Upper Airway Imaging in Pediatric Obstructive Sleep Apnea

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Monique A. L. J. Slaats and Stijn L. Verhulst

Abbreviations

2D	2-dimensional
3D	3-dimensional
AHI	Apnea hypopnea index
AN	Adenoidal-nasopharyngeal
ATE	Adenotonsillectomy
BMI	Body-mass index
CAD	Computer aided design
CBCT	Cone beam computed tomography
CFD	Computational fluid dynamics
CI	Confidence interval
CSA	Cross-sectional area
CT	Computed tomography
DS	Down syndrome
LR-OCT	Long-range optical coherence tomography
mCSA	Minimal cross-sectional area
MCW	Mandibular cortical width
MDCT	Multiple detector computed tomography MRI magnetic resonance imaging
mSv	Milisievert
oAHI	Obstructive apnea hypopnea index
OCT	Optical coherence tomography
OSA	Obstructive sleep apnea
PSG	Polysomnography
RDI	Respiratory disturbance index
SNA	Sella, nasion, and A-point
SNB	Sella, nasion, and B-point
T1	Longitudinal relaxation time
T2	Transverse relaxation time
TP	Tonsillar-pharyngeal
UA	Upper airway

Introduction

Adenotonsillar hypertrophy is the most important predisposing factor in children with obstructive sleep apnea (OSA) [1–3]. The association between the subjective evaluation of tonsillar size and OSA severity as determined by polysomnography is weak. High-quality studies suggest no association [4–6]. Additionally, the pathogenesis of upper airway (UA) narrowing is more complex in children with risk factors such as obesity, craniofacial malformations, Down syndrome (DS), or neuromuscular disorders [7].

The first line treatment of pediatric OSA is adenotonsillectomy (ATE) [7, 8]. There are other non-surgical and surgical options for treatment that are used in residual OSA or complex OSA (children with risk factors) [7]. Treatment outcomes for ATE have been extensively studied and there is a high incidence of residual OSA after ATE, especially in children with risk factors such as obesity (up to 59%) and Down syndrome (up to 87%) [9–18]. Commonly described anatomical causes of persistent disease include mandibular deficiency, glossoptosis, macroglossia, soft palate enlargement, lymphoid hypertrophy surrounding the UA, and inferior displacement of the hyoid bone or abnormal neuromuscular control [3, 17, 19, 20].

Polysomnography gives the diagnosis of OSA but not the anatomical level of obstruction in the UA. In a time of personalized medicine, it seems crucial to couple the exact individual anatomical risk factor with the most appropriate treatment to avoid unnecessary risks and ineffective surgeries. Several studies investigated the role of UA imaging as noninvasive evaluation of UA obstruction. These techniques include lateral neck radiographs, cephalometry, computerized tomography (CT), cone beam CT, magnetic resonance imaging (MRI) and post-processing of these images using computational fluid dynamics (CFD) for functional respiratory imaging (FRI), long-range optical coherence tomography (LR-OCT), and drug induced sleep (sedation) endoscopy (DISE). Every technique has advantages and disadvantages, while an overview is presented in Table 16.1 [21].

M. A. L. J. Slaats (✉) · S. L. Verhulst
Department of Pediatrics, Antwerp University Hospital, Edegem, Antwerp, Belgium
e-mail: monique.slaats@uza.be

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Table 16.1 Advantages and disadvantages of imaging techniques

	Advantages	Disadvantages
Lateral neck radiography	Fast procedure Widely accessible Low cost	Awake (Low) radiation 2D Limited differentiation of soft tissue
Cephalometry	No sedation Low cost	Awake (Low) radiation 2D Need for expertise Limited differentiation of soft tissue
(Cine) magnetic resonance imaging (MRI)	No radiation Sleep-like state 3D High resolution and high contrast visualizations of the UA Visualize multiple levels of obstruction	Sedation Not widely available Expensive
Computerized tomography (CT)	No sedation Widely accessible 3D	Radiation Limited differentiation of soft tissue Expensive
Cone beam CT	No sedation Low cost 3D	(Low) radiation Not widely accessible Limited differentiation of soft tissue
Functional imaging	No sedation (CT) 3D Differentiation of soft tissue (MRI) Sleep-like state (MRI)	Radiation (CT) Limited differentiation of soft tissue (CT images) Not widely available Expensive
Long-range optical coherence tomography	No sedation No radiation 3D Low cost	Not widely available Limited differentiation of soft tissue
Drug induced sleep (sedation) endoscopy	Fast procedure before surgery No radiation Sleep-like state Live video Visualize multiple levels of obstruction Supine position	Sedation Not widely available Cannot simultaneously view multiple levels of obstruction Need for expertise

This chapter reviews studies using imaging techniques that may further enhance our understanding about the mechanisms of UA obstruction leading to pediatric OSA and could assist in the selection of treatment.

Lateral Neck Radiography

Lateral neck radiography is relatively simple, is widely accessible, and has a low cost. However, the images are taken in an upright position in awake patients. One study in adults investigated the difference between supine and upright lateral cephalograms and observed no additional anatomical differences [22]. Another study in five adults with OSA measured the total volume and cross-sectional area (CSA) change in supine versus upright position by computerized tomography (CT). They concluded that the airway was significantly smaller when patients were in a supine position [23]. There are currently no such studies available in children. Furthermore, the airway is depicted in a two-dimensional (2D) view, resulting in a possible loss of information.

Another disadvantage is that this technique utilizes ionizing radiation. Effective dose is expressed in Sieverts which is a single dose parameter that reflects the risk of exposure in terms of whole-body exposure. An annual effective dose from natural background radiation is about 2.5–3 millisievert (mSv), