary and were either combined to each of the other keywords individually or used in groups of three. Reference lists from the retrieved articles were also manually searched.

Thirty-one related studies were found and analyzed. The retrieved studies were critically appraised, according to evidence-based guidelines for the categorization of medical studies (Tables 1-3).[2,6,10-23] Language restrictions

Table 3. Overview of Pediatric FESS Studies.

Authors	Study Type	Level of Evidence	Number of Patients	Mean Age (Years)	Mean Follow-Up (Months)	Comorbidity	Remarks
Siedek et al (2009)[2]	Retrospective	IV	115	12	≥60	Asthma cystic fibrosis	(*a*) Adolescents who have started or continued active smoking postoperatively demonstrate a worse outcome (*b*) CF, asthma, and a high graded CT scan are negative prognostic factors of outcome after FESS
Rudnick and Mitchell (2007)[10]	Prospective comparative	II	22	6.1	≥6	Asthma	(*a*) The emotional impact of chronic rhinosinusitis cannot be underestimated, and FESS has significant and positive impact on the child and family (*b*) There are long-term improvements in the quality-of-life of children after FESS
Chang et al (2004)[14]	Retrospective	IV	101	14.5	27.2	None	(*a*) Pediatric FESS should be limited; the concept of "the same procedure in a smaller patient" is not entirely accurate (*b*) Second-look operations may be necessary when there is strong clinical suspicion of recurrence during postoperative wound debridement, in the presence of diffuse preoperative sinonasal polyposis, and in revision cases with extensive disease
Ramadan (2004)[15]	Retrospective comparative	III	119	6.2 ± 2.8	NR	Asthma allergy	(*a*) Asthma, age, and cigarette exposure are significant parameters of success after FESS (*b*) When a decision to proceed with FESS is made, an adenoidectomy should also be performed (*c*) Children younger than 6, low CT score, and nonasthmatics may only require an adenoidectomy
Cunningham et al (2000)[11]	Prospective observational	II	21	10.2 ± 3.5	NR	None	(*a*) Children with chronic rhinosinusitis warranting surgical treatment have a significant chronic illness (*b*) There are appreciable differences in parent versus child reporting of general health concepts in chronic rhinosinusitis, highlighting the importance of acquiring both perspectives
Hebert and Bent (1998)[16]	Retrospective comparative	III	50	NR[b]	NR	Asthma	FESS is an effective and safe procedure for the treatment of chronic sinusitis which is refractory to the appropriate medical therapy
Triglia and Nicollas (1997)[17]	Retrospective comparative	III	41	NR[b]	44.4	Asthma cystic fibrosis	(*a*) The great majority of patients experience a radical change in their lives after sinus surgery (*b*) Surgical management of nasal polyps reduces the need for ABx therapy in CF patients (*c*) Sinus surgery greatly alleviated pulmonary symptoms in patients with asthma
Younis and Lazar (1996)[18]	Retrospective comparative	III	500	NR[b]	≥12	Asthma allergy immune-deficiency cystic fibrosis immotile cilia syndrome	(*a*) CF patients have 100% improvement of their sinusitis symptoms postoperatively (*b*) 83% of operated CF children require a revision 3-5 years after the first operation (*c*) Passive smoking has significantly worse outcome than patients from smoke-free environments (*d*) Postoperative granulation, synechiae, active infection, or polypoid disease are predictors of poorer outcome
Rosenfeld (1995)[12]	Prospective comparative	II	18	8[a]	12	None	(*a*) There is an 85% to 100% chance of at least improving all major symptoms, but only a 15% to 60% chance of cure (*b*) FESS should be performed with caution when families define a successful outcome as complete resolution of all major symptoms (*c*) There are mutually dependent conditions as reasonable criteria for pediatric FESS
Stankiewicz (1995)[19]	Retrospective	IV	77	NR[b]	42	Asthma allergy immune-deficiency cystic fibrosis	(*a*) 44% of children required second-look operations because of the inability to debride or cleanse the nose postoperatively (*b*) FESS is an effective tool for treating medical failure sinusitis (*c*) The real benefit of FESS is that children have fewer infections postoperatively, and are able to clear the infection either on their own or with ABx
Wolf et al (1994)[6]	Retrospective	IV	124	12	NR	Asthma allergy immune-deficiency cystic fibrosis	(*a*) Sinusitis requiring surgery may develop in the older pediatric age group (*b*) Headache and behavioral disturbances may be more frequent in children with chronic recurrent sinusitis than previously assumed

