

# *Surgical Management of Pediatric Rhinosinusitis*

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## **Introduction**

Chronic rhinosinusitis is a common disease of childhood that can significantly impact quality of life<sup>1</sup>. The prevalence of pediatric rhinosinusitis is difficult to determine as children oftentimes have nonspecific upper respiratory symptoms. They can have up to 8 viral upper respiratory tract infections in a year and only 0.5% to 5% progress to acute rhinosinusitis<sup>2</sup>. An even smaller percentage of these cases go on to become chronic rhinosinusitis. Special considerations must be taken into account when managing chronic rhinosinusitis in children. The treatment paradigms used for adults do not necessarily apply to children. The objective of this paper is to review current trends in the surgical treatment of pediatric chronic rhinosinusitis.

## **Diagnosis**

The diagnosis of chronic rhinosinusitis is based on the presence of symptoms and clinical signs persisting for more than 12 weeks<sup>3</sup>. At least 2 symptoms such as nasal congestion, nasal discharge (anterior or posterior), facial pressure or pain, and cough should be present. Children are less likely to complain about headache although parents may report irritability or behavior problems. Symptoms of chronic rhinosinusitis should be accompanied by clinical signs on endoscopy such as nasal polyps, mucosal edema, or mucopurulent discharge or radiographic findings such as mucosal thickening and sinus opacification<sup>4</sup>. Differentiation from other common childhood nasal diseases such as allergic rhinitis, chronic adenoiditis, adenoid hypertrophy, and viral upper respiratory tract infections can be difficult due to the overlap of symptoms.

Plain film radiography such as Waters' view and/or Caldwell-Luc view may be helpful in diagnosing chronic rhinosinusitis but the findings can be very nonspecific<sup>5,6</sup>. Although computed tomography (CT) is the diagnostic modality of choice, it should be reserved for situations where sinus surgery is imminent, complications of sinusitis are suspected, or in atypical presentations<sup>7</sup>. Care should be taken to reduce radiation exposure and minimize the number of CT scans used in children. The decision to proceed with CT imaging should not be taken lightly as recent studies have demonstrated a link between childhood exposure to CT scan radiation and increased risk of developing malignancies such as leukemia and brain cancer<sup>8,9</sup>.

Additionally, incidental findings of abnormalities are often present on imaging in the absence of disease. Common anatomic abnormalities such as concha bullosa, paradoxical middle turbinate, and Haller cells do not necessarily correlate with sinusitis on a CT scan<sup>10</sup>. A mean Lund score of 2.81 in pediatric patients without evidence of chronic rhinosinusitis has been reported in the literature<sup>11</sup>.

A follow-up study by Bhattacharyya *et al.* recommended adopting a Lund score cutoff of 5 to represent true disease with a sensitivity and specificity of 86% and 85%<sup>12</sup>. CT imaging can be useful for surgical planning and diagnosis but should be used judiciously in the pediatric population.

### **Surgical Management**

Medical management is the primary treatment modality for pediatric chronic rhinosinusitis. **Surgery is reserved for refractory cases that have failed maximal medical therapy.** However, the concept of maximal medical therapy is not well defined and there are variations amongst practitioners. Medical therapy regimens typically include a combination of any of the following: oral antibiotic, oral steroid, nasal steroid spray, oral antihistamine, and nasal saline irrigations. Antibiotic therapy should be directed at the most common organisms such as alpha-hemolytic streptococci, *S. aureus*, *S. pneumoniae*, *H. influenza*, and *M. cattarrhalis*<sup>13-15</sup>. If symptoms persist after 3-6 weeks of medical management, surgical options should be considered<sup>16</sup>.

### **Adenoidectomy**

**Adenoidectomy is an effective first-line surgical option for chronic rhinosinusitis in children**<sup>17</sup>. A meta-analysis by Brietzke and Brigger concluded that adenoidectomy led to significant improvement in 69.3% of patients<sup>18</sup>. A more recent prospective interventional study by Bettadahalli and Chakravarti reported improvement in sinus and nasal quality of life in 88.3% of children ages 4 to 12 years old after adenoidectomy for refractory chronic rhinosinusitis<sup>19</sup>.

**Several lines of evidence suggest that bacterial biofilms on the adenoids are associated with chronic rhinosinusitis in children.** Electron microscopy studies of adenoid specimens obtained from children with chronic rhinosinusitis demonstrated near complete coverage of mucosal surfaces by dense bacterial biofilms. In contrast, adenoid specimens from children with sleep apnea demonstrated on average 1.9% surface coverage by biofilms<sup>20</sup>. Adenoid core cultures can be used to predict middle meatal culture results<sup>21</sup>. Bacterial isolation rates from the adenoids increased significantly with sinusitis grade on Waters' view X-ray<sup>22</sup>. Finally, the severity of sinusitis on CT imaging does not correlate with adenoid size suggesting that the contribution of the adenoids to chronic rhinosinusitis is less likely an issue with mechanical obstruction<sup>23,24</sup>.

