



Management of Pediatric Chronic Rhinosinusitis

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Abstract

Purpose of Review Chronic pediatric rhinosinusitis is a common entity, with an annual incidence of 4% in the US schoolchildren's population. The predominant contributing factor in younger children is adenoid pathology and in older children, allergic rhinitis. Recent research on sinus microbiome, biofilm, inflammatory response, and therapeutic alternatives is providing new insights in this prevalent disease.

Recent Findings Adenoid size does not correlate with the severity of the disease suggesting that it is due to the biofilms observed in both adenoiditis and hypertrophic adenoids. There is new consensus among the experts on the definition and clinical diagnosis of pediatric chronic rhinosinusitis (PCRS). In PCRS, inflammation is mediated by helper T lymphocyte type 2 with limited glandular hyperplasia or fibrosis observed histologically. Both innate and adaptive immunity contribute to the heterogeneous inflammatory pathogenesis of PCRS that is driven by genetic, environmental, and microbiome factors. Medical treatment includes nasal hygiene, anti-inflammatory, and antibiotic therapy. When medical treatment fails, adenoidectomy is the surgical treatment of choice in children less than 6 years old, adenoidectomy plus possible endoscopic endonasal surgery (EES) between ages 6 and 12, and EES for children 12 and older. Balloon sinuplasty has been reported to be effective between 70 and 80% in older children.

Summary This review focuses on the most recent PCRS consensus statements, novel research in histopathology and microbiome, and the evolving medical and surgical therapeutic options for this challenging disease.

Introduction

Rhinosinusitis (RS) is an inflammatory sinus pathology very common in children. In the pediatric population, approximately 5–13% of the upper respiratory tract infections evolve to acute rhinosinusitis (ARS) and a proportion of these progresses to pediatric chronic rhinosinusitis (PCRS) [1•, 2•].

Chronic rhinosinusitis (CRS) is reported in 12% of the general US population [3••, 4]. Gilani et al. report that school-age children with PCRS account for 2.1% of the outpatient visits in the USA, but some authors

consider that this incidence is under reported. Patients between the ages 10 and 15 are the most affected by this pathology [5•].

Allergic rhinitis, asthma (57.3%), and gastroesophageal reflux (28.2%) are the prevailing comorbidities in PCRS [6].

Adenoid hypertrophy and adenoiditis are often associated as a predisposing factor of PCRS and confirms that the medical and surgical therapy aimed at the adenoids is effective on the treatment of PCRS [7•].

Definition

Pediatric Rhinosinusitis (PRS)

Rhinosinusitis, defined as inflammation of the nose and paranasal sinuses, is characterized by two or more symptoms, one of which must be blockage/obstruction/nasal congestion or runny nose (post-nasal drip), associated or not to facial pressure/pain. There is good agreement between the European position paper on rhinosinusitis and nasal polyps (EPOS) [8••] and the AAO-HNS clinical consensus statement on pediatric chronic rhinosinusitis [9••] regarding definition, diagnosis, and classification. Depending on the duration of the symptoms, PRS is classified as acute or chronic.

Acute rhinosinusitis (ARS) in children is defined as the sudden onset of two or more of the following symptoms: nasal obstruction or congestion, discolored nasal discharge, and cough which are present for less than 12 weeks [8••, 9••].

Chronic Rhinosinusitis (CRS)

It is defined as the process with a duration greater than 90 continuous days of two or more symptoms of nasal obstruction or congestion, nasal discharge, facial pressure/pain, cough with endoscopic signs of mucosal edema, purulent discharge, and/or changes in CT in children and adolescents under 18 years of age [8••, 9••].

In a survey of 144 patients with PCRS, the predominant symptoms were: congestion (95.2%), cough (79.8%), rhinorrhea (60.6%), headache (48.1%), and fatigue (40.4%) [6].

The classification in phenotypes and endotypes of CRS is intended to optimize the indications of medical and surgical treatment. Clinical parameters are used to classify by phenotype, while molecular and cellular parameters are used in endotype classification. Currently most studies are done in adults and then standardize the classification in children [2•, 10, 11•, 12].

Contributing Factors

PCRS could be caused by different triggering factors [13].