(continued)

Table 3. (continued)

Authors	Study Type	Level of Evidence	Number of Patients	Mean Age (Years)	Mean Follow-Up (Months)	Comorbidity	Remarks
Bolt et al (1995)[20]	Retrospective	IV	21	13.4	29	Asthma cystic fibrosis	(*a*) Subjective results in children with nasal polyposis are good (*b*) Recurrences occurred less frequently after primary operations than in children with previous polypectomies (*c*) Revisions in pediatric nasal polyposis tend to perform worse than primary operations
Parsons and Phillips (1993)[21]	Retrospective comparative	III	52	7.4	21.8	Asthma allergy immune-deficiency cystic fibrosis	(*a*) sinusitis-associated behavioral problems demonstrate significant improvement postoperatively (*b*) FESS is not effective for allergy-associated symptoms (*c*) There is a positive rate of improvement in asthmatic symptomatology following FESS
Jones et al (1993)[22]	Retrospective	IV	9[c]	10 ± 6	29	Cystic fibrosis[d]	There was a positive change in the frequency of nasal congestion, purulent nasal discharge, and postnasal drainage postoperatively, positively affecting the patients' physical comfort and general well-being
Lusk and Muntz (1990)[23]	Prospective comparative	II	31	6.6	≥12	Asthma allergy immune-deficiency cystic fibrosis	(*a*) The vast majority of patients noted significant symptom improvement (*b*) No patient experienced worsening of his/her symptoms (*c*) 71% of parents felt that their children were essentially normal (*d*) Functional endoscopic ethmoidectomy can be safely performed in children

Abbreviations: FESS, functional endoscopic sinus surgery; CF, cystic fibrosis; CT, computed tomography; ABx, antibiotics; NR, not reported.
[a]Median value.
[b]The study population comprises pediatric patients.
[c]Eight children were excluded to avoid double-counting.
[d]Only cystic fibrosis children were included.

limited the included literature into English-speaking articles. Twenty studies continued to meet the defined criteria and were further analyzed.

In addition, the clinical effectiveness and impact regarding the quality of life of pediatric FESS in special subpopulations of children with chronic rhinosinusitis (ie, cystic fibrosis) was also assessed.

Results

Among the 20 eligible studies, 2 had been incorporated in a larger patient series by the same principle author and were not included in the analysis of pooled data in order to avoid double-counting.[24,25] The same exclusion process was followed with regard to another study, the pediatric FESS population of which had also been incorporated in a larger patient series by the same authors.[26] Another study primarily included adult patients[27]; in the absence of clear-cut data referring to pediatric patients, this study was also excluded from the analysis of pooled data. Finally, one study exclusively referred to extensive endoscopic sinus surgery and not FESS, and was further excluded to avoid sample heterogeneity.[28] Two further studies included 8 overlapping children operated at the same center, by the same author.[21,22] However, both studies were included in the analysis of pooled data, as we were able to identify the overlaps and avoid double-counting of the operations.

Overall, 4 prospective, 5 retrospective comparative, and 6 retrospective studies were systematically analyzed. Four studies represented Level II, 5 studies Level III, and 6 studies Level IV evidence (Table 1). The total number of treated patients was 1301; an underlying systematic disease (ie, cystic fibrosis, ciliary dyskinesia, immune deficiency) was reported in 155 patients.

All the 13 research groups that had assessed the effectiveness of pediatric FESS concluded that FESS is an effective treatment for chronic rhinosinusitis in children. Among the analyzed studies, 3 represented Level II, 4 Level III, and 6 Level IV evidence. The reported positive outcome ranged between 71% and 100% of operated children. In addition, 5 studies concluded that FESS is associated with significant improvement in the children's postoperative quality of life. Two of the analyzed studies represented Level II, 1 study Level III, and 2 studies Level IV evidence.

Pediatric FESS seems to be less effective in the presence of a systematic underlying disease, and revision operations are usually necessary. Although the respective recurrence rates were not properly recorded in the majority of studies, pooled data for a subpopulation of 36 children with cystic fibrosis revealed that 18 of them required at least 1 revision operation (50% recurrence rate). Furthermore, 8 research groups studied the clinical effectiveness of FESS in children with cystic fibrosis. Among these studies, 1 represented Level II, 2 Level III,

Table 4. Complications of Pediatric FESS.