### **Sinonasal Lavage**

**The addition of sinonasal lavage at the time of adenoidectomy may also improve outcomes.** Lavage helps remove inspissated secretions and infection from the sinus as well as provide culture specimens for directed antibiotic therapy<sup>16</sup>. Two early studies investigated the use of long-term intravenous antibiotic therapy after sinus lavage with adenoidectomy. They demonstrated treatment success rates of greater than 89% but there were several reported complications associated with long-term intravenous antibiotic therapy such as thrombophlebitis, serum sickness, and drug fevers<sup>25,26</sup>. A study by Ramadan and Cost in 2008 compared the efficacy of adenoidectomy with and without maxillary sinus washout and found that success rates in children with more severe sinus disease on CT had a higher rate of success with maxillary sinus washout<sup>27</sup>.

### **Balloon Catheter Dilation**

**Balloon catheter dilation may be considered as a potential minimally invasive surgical technique for managing pediatric chronic rhinosinusitis.** This technique could be used as an adjunct treatment with adenoidectomy. Ramadan reported successful dilation of 51 out of 56 sinuses without any reported complications or side effects in children<sup>28</sup>. Sinuses that were not amenable to dilation were 4 hypoplastic maxillary sinuses and 1 frontal sinus. A follow up study by the same author reported that balloon dilation with adenoidectomy was more effective than adenoidectomy alone<sup>29</sup>. Wang *et al.* published a prospective case control study demonstrating significantly decreased SN-5 and Visual Analog Scale scores in patients who underwent balloon dilation 1 year after the procedure<sup>30</sup>. A prospective, single arm study by Soler *et al.* reported moderate to significant improvement in SN-5 and QOL scores in 92% of children treated with balloon dilation. No serious adverse events related to device use were reported and 100% of sinuses targeted were successfully dilated<sup>31</sup>. In cases where adenoidectomy has failed, balloon dilation successfully treated 81% of children with persistent symptoms as measured by a post-operative reduction in SN-5 scores<sup>32</sup>.

However, there are limitations to this technique. Dilation cannot address the uncinate process, an accessory sinus ostium, a concha bullosa, or a Haller cell<sup>28</sup>. Additionally, hypoplastic maxillary sinuses cannot be effectively treated with this technique. There are also concerns about radiation exposure in children from fluoroscopy during the procedure. The introduction of new balloon catheters with lighted guidewires may obviate the need for fluoroscopy.

### **Functional Endoscopic Sinus Surgery**

**Functional endoscopic sinus surgery has been shown to be an effective and safe treatment option for children with chronic rhinosinusitis.** A meta-analysis by Hebert and Bent in 1998 reported a favorable outcome in at least 88% of patients with a mean follow up of 3.7 years and a low complication of 0.6%<sup>33</sup>. A retrospective chart review of 115 children undergoing functional endoscopic sinus surgery for chronic rhinosinusitis by Siedek *et al.* demonstrated an improvement in quality of life in 71% of patients and a reduction of symptoms in 76% of patients<sup>34</sup>. A subsequent literature review by Makary and Ramadan in 2013 reported an overall success rate of children undergoing functional endoscopic sinus surgery for chronic rhinosinusitis of 82% to 100%.

**Many believe that a conservative approach in children undergoing functional endoscopic sinus surgery for chronic rhinosinusitis is more appropriate<sup>35</sup>.** A limited approach would include removal of obvious anatomical obstructions, polypectomy, anterior ethmoidectomy (ethmoid bullectomy), and/or maxillary sinus antrostomy. Chang *et al.* demonstrated that, using this approach, the majority of patients reported improved sinonasal symptoms and 86% were satisfied with their surgery<sup>36</sup>. Pre-operative administration of systemic steroids in patients with nasal polyposis can potentially reduce intraoperative bleeding and improve visualization<sup>37,38</sup>. Concerns regarding the impact on the developing facial skeleton have been allayed by long-term studies on the effect of sinus surgery on facial growth<sup>39,40</sup>. Reasons for treatment failure after sinus

surgery have not been well studied in pediatrics. Ramadan reported that adhesions and maxillary sinus ostia stenosis were the most common findings at the time revision of surgery<sup>41</sup>.