Both innate and adaptive immunity contribute to the heterogeneous inflammatory pathogenesis of PCRS that is driven by genetic, environmental, and microbiome factors [14].

PCRS may start as an upper respiratory infection that progresses to chronic disease in 13% of these patients [3••, 9••]. Heath et al.'s hypothesis is that recurrent sinus infections are responsible for inflammatory changes, causing obstruction of the outflow pathways, compromised mucociliary function, thick mucus, and decreased ventilation of the sinuses [13].

Adenoiditis and adenoid hypertrophy are the most common predisposing factors for PCRS development in young children. Adenoid size does not correlate with the severity of the disease suggesting that it is due to the reservoir of bacteria in the adenoids, evidenced by the biofilms observed in both adenoiditis and hypertrophic adenoids [1•, 8••, 9••, 15••].

The most common predisposing factor in adolescents is allergic rhinitis, which presents between 26 and 29% of patients with PCRS [13, 16].

Children with asthma and PCRS manifest a different inflammatory response, which needs special medical and surgical treatment to achieve good results. In these patients, it has been shown that improving CRS also improves asthma [15••].

Gastroesophageal reflux has been suggested as a predisposing factor. Bachert et al. state that acid reaching the nasopharynx can lead to inflammation of the sinonasal mucosa and obstruction of the ostium [2•]. There is no convincing evidence to support this association [9••, 15••].

Cystic fibrosis is an autosomal recessive genetic disease associated with a high incidence of PCRS with nasal polyps [2•]. Immotile ciliary syndrome is a rare cause of PCRS.

Immunodeficiencies due to B cell defects have been associated to PCRS [2•] including IgG subclass immunodeficiencies, selective IgA deficiency, hypogammaglobulinemia, and agammaglobulinemia.

Other contributing factors are immaturity of the immune system, biofilm, anatomical abnormalities, or blockage [8••]; environmental pollution [17]; daycare attendance [18]; and passive and active smoking [19].

Histopathological Differences Between PCRS and Adult CRS

In PCRS, maxillary sinus biopsies had a higher density of submucosal lymphocytes, lower density of submucosal eosinophils, thinner and more intact epithelium, thinner basement membranes, and fewer submucosal glands [20]. The inflammatory mechanism is mediated by the T lymphocyte helper type 2. In adults with CRS with nasal polyps, the predominant infiltration is eosinophilic with marked glandular hyperplasia, increased epithelial detachment and extensive fibrosis, and mediated inflammation by eosinophils [21].

In children, two forms of PCRS may coexist: transient that is usually observed in children under 13 years of age and the other intended to evolve to persistent, adult-like PCRS, more common in those over 13 years of age [21].

Sinus Microbiome

The microbiology concepts in CRS in adults progressed from individual bacterial involvement to factors such as biofilm development, intracellular bacteria, and

changes in the microbiome [22]. Lactobacillales were found to be defensive against the progression to CRS although this has not been supported in all studies [23].

Recent bacteriologic studies showed the presence of alpha hemolytic *Streptococcus* as the most common species followed by *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, and anaerobes in 8% of surgical specimens. Both *H. influenzae* and *S. pneumoniae* species showed increased resistance [15••, 24].

Diagnosis

As described above, the diagnosis of PCRS is based on the persistence of symptoms for more than 12 weeks along with inflammatory signs by CT scan and/or endoscopic findings [8••, 9••].

CT scan has a good sensitivity and specificity when Lund-Mackay scores are equal or higher than 5 [8••, 9••, 25–27, 28••].

CT scan is indicated in the diagnosis of PCRS when there is [11•, 25, 29] little or no response to medical treatment (severe illness), suspected intracranial or ophthalmologic complications, suspected tumor, or previous sinus surgery.

Nasal endoscopy provides direct visualization of meatal purulent drainage, mucosal edema, nasal polyps, and/or adenoid pathology (hyperplasia or infection) [28••]. When nasal endoscopy is not feasible or not available, soft tissue lateral X-ray is an option to evaluate adenoid size [11•].

Sinus aspiration and cultures are recommended in certain cases that do not respond to medical treatment or in patients with immunodeficiencies, complications, or nosocomial infections [2•].