Complications	
Severity	Type
Major	Bleed (n = 5)
	CSF leak (n = 1)
	Meningitis (n = 2)
Minor	Lamina papyracea breach (n = 2)
	Orbital chymosis/surgical emphysema (n = 4)
	Bleed (n = 7)
	Meatal scarring/adhesions/synechiae (n = 13)

Abbreviation: CSF, cerebrospinal fluid.

and 5 Level IV evidence. Moreover, 3 studies assessed the impact of FESS on the quality of life of this specific subpopulation of children. One study represented Level III and 2 studies Level IV evidence. FESS in children with cystic fibrosis was found to improve both their sinusitis symptoms and their quality of life, albeit for a more limited time period compared to otherwise healthy children in most cases.

The majority of treated patients were followed-up for over 1 year. The incidence of major complications was 0.6%. The rest of the reported complications were minor and are summarized in Table 4.

Discussion

In the era of endoscopy and imaging, it became clear that rhinitis and adenoid hypertrophy are not the only reasons of a runny nose in children, as in the majority of cases the sinuses are involved as well. Indeed, van der Veken et al showed that 64% of children with a history of chronic purulent rhinorrhea and nasal obstruction demonstrate sinus involvement in the computed tomography scan.[29] It is therefore obvious that rhinosinusitis, a common problem in children, is often overlooked. Moreover, the presentation of chronic pediatric rhinosinusitis may be extremely variable, often making accurate diagnosis very difficult.[30] On the other hand, as children may not be able to describe reliably their exact symptoms, parents may cling to the diagnosis of sinusitis as the source of all symptoms and problems.[23]

Irrespective of the difficulties in diagnosis, chronic rhinosinusitis may indeed have a serious impact on children's quality of life and their respective health status. Therefore, timely and appropriate management is of great importance.

It is widely agreed that the optimal management of chronic rhinosinusitis includes 2 to 6 weeks of adequate antibiotics with treatment of any concomitant disease. Nevertheless, in cases of chronic rhinosinusitis with frequent exacerbations that persist despite optimal medical management (and after systemic disease has been excluded), FESS can be a reasonable alternative to continuous medical treatment.[4] Demographic parameters, environmental factors, and comorbidities may also warrant an adenoidectomy in these children at the time of the endoscopic procedure (ie, age greater than 6, asthma, cigarette smoke exposure[15]). There are also absolute indications for pediatric FESS: (*a*) complete nasal obstruction in cystic fibrosis due to massive polyposis or due to medialization of the lateral nasal wall, (*b*) orbital abscess, (*c*) intracranial complications, (*d*) antrochoanal polyp, (*e*) mucocoele/mucopyocoele, and (*f*) fungal rhinosinusitis.[4]

Whereas little debate exists regarding the latter indications, the surgical management of chronic rhinosinusitis, which persists despite optimal medical management, can be a controversial issue. Already established beliefs in pediatric textbooks that "in chronic sinusitis every effort should be made to avoid operative procedures,"[31] the potential intraoperative complications of endoscopic surgery, along with a fear about the impact of this type of surgery on the growing facial structures supported in part by animal experiments,[32] represent some of the sources of concern.

The present study, taking into account the results of more than 1000 patients and applying strict inclusion criteria, demonstrated that pediatric FESS is an effective treatment in chronic rhinosinusitis, with a reported positive outcome ranging between 71% and 100% of operated children. The uniform nature of the reported results, along with the quality of the studies performed, allow us to adopt a grade B strength of recommendation regarding the effectiveness of FESS in the treatment of chronic rhinosinusitis when optimal medical management proves unsuccessful and strict selection criteria are applied (Table 3).