**The role of second-look sinus endoscopy is controversial<sup>42</sup>.** Young children are unlikely to tolerate nasal debridement in the clinic. Previously, second-look sinonasal endoscopy in the pediatric population was recommended to improve post-operative outcomes<sup>43</sup>. However, more recent studies have demonstrated that this belief is not necessarily true<sup>44,45</sup>. **Second-look endoscopy can be considered in young children who are unable to clear their nose themselves or in children with risk factors for severe, persistent disease such as cystic fibrosis, ciliary dyskinesia, and allergic fungal sinusitis<sup>42,46</sup>.** Overall, endoscopic sinus surgery is a very effective treatment for pediatric chronic rhinosinusitis with low rates of complications.

### Special populations

Certain co-morbid conditions are associated with refractory chronic rhinosinusitis and surgery is more likely to play a much larger role in treatment in these children.

#### Cystic Fibrosis

Cystic fibrosis occurs in approximately 1 in 3500 births and is mediated by an autosomal-recessive mutation in the CFTR gene. Disruption of cAMP-mediated chloride secretion in epithelial cells and exocrine glands leads to increased viscosity of secretions. Inspissated secretions, impaired mucociliary transport, and chronic bacterial infections may increase the risk of chronic rhinosinusitis. The prevalence of chronic rhinosinusitis in this population is up to 90% and polyps occur in at least one-third of cases<sup>47-50</sup>. Additionally, the presence of nasal polyps in a child is highly unusual and the diagnosis of cystic fibrosis should be considered until proven otherwise. Causative microorganisms are different in cystic fibrosis as *Pseudomonas aeruginosa* and Methicillin Resistant *Staphylococcus aureus* (MRSA) are common bacterial isolates<sup>51,52</sup>.

There are no established indications for endoscopic sinus surgery in children with cystic fibrosis associated chronic rhinosinusitis. It is safe and well tolerated in children with cystic fibrosis<sup>53</sup>. Wide opening in sinus ostia may help with drug delivery such as antibiotic irrigations. Surgical intervention can potentially reduce symptoms of nasal obstruction and discharge and improve quality of life<sup>54</sup>. However, the impact on pulmonary function test values is equivocal<sup>55-58</sup>. It may also benefit patients with refractory CRS after lung transplantation<sup>59</sup>. After surgery, the use of nasally inhaled dornase alfa, a recombinant human deoxyribonuclease I that hydrolyzes DNA polymers in the mucus of cystic fibrosis patients, may improve post-operative outcomes<sup>60-62</sup>. Ultimately, the decision to proceed with surgical intervention in a child with cystic fibrosis should involve a multidisciplinary approach that includes the input from the patient's pulmonologist.

#### Primary Ciliary Dyskinesia

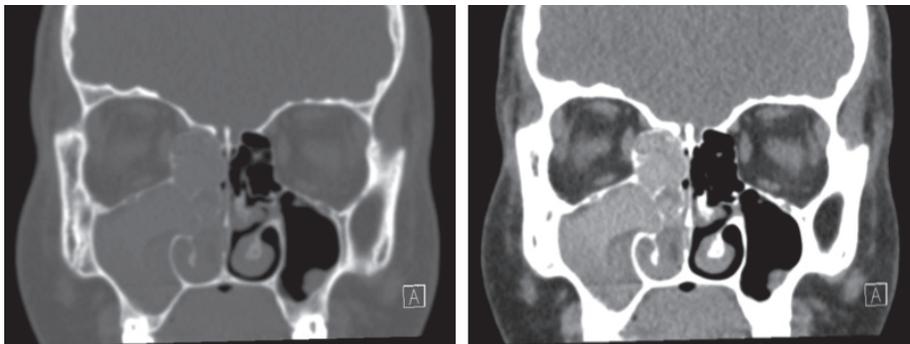
Primary ciliary dyskinesia (PCD) is an autosomal recessive disease that affects approximately 1:15000 individuals<sup>63</sup>. It should be suspected in children who have a history of neonatal respiratory distress, chronic nasal congestion, constant

wet cough, chronic ear disease, bronchiectasis, and situs inversus or ambiguous<sup>64</sup>. The detection of reduced nasal nitric oxide levels can be used as an initial screening test<sup>65-67</sup>. The diagnosis can then be confirmed by evaluating nasal or tracheal biopsies under videomicroscopy or transmission electron microscopy<sup>68-70</sup>.

Chronic rhinosinusitis affects 100% of patients with PCD and up to 30% will have nasal polyps<sup>71,72</sup>. Effective management of sinonasal disease may improve pulmonary function<sup>73</sup>. Overall, there is a paucity of data regarding the surgical management of children with PCD and most treatment paradigms are derived from experiences with cystic fibrosis<sup>7</sup>.