Allergic rhinitis: The association between allergic rhinitis and the development of PCRS is controversial [15••]. While some studies show association, others have not shown significant association at all [8••, 9••]. Allergies may be a contributing factor in CRS in older children [30].

Cystic fibrosis [13, 31, 32] allergic fungal sinusitis [13, 33] and aspirin-exacerbated respiratory disease [13, 34] have a high prevalence of nasal polyps, but in general, PCRS has a lower prevalence of nasal polyps when compared with adults [21].

Immunologic deficiencies have been implicated in the pathogenesis of rhinosinusitis; however, the prevalence of immunologic disease in pediatric rhinosinusitis is poorly defined. High-yield testing in pediatric rhinosinusitis should include titers to polysaccharide antigens, specifically *Streptococcus pneumoniae* and *H. influenzae* [35•].

Medical Treatment of Pediatric Chronic Rhinosinusitis

The treatment of PCRS is based on nasal hygiene control of mucosal edema and directed antibiotic therapy [15••].

Medical treatment is considered first-line in the management of PCRS [7•, 8••, 9••] which is achieved by relieving the obstruction, fluidifying mucus, improving the mucociliary clearance, permeating the outflow of the sinuses [11•, 29, 36] and eradicating pathogens [37, 38].

Appropriate medical therapy is the combination and duration of treatment. The first line of medical therapy includes intranasal corticosteroids (INCS) used daily, saline irrigation [3••, 8••, 9••, 11•, 15••, 28••, 39•] and antibiotics for 3 weeks [3••, 9••, 11•, 15••, 28••, 39•]. Systemic corticosteroids and antibiotics for the treatment of PCRS have been shown to be effective in improving symptoms and radiographic findings in double blinded, randomized prospective studies [40].

Nasal Saline Irrigation

It is hypothesized to function by thinning mucous, improving mucociliary clearance, decreasing edema, and reducing antigen load in the nasal and sinus cavities [6, 41, 42, 43•]. A Cochrane review of eight RCT, three of which were done in children, showed evidence that nasal saline irrigations as a single therapy was advantageous in PCRS [44].

A randomized prospective double-blind-study of forty PCRS patients compared daily saline irrigations to saline plus gentamicin for 6 weeks [41]. It showed statistically significant improvement in both groups but no differences between them.

Low concentration hypochlorous nasal irrigation was compared to normal saline irrigations in PCRS. This randomized prospective study showed that the total symptom score improved significantly in both groups with no differences between them. [45]

Parents-children compliance with nasal irrigations has been reported at 64% [46]. Compliant patients showed a 73% improvement in their symptoms and endoscopic findings requiring surgery in only 16.3% of the cases.

The most recent consensus statements and Cochrane Review recommend the use of nasal saline irrigations for PCRS based on a preponderance of lower level evidence [42, 43•]. There is no benefit in adding antibiotics to the nasal saline irrigation. [8••, 9••].

Intranasal Corticosteroids

Although there is no sufficient evidence that proves the effectiveness of INCS in PCRS, their efficacy in adults with CRS and in children with allergic rhinitis supports the recommendation to include them as first-line therapy in PCRS [8••].

In intranasal allergen challenges, INCS have a strong anti-inflammatory effect by downmodulating cytokine release and inflammatory cells recruitment [47].

Fokkens et al. showed that budesonide was significantly more effective than placebo in treating perennial allergic rhinitis in children [48].

Maspero et al. demonstrated that fluticasone furoate was effective in treating perennial allergic rhinitis in children 2 to 11 years old when compared with placebo [49].

Reports on the efficacy of INCS such as fluticasone and mometasone are conflicting. However, they are still recommended as first-line therapy to decrease inflammation and their low risk profile [8••, 9••, 15••, 28••].

In the American Society of Pediatric Otolaryngology survey of appropriate medical therapy in PCRS, 96% of the respondents used INCS, 93% nasal saline irrigations, and 91% utilized oral antibiotics [26].

In a Latin American survey of Pediatric Otolaryngologists, 100% of the respondents used INCS, antibiotics, and saline nasal irrigations and 30% used oral corticosteroids [11•].