It should also be mentioned that children with chronic rhinosinusitis warranting surgical treatment have a significant chronic illness.[11] The nasal congestion, the purulent nasal discharge, the postnasal drainage, and the recurring headache inevitably affect the children's physical and emotional well-being and thus their quality of life. Based on the quality of studies, which reported that children with sinonasal disease experience an improvement in their quality of life after surgical intervention, the strength of the respective recommendation can be graded as B. However, quality of life issues are often very complicated. On the one hand, quality of life data are as important as objective parameters measuring positive outcome and can be used in conjunction with these parameters and computed tomography findings to set criteria for medical or surgical treatment.[11] On the other hand, appreciable differences between parental and child reporting do exist[11] and need to be taken into

consideration by the physician, depending on whether the parent or child is primarily interviewed. That being said, it has been suggested that children older than 8 years of age can accurately report on subjective issues.[33] Hence, although parents may serve as proxy reporters for the children both pre- and postoperatively, under the notion that they may have a better understanding of the condition that is being treated, the real issue is not to determine who the optimal respondent is but to develop assessment tools that can make use of the valuable information from both sources, in order to estimate the burden of pediatric chronic rhinosinusitis and the outcome of a surgical intervention. This will further enhance the related research and give us a better insight into the problems that children with chronic rhinosinusitis face.

Systemic diseases, immunodeficiencies, but also modifiable factors, such as gastroesophageal reflux disease, urban pollution, smoking, and passive smoking, may have unfavorable prognostic effects.[2,18] Unfortunately, the presence of these factors was not uniformly recorded in our study population. Nevertheless, it seems that cystic fibrosis is associated with a 50% recurrence rate of nasal polyps, whereas rates as high as 100% have also been reported.[18] It was therefore deemed important to assess the impact of FESS in cystic fibrosis children with nasal polyps in the present meta-analysis. The association of cystic fibrosis with nasal polyps in children was first reported by Lurie,[34] but its importance has been reiterated by other authors.[35,36] Our meta-analysis showed that FESS in these children improves both their sinusitis symptoms and their quality of life, albeit for a more limited time period compared to otherwise healthy children (not exceeding 3 to 5 years according to Younis and Lazar[18]). Despite the uniform nature of the aforementioned results, the quality of the related studies, and the lack of a specific suggestion about the clinical effectiveness of FESS in the only Level II study within this group of studies, allows us to adopt a grade C strength in the respective recommendations.

In addition to the expected clinical effectiveness of pediatric FESS, and the improvement of the children's quality of life, appropriate preoperative informed consent requires that the patient and parents are aware of the potential risks that can be associated with this specific type of surgery. Regarding the concerns about the potential impact of endoscopic surgery on facial growth, a quantitative anthropomorphic analysis using 12 standard facial measurements as well as a qualitative facial analysis conducted by Bothwell et al showed no statistical significance in facial growth between children who had undergone FESS surgery and those who had not after a mean follow-up period of 13.2 years.[37] In addition, despite the relative underdevelopment of the pediatric sinuses, and the proximity of the operated areas to noble structures (ie, orbit, optic nerve anterior cranial fossa), pediatric FESS can be overall considered as a safe procedure. The rate of major complications identified in the present meta-analysis of 1301was 0.6%, none of which proved fatal, or irreversible. Moreover, the respective rate of minor complications did not exceed 2%; some of these complications are associated with difficulties in the postoperative assessment and care of pediatric patients (Table 4).

It is worth mentioning, however, that the concept of "the same procedure in a smaller patient" for pediatric FESS is not exactly correct. A more liberal use of FESS in children without strict inclusion criteria, or without respecting the limitations related to the patient and/or the surgeon, may increase morbidity; this should be taken into account before deciding the surgical management of children with chronic rhinosinusitis.

Conclusions

The results of the present study suggest that surgical management in children with chronic rhinosinusitis, despite the reservations expressed by many clinicians, is effective when optimal medical treatment proves unsuccessful (grade B strength of recommendation) and when strict criteria are followed. It is also associated with improvement in the children's quality of life (grade B strength of recommendation).

Systemic diseases, immunodeficiencies, and other factors may have an unfavorable effect on the outcome. Nevertheless, FESS improves both the sinusitis-associated symptoms and the quality of life in children with cystic fibrosis (grade C strength of recommendation), although recurrence rates in the associated polyposis is high.

Most complications of pediatric FESS reported in the literature are minor and are associated with difficulties in the postoperative assessment and care of pediatric patients. However, extreme caution and strict inclusion criteria by experienced surgeons should be the rule in the surgical management of pediatric rhinosinusitis.

Authors' Notes

Drs Vlastarakos and Fetta have equally contributed to the preparation of this article.

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