### Allergic Fungal Rhinosinusitis

Allergic fungal rhinosinusitis is a subtype of eosinophilic chronic rhinosinusitis. It is thought to be caused by an abnormally intense allergic reaction towards colonizing fungi and the pathophysiology is believed to be very similar to that of allergic bronchopulmonary aspergillosis<sup>74,75</sup>. It is frequently unilateral, more aggressive, and more likely to present with facial deformity in children<sup>76-78</sup>. The Bent and Kuhn criteria for diagnosing allergic fungal sinusitis is most widely used<sup>79</sup>. Major criteria include: 1. Type I hypersensitivity to fungi, 2. Nasal polyposis, 3. Histologic evidence of eosinophilic mucus without evidence of fungal invasion, 4. Positive fungal stain of sinus contents, 5. Characteristic computed tomography findings. Typical CT findings (**Figure 1**) include multiple opacified sinuses, centrally hyperdense material with a peripheral rim of hypodense mucosa, expansion of affected sinuses, remodeling and thinning of bone, erosion of sinus walls<sup>80,81</sup>.



**Figure 1.** Allergic fungal sinusitis. A fifteen year-old male presented to ENT clinic with a one-year history of right-sided nasal congestion and obstruction. A right nasal polyp was identified during clinical examination. CT sinus without contrast was obtained. Bony and soft tissue windows are shown above. There is unilateral opacification of the paranasal sinuses by centrally hyperdense material along with expansion, remodeling, and thinning of the sinus walls.

Almost all cases of allergic fungal sinusitis will require treatment with functional endoscopic sinus surgery. Careful review of pre-operative imaging and use of image guidance are essential as the disease process can alter anatomy through osseous expansion and erosion<sup>82</sup>. Removal of polyps and mechanical obstruction, reduction of fungal antigen burden, clearance of eosinophilic mucin, and widely

opening the sinuses (for ventilation, access, and topical therapy) are key goals in the surgical management of allergic fungal sinusitis. Postoperatively, patients must continue to use medical therapies that reduce eosinophilic inflammation such as topical glucocorticosteroids and nasal irrigations<sup>83</sup>.

### **Aspirin Exacerbated Respiratory Disease (AERD)**

Aspirin exacerbated respiratory disease, also known as Samter's Triad, is characterized by chronic rhinosinusitis with nasal polyposis, asthma, and hypersensitivity to COX-1 inhibitors such as aspirin. Oral aspirin challenge is the gold standard for diagnosis<sup>84</sup>. Management of AERD should incorporate a multi-disciplinary approach. Medical management should include nasal saline irrigation, topical nasal steroid therapy, leukotriene modifying agents, avoidance of non-steroidal anti-inflammatory agents, and aspirin desensitization therapy<sup>85-89</sup>. Functional endoscopic sinus surgery to reduce disease burden has been recommended as a potential adjunctive therapy prior to aspirin desensitization<sup>90,91</sup>. Additionally, comprehensive surgery rather than "targeted" surgery may lead to better post-operative outcomes<sup>92,93</sup>.

### **Conclusion**

Many factors must be taken into account when treating pediatric chronic rhinosinusitis. Diagnosis of the disease can be difficult to discern from many common pediatric conditions such as upper respiratory tract infections, gastroesophageal reflux, and allergic rhinitis. Imaging can be helpful with diagnosis and surgical planning but should be ordered judiciously due to the risk radiation exposure.

Several surgical treatment options can be used in children when maximal medical treatment has failed. **Surgical options such as adenoidectomy, sinonasal lavage, balloon sinuplasty, and endoscopic sinus surgery have all been shown to be safe and effective in children. The choice of treatment should be tailored to the disease process and the child in question.** For most children, a staged surgical approach **starting with adenoidectomy with or without sinonasal lavage and balloon sinuplasty before endoscopic sinus surgery is appropriate.** Children with cystic fibrosis, AERD, PCD, and immunodeficiency tend to present with severe disease refractive to medical management. They often require endoscopic sinus surgery for the treatment of their sinus disease.

The majority of the current literature on treating chronic rhinosinusitis pertains to the adult population. As such, treatments in the pediatric population are often extrapolated from the adult literature. More studies are needed to help establish guidelines for the effective management of pediatric chronic rhinosinusitis.

### **References**

1. Cunningham M, Chiu E, Landgraf J, Glicklich R. The health impact of chronic recurrent rhinosinusitis in children. *Arch Otolaryngol Head Neck Surg* 2000; 126:1363-1368.
2. Lusk R. Pediatric chronic rhinosinusitis. *Curr Opin Otolaryngol Head Neck Surg* 2006; 14:393-396.
3. Barody FM. Pediatric Chronic Rhinosinusitis. In: Lesperance MM, Flint PW, eds. *Cummings Pediatric Otolaryngology*: Elsevier, 2015.