Antibiotic Therapy

The use of antibiotics in PCRS is indicated only in acute exacerbations being the antibiotic of choice amoxicillin/clavulanic acid (90–120 mg/kg/day BID) [11•, 15••, 29, 50], which is intended to treat polymicrobial and beta-lactamase infections. Other alternatives are second-generation (cefuroxime) and third-generation (cefdinir and cefixime) cephalosporins. In case of allergy to penicillin and cephalosporins, the alternative antibiotics are macrolides or clindamycin [15••].

There is insufficient evidence regarding the appropriate length of antibiotic treatment. EPOS 2020 does not recommend a precise length of treatment, while the AAOHNSF consensus statement recommends 20 days over 10 days of antibiotic therapy [8••, 9••].

A case control PCRS study by Shin et al. looked at the predictors of response to treatment after a 12-week trial of antibiotics. They concluded that allergic patients with elevated IgE levels and high eosinophils in serum were statistically significantly higher in the non-responder cohort [51].

The use of oral or intravenous antibiotics in PCRS is not recommended by the EPOS 2020 due to the lack of supportive evidence [8••], and the AAO-HNS Clinical Consensus Statement on PCRS does not recommend the use of topical antimicrobials [9••].

Randomized prospective studies are needed to support the use of nasal decongestants or antihistamines in PCRS [15••]. Novel therapeutic possibilities for the management of eosinophilic inflammation include biologics targeting IgE, IL-5, and IL-4, but these options need to be studied in the pediatric population [13]. Table 1.

Surgical Indications

Most children with PCRS respond to medical treatment that includes nasal hygiene and topical and oral medications. Consideration for surgical intervention is made after failed appropriate medical therapy [15••]. Surgical options are age-dependent and anatomy-dependent.

Table 1. PCRS medical therapy: levels of evidence

Medical therapy	Study summary	Level Of Evidence
Intranasal corticosteroids	First-line therapy to decrease inflammation and treat allergies [8••]	5: Expert opinion without explicit critical appraisal
Nasal saline irrigations	Effective first-line treatment in PCRS [6, 8••]	2b: Individual cohort studies
Oral/Intravenous Antibiotics	Only in acute rhinosinusitis. No evidence to support its use in PCRS [8••]	1b: Individual cohort studies
Systemic steroids	Effective in conjunction with antibiotics [8••, 40]	1b: Individual cohort studies

PCRS in children 6 years of age and younger is effectively managed with adenoidectomy alone and could be considered up to age 12. However, there is not enough evidence to treat PCRS with adenoidectomy in children age 12 or older [8••, 9••].

The AAO-HNS consensus found strong evidence in surgical indications for PCRS according to age group [1•, 9••, 11•]. Under 6 years old, the consensus recommends adenoidectomy; 6 to 12 years old, adenoidectomy and probable EES; and over 12 years old, the most highly probable procedure recommended is EES.

Adenoidectomy

Adenoidectomy is effective in children under 6 years of age and serves as a mechanical degradation of pathogenic organisms that infect the sinuses. Adenoiditis, whether hypertrophic or hypotrophic, functions as a bacterial reservoir, where biofilm is evident in 97% of cases [2•, 8••, 9••, 52, 53]. Adenoidectomy alone is successful in the surgical treatment of PCRS in 61% of the children and improves to 88% when combined with maxillary sinus lavage [54].

Ramadan et al. [55•] showed that the inflammatory response in the upper airway mucosa of asthmatic children with CRS is similar but is more severe compared with that of non-asthmatic children with CRS. This observation may provide the basis that asthmatic children are at risk for worse surgical outcomes after sinus surgery and/or adenoidectomy compared with non-asthmatic children [56]. The non-asthmatic PCRS group who underwent adenoidectomy alone had a success rate of 43%, while those children who were asthmatic and had PCRS had a success rate of 28% [57].

A meta-analysis of 8 studies [58] showed that adenoidectomy significantly improved PCRS symptoms with a 69.3% subjective success rate.

A prospective study of 37 patients with adenoid hypertrophy and PCRS showed that adenoidectomy was beneficial in younger children as a surgical option before EES [59]. Another prospective cohort study demonstrated that additional antibiotic therapy and adenoidectomy should be considered before EES, even in non-obstructing adenoids [60].

Endoscopic Endonasal Surgery

Endoscopic Endonasal Surgery (EES) aims to expand obstructed ostia to improve ventilation and drainage of the paranasal sinuses and topical therapy delivery. EES is indicated in children over the age of 12 or when adenoidectomy fails in the 6 to 12 age group [8••, 9•, 11•, 61, 62•].

Pre-op CT scan allows for the assessment of sinus anatomy and risk areas. It is also necessary when computer image guidance is used in revision cases or polyposis where the anatomy is distorted [9••, 63].

In a 10-year follow-up retrospective age-matched outcome study, Lusk et al. [64] concluded that patients who underwent EES resulted in a greater relief of nasal obstruction and purulent discharge, as well as higher parent satisfaction when compared with medical management alone.

In a meta-analysis of pooled data of 1301 children in 15 studies, Vlastarakos et al. [65] demonstrated that EES had a success rate between 71 and 100% with significant improvement in quality of life and a major complication rate of 0.6%.

A meta-analysis of eight studies including 831 patients showed a “positive” outcome rate in 88.4% of the children with an average follow-up of 3.7 years, with a major complication rate of 0.6% [66].

Makary et al. published that EES in PCRS has an 82% success rate with complication rate of 1.4%. [67]. The most common complications of this surgery are bleeding and synechia [15••, 68]. Other less common complications observed are CSF fistula, intracranial infections, and orbital complications such as orbital hematoma [66, 69]. There is no evidence that EES produces delay in craniofacial growth [8••, 9•]. Unlike the adult population, postoperative debridement is not considered essential [15••].

A prospective study of 270 EES children and 273 healthy controls comparing SNOT-20 pre-op to 3- and 8-year post-op showed significant improvement in quality of life after EES [70].

A combined prospective/retrospective study of 44 pediatric EES found a significant improvement in the rhinosinusitis outcome measure quality of life after a 4-year follow-up [71].

A few studies have shown that in the majority of children without systemic conditions, a postoperative debridement under general anesthesia was not necessary in children [72].

A retrospective age-matched cohort outcome study of 67 children showed no detrimental effects in facial growth in children who underwent EES by quantitative anthropomorphic analyses [73].

Longitudinal review of eight pediatric patients treated with unilateral sinus surgery using volumetric computed tomography showed only minimal changes in facial volume measurements [74].

Balloon catheter sinuplasty (BCS)

Balloon catheter sinuplasty (BCS): It is a less invasive and safe technique for the pediatric population that expands the ostium of the sinuses with less distortion of the original anatomy and preservation of the mucosa [75•]. The 2014 AAO-HNS Clinical Consensus Statement on PCRS concluded that there was insufficient current evidence to compare balloon sinuplasty to EES for PCRS and did not reach consensus on the effectiveness of BCS [8••, 9••]. Subsequent research has reported its efficacy between 70 and 80%, associated with adenoidectomy or as a standalone procedure [1•, 76, 77]. Soler et al. conducted a prospective, multicenter, single-arm study of 50 children (2 to 21 years old) with CRS who had failed medical management. At 6-month follow-up, 92% improved by a minimal clinically important difference (MCID) of 1.0 or more in the SN-5 [77]. Ramadan et al. reviewed sinus balloon catheter dilation after adenoidectomy failure for children with chronic rhinosinusitis and reported a success rate of 81% [76]. Gerber et al. did a prospective, two-arm, randomized, and blinded trial of children ages 2 to 12 that underwent either BCS + adenoidectomy + maxillary sinus irrigation or adenoidectomy + maxillary sinus irrigation alone. The authors concluded that the addition of BCS did not provide additional QOL and sinonasal symptom improvement [79]. The EPOS 2020 steering group evaluated the most recently published literature and concluded that there is no convincing evidence to recommend balloon sinuplasty for the treatment of PCRS [8••]. Figure 1 and Table 2.