4. Magit A. Pediatric rhinosinusitis. *Otolaryngol Clin North Am* 2014; 47:733-746.
5. Mafee M, Tran B, Chapa A. Imaging of rhinosinusitis and its complications: plain film, CT, and MRI. *Clin Rev Allergy Immunol* 2006; 30:165-186.
6. Triulzi F, Zirpoli S. Imaging techniques in the diagnosis and management of rhinosinusitis in children. *Pediatr Allergy Immunol* 2007; 18:46-49.
7. Rizzi M, Kazahaya K. Pediatric chronic rhinosinusitis: when should we operate? *Curr Opin Otolaryngol Head Neck Surg* 2014; 22:27-33.
8. Pearce M, Salotti J, Little *Met al.* Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumors: a retrospective cohort study. *Lancet* 2012; 380:499-505.
9. Miglioretti D, Johnson E, Williams *Aet al.* The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. *JAMA Pediatr* 2013; 167:700-707.
10. Al-Qudah M. The relationship between anatomical variations of the sino-nasal region and chronic sinusitis extension in children. *Int J Pediatr Otorhinolaryngol* 2008; 72:817-821.
11. Hill M, Bhattacharyya N, Hall T, Lufkin R, Shapiro N. Incidental paranasal sinus imaging abnormalities and the normal Lund score in children. *Otolaryngol Head Neck Surg* 2004; 130:171-175.
12. Bhattacharyya N, Jones D, Hill M, Shapiro N. The diagnostic accuracy of computed tomography in pediatric chronic rhinosinusitis. *Arch Otolaryngol Head Neck Surg* 2004; 130:1029-1032.
13. Muntz H, Lusk R. Bacteriology of the ethmoid bullae in children with chronic sinusitis. *Arch Otolaryngol Head Neck Surg* 1991; 117:179-181.
14. Slack C, Dahn K, Abzug M, Chan K. Antibiotic-resistant bacteria in pediatric chronic sinusitis. *Pediatr Infect Dis J* 2001; 20:247-250.
15. Hsin C, Su M, Tsao C, Chuang C, Liu C. Bacteriology and antimicrobial susceptibility of pediatric chronic rhinosinusitis: a 6-year result of maxillary sinus punctures. *Am J Otolaryngol* 2010; 31:145-149.
16. Wu A, Shapiro N, Bhattacharyya N. Chronic rhinosinusitis in children: what are the treatment options? *Immunol Allergy Clin North Am* 2009; 29:705-717.
17. Brietzke S, Shin J, Choi *Set al.* Clinical consensus statement: pediatric chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2014; 151:542-553.
18. Brietzke S, Brigger M. Adenoidectomy outcomes in pediatric rhinosinusitis: a meta-analysis. *Int J Pediatr Otorhinolaryngol* 2008; 72:1541-1545.
19. Bettadahalli V, Chakravarti A. Post-adenoidectomy quality of life in children with refractory chronic rhinosinusitis. *J Laryngol Otol* 2017; 131:773-778.
20. Coticchia J, Zuliani G, Coleman *Cet al.* Biofilm surface area in the pediatric nasopharynx: Chronic rhinosinusitis vs obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg* 2007; 133:110-114.
21. Elwany S, El-Dine A, El-Medany A, Omran A, Mandour Z, El-Salam A. Relationship between bacteriology of the adenoid core and middle meatus in children with sinusitis. *J Laryngol Otol* 2011; 125:279-281.
22. Shin K, Cho S, Kim *Ket al.* The role of adenoids in pediatric rhinosinusitis. *Int J Pediatr Otorhinolaryngol* 2008; 72:1643-1650.
23. Bercin A, Ural A, Kutluhan A, Yurttas V. Relationship between sinusitis and adenoid size in pediatric age group. *Ann Otol Rhinol Laryngol* 2007; 116:550-553.
24. Fukuda K, Matsune S, Ushikai M, Imamura Y, Ohyama M. A study on the relationship between adenoid vegetation and rhinosinusitis. *Am J Otolaryngol* 1989; 10:214-216.
25. Buchman C, Yellon R, Bluestone C. Alternative to endoscopic sinus surgery in the management of pediatric chronic rhinosinusitis refractory to oral antimicrobial therapy. *Otolaryngol*