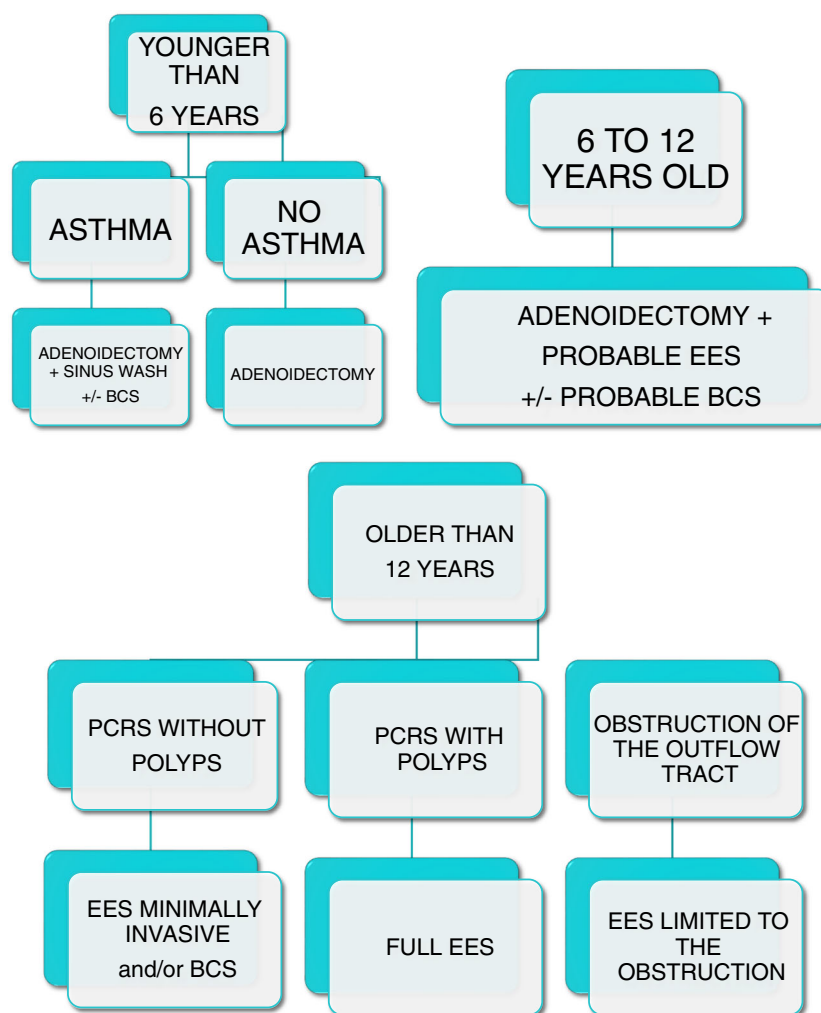


Fig. 1. Algorithm for the surgical treatment of PCRS by age. Published with permission from Manual de Otorrinolaringologia Pediátrica da IAPO [11•]

Table 2. PCRS surgical therapy: levels of evidence

Surgical treatment	Study summary	Level of evidence
Adenoidectomy alone	Effective in children under 6 [2•, 8••, 9••, 53, 54]	4: Case series
Balloon catheter sinuplasty	There is no convincing evidence to recommend balloon sinuplasty for the treatment of PCRS [8••, 78]	4: Case series
Endoscopic sinus surgery	Effective in PCRS after failure of adenoidectomy in older children not responsive to appropriate medical therapy [8••]	4: Case series

Conclusions

The 2.1% incidence of PCRS in school-age children is considered under reported. Its diagnosis is based on the persistence of symptoms for more than 12 weeks along with inflammatory signs by CT scan and/or endoscopic findings. Adenoid pathology is the most common predisposing factor in young children, and allergic rhinitis is the most common in older children.

The first line of treatment is INCS, nasal saline irrigations, and oral antibiotics.

When medical treatment fails, adenoidectomy is the procedure of choice in children under 6 years of age; adenoidectomy with probable EES or BCS in children 6 to 12; and EES in children 12 and above.

Compliance with Ethical Standard

Conflict of Interest

Pablo Stolovitzky reports personal fees from INTERSECTENT, personal fees from SPIROX/STRYKER, and personal fees from ACCLARENT outside the submitted work. Jacqueline Alvarado declares no conflict of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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