- Head Neck Surg 1999; 120:219-224.
26. Don D, Yellon R, Casselbrant M, Bluestone C. Efficacy of a stepwise protocol that includes intravenous antibiotic therapy for the management of chronic sinusitis in children and adolescents. *Arch Otolaryngol Head Neck Surg* 2001; 127:1093-1098.
  27. Ramadan H, Cost J. Outcome of adenoidectomy versus adenoidectomy with maxillary sinus wash for chronic rhinosinusitis in children. *Laryngoscope* 2008; 118:871-873.
  28. Ramadan H. Safety and feasibility of balloon sinuplasty for treatment of chronic rhinosinusitis in children. *Ann Otol Rhinol Laryngol* 2009; 118:161-164.
  29. Ramadan H, Terrell A. Balloon catheter sinuplasty and adenoidectomy in children with chronic rhinosinusitis. *Ann Otol Rhinol Laryngol* 2010; 119:578-582.
  30. Wang F, Song Y, Zhang X, Tan G. Sinus balloon catheter dilation in pediatric chronic rhinosinusitis resistant to medical therapy. *JAMA Otolaryngol Head Neck Surg* 2015; 141:526-531.
  31. Soler Z, Rosenbloom J, Skarada D, Gutman M, Hoy M, Nguyen S. Prospective, multicenter evaluation of balloon sinus dilation for treatment of pediatric chronic rhinosinusitis. *Int Forum Allergy Rhinol* 2017; 7:221-229.
  32. Ramadan H, Bueller H, Hester S, Terrell A. Sinus balloon catheter dilation after adenoidectomy failure for children with chronic rhinosinusitis. *Arch Otolaryngol Head Neck Surg* 2012; 138:635-637.
  33. Hebert R, Bent J. Meta-analysis of outcomes of pediatric functional endoscopic sinus surgery. *Laryngoscope* 1998; 108:796-799.
  34. Siedek V, Stelter K, Betz C, Berghaus A, Leunig A. Functional endoscopic sinus surgery—a retrospective analysis of 115 children and adolescents with chronic rhinosinusitis. *Int J Pediatr Otorhinolaryngol* 2009; 73:741-745.
  35. Makary C, Ramadan H. The role of sinus surgery in children. *Laryngoscope* 2013; 123:1348-1352.
  36. Chang P, Lee L, Huang C, Lai C, Lee T. Functional endoscopic surgery in children using a limited approach. *Arch Otolaryngol Head Neck Surg* 2004; 130:1033-1036.
  37. Sieskiewicz A, Olszewska E, Rogowski M, Grycz E. Preoperative corticosteroid oral therapy and intraoperative bleeding during functional endoscopic sinus surgery in patients with severe nasal polyposis: a preliminary investigation. *Ann Otol Rhinol Laryngol* 2006; 115:490-494.
  38. Hwang S, Seo J, Joo Y, Kang J. Does the preoperative administration of steroids reduce intraoperative bleeding during endoscopic surgery of nasal polyps? *Otolaryngol Head Neck Surg* 2016; 155:949-955.
  39. Senior B, Wirtschafter A, Mai C, Becker C, Belenky W. Quantitative impact of pediatric sinus surgery on facial growth. *Laryngoscope* 2000; 110:1866-1870.
  40. Bothwell M, Piccirillo J, Lusk R, Ridenour B. Long-term outcome of facial growth after functional endoscopic sinus surgery. *Otolaryngol Head Neck Surg* 2002; 126:628-634.
  41. Ramadan H. Revision endoscopic sinus surgery in children: surgical causes of failure. *Laryngoscope* 2009; 119:1214-1217.
  42. Younis R. The pros and cons of second-look sinonasal endoscopy after endoscopic sinus surgery in children. *Arch Otolaryngol Head Neck Surg* 2005; 131:267-269.
  43. Lazar R, Younis R, Gross C. Pediatric functional endonasal sinus surgery: review of 210 cases. *Head Neck* 1992; 14:92-98.
  44. Mitchell R, Pereira K, Younis R, Lazar R. Pediatric functional endoscopic sinus surgery: is a second look necessary? *Laryngoscope* 1997; 107:1267-1269.
  45. Walner D, Falciglia M, Willging J, Myer C. The role of second-look nasal endoscopy after pediatric functional endoscopic sinus surgery. *Arch Otolaryngol Head Neck Surg* 1998;

- 124:452-458.
46. Ramadan H, Rosen D. Endoscopic sinus surgery in the developmentally delayed child. *Laryngoscope* 1996; 106:121-123.
  47. Gentile V, Isaacson G. Patterns of sinusitis in cystic fibrosis. *Laryngoscope* 1996; 106:1005-1009.
  48. Hadfield P, Rowe-Jones J, Mackay I. The prevalence of nasal polyps in adults with cystic fibrosis. *Clin Otolaryngol Allied Sci* 2000; 25:19-22.
  49. Babinski D, Trawinska-Bartnicka M. Rhinosinusitis in cystic fibrosis: not a simple story. *Int J Pediatr Otorhinolaryngol* 2008; 72:619-624.
  50. Weber S, Iyomasa R, Correa C, Florentino W, Ferrari G. Nasal polyposis in cystic fibrosis: follow-up in children and adolescents for a 3-year period. *Braz J Otorhinolaryngol* 2016.
  51. Lavin J, Bhushan B, Schroeder J. Correlation between respiratory cultures and sinus cultures in children with cystic fibrosis. *Int J Pediatr Otorhinolaryngol* 2013; 77:686-689.
  52. Sobin L, Kawai K, Irace *Aet al.* Microbiology of the upper and lower airways in pediatric cystic fibrosis patients. *Otolaryngol Head Neck Surg* 2017; 157:302-308.
  53. Tumin D, Hayes D, Kirkby S, Tobias J, McKee C. Safety of endoscopic sinus surgery in children with cystic fibrosis. *Int J Pediatr Otorhinolaryngol* 2017; 98:25-28.
  54. Duplechain J, White J, Miller R. Pediatric sinusitis. The role of endoscopic sinus surgery in cystic fibrosis and other forms of sinonasal disease. *Arch Otolaryngol Head Neck Surg* 1991; 117:422-426.
  55. Madonna D, Isaacson G, Rosenfeld R, Panitch H. Effect of sinus surgery on pulmonary function in patients with cystic fibrosis. *Laryngoscope* 1997; 107:328-331.
  56. Rosbe K, Jones D, Rahbar R, Lahiri T, Auerbach A. Endoscopic sinus surgery in cystic fibrosis: do patients benefit from surgery? *Int J Pediatric Otorhinolaryngol* 2001; 61:113-119.
  57. Jarrett W, Militsakh M, Anstad M, Manaligod J. Endoscopic sinus surgery in cystic fibrosis: effects on pulmonary function and ideal body weight. *Ear Nose Throat J* 2004; 83:118-121.
  58. Osborn A, Leung R, Ratjen F, James A. Effect of endoscopic sinus surgery on pulmonary function and microbial pathogens in a pediatric population with cystic fibrosis. *Arch Otolaryngol Head Neck Surg* 2011; 137:542-547.
  59. Vital D, Hofer M, Benden C, Holzmann D, Boehler A. Impact of sinus surgery on pseudo-normal airway colonization, bronchiolitis obliterans syndrome and survival in cystic fibrosis lung transplant recipients. *Respiration* 2013; 86:25-31.
  60. Raynor E, Butler A, Guill M, Bent J. Nasally inhaled dornase alfa in the postoperative management of chronic sinusitis due to cystic fibrosis. *Arch Otolaryngol Head Neck Surg* 2000; 126:581-583.
  61. Cimmino M, Nardone M, Cavaliere *Met al.* Dornase alfa as postoperative therapy in cystic fibrosis sinonasal disease. *Arch Otolaryngol Head Neck Surg* 2005; 131:1097-1101.
  62. Mainz J, Schien C, Schiller *Iet al.* Sinonasal inhalation of dornase alfa administered by vibrating aerosol to cystic fibrosis patients: a double-blind placebo-controlled cross-over trial. *J Cyst Fibros* 2014; 13:461-470.
  63. Knowles M, Daniels L, Davis S, Zariwala M, Leigh M. Primary ciliary dyskinesia. Recent advances in diagnostics, genetics, and characterization of clinical disease. *Am J Respir Crit Care Med* 2013; 188:913-922.
  64. Rubbo B, Lucas J. Clinical care for primary ciliary dyskinesia: current challenges and future directions. *Eur Respir Rev* 2017; 26.
  65. Horvath I, Loukides S, Wodehouse *Tet al.* Comparison of exhaled and nasal nitric oxide and exhaled carbon monoxide levels in bronchiectatic patients with and without primary ciliary dyskinesia. *Thorax* 2003; 58:68-72.
  66. Corbelli R, Bringolf-Isler B, Amacher A, Sasse B, Spycher M, Hammer J. Nasal nitric oxide

- measurements to screen children for primary ciliary dyskinesia. *Chest* 2004; 126:1054-1059.
67. Leigh M, Hazucha M, Chawla *et al.* Standardizing nasal nitric oxide measurement as a test for primary ciliary dyskinesia. *Ann Am Thorac Soc* 2013; 10:574-581.
  68. Chilvers M, Rutman A, O'Callaghan C. Ciliary beat pattern is associated with specific ultra-structural defects in primary ciliary dyskinesia. *J Allergy Clin Immunol* 2003; 112:518-524.
  69. Stannard W, Chilvers M, Rutman A, Williams C, O'Callaghan C. Diagnostic testing of patients suspected of primary ciliary dyskinesia. *Am J Respir Crit Care Med* 2010; 181:307-314.
  70. Jackson C, Behan L, Collins *et al.* Accuracy of diagnostic testing primary ciliary dyskinesia. *Eur Respir J* 2016; 47:837-848.
  71. Leigh M, Pittman J, Carson *et al.* Clinical and genetic aspects of primary ciliary dyskinesia/Kartagener syndrome. *Genet Med* 2009; 11:473-487.
  72. Campbell R. Managing upper respiratory tract complications of primary ciliary dyskinesia in children. *Curr Opin Otolaryngol Head Neck Surg* 2012; 12:32-38.
  73. Alanin M, Aanaes K, Hoiby *et al.* Sinus surgery can improve quality of life, lung infections, and lung function in patients with primary ciliary dyskinesia. *Int Forum Allergy Rhinol* 2017; 7:240-247.
  74. Ryan M, Marple B. Allergic fungal rhinosinusitis: diagnosis and management. *Curr Opin Otolaryngol Head Neck Surg* 2007; 15:18-22.
  75. Ryan M, Clark C. Allergic fungal rhinosinusitis and the unified airway: the role of antifungal therapy in AFRS. *Curr Allergy Asthma Rep* 2015; 15:75.
  76. McClay J, Marple B, Kapadia *et al.* Clinical presentation of allergic fungal sinusitis in children. *Laryngoscope* 2002; 112:565-569.
  77. Patro S, Verma R, Panda N, Chakrabarti A. Understanding paediatric allergic fungal sinusitis: Is it more aggressive? *Int J Pediatr Otorhinolaryngol* 2015; 79:1876-1880.
  78. Gupta A, Bansal S, Gupta A, Mathur N. Is fungal infestation of paranasal sinuses more aggressive in pediatric population? *Int J Pediatr Otorhinolaryngol* 2006; 70:603-608.
  79. Bent J, Kuhn F. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1994; 111:580-588.
  80. Mukherji S, Figueroa R, Ginsberg *et al.* Allergic fungal sinusitis: CT findings. *Radiology* 1998; 207:417-422.
  81. Nussenbaum B, Marple B, Schwade N. Characteristics of bony erosion in allergic fungal rhinosinusitis. *Otolaryngol Head Neck Surg* 2001; 124:150-154.
  82. Lusk R. Computer-assisted functional endoscopic sinus surgery in children. *Otolaryngol Clin N Am* 2005; 38:505-513.
  83. Thorp B, McKinney K, Rose A, Ebert C. Allergic fungal sinusitis in children. *Otolaryngol Clin N Am* 2012; 45:631-642.
  84. Williams A. Diagnostic evaluation in aspirin-exacerbated respiratory disease. *Immunol Allergy Clin North Am* 2016; 36:657-668.
  85. Dahlen S, Malmstrom K, Nizankowska *et al.* Improvement of aspirin-intolerant asthma by montelukast, a leukotriene antagonist: a randomized, double-blind, placebo-controlled trial. *Am J Respir Crit Care Med* 2002; 165:9-14.
  86. Stevenson D, Hankammer M, Mathison D, Christiansen S, Simon R. Aspirin desensitization treatment of aspirin-sensitive patients with rhinosinusitis-asthma: long-term outcomes. *J Allergy Clin Immunol* 1996; 98:751-758.
  87. Kennedy J, Stoner A, Borish L. Aspirin-exacerbated respiratory disease: Prevalence, diagnosis, treatment, and considerations for the future. *Am J Rhinol Allergy* 2016; 30:407-413.
  88. Waldram J, Walters K, Simon R, Woessner K, Waalen J, White A. Safety and outcomes of aspirin desensitization for aspirin-exacerbated respiratory disease: A single-center study. *J*

Allergy Clin Immunol 2017.

89. Levy J, Rudmik R, Peters A, Wise S, Rotenberg B, Smith T. Contemporary management of chronic rhinosinusitis with nasal polyposis in aspirin-exacerbated respiratory disease: an evidence-based review with recommendations. *Int Forum Allergy Rhinol* 2016; 6:1273-1283.
90. Cho K, Soudry E, Psaltis *Aet al*. Long-term sinonasal outcomes of aspirin desensitization in aspirin exacerbated respiratory disease. *Otolaryngol Head Neck Surg* 2014; 151:575-581.
91. Adelman J, McLean C, Shaigany K, Krouse J. The role of surgery in management in Samter's Triad: A systematic review. *Otolaryngol Head Neck Surg* 2016; 155:220-237.
92. DeConde A, Suh J, Mace J, Alt J, Tmith T. Outcomes of complete vs targeted approaches to endoscopic sinus surgery. *Int Forum Allergy Rhinol* 2015; 5:691-700.
93. Morrissey D, Bassiouni A, Psaltis A, Naidoo Y, Wormald P. Outcomes of modified endoscopic Lothrop in aspirin-exacerbated respiratory disease with nasal polyposis. *Int Forum Allergy Rhinol* 2016; 6:820-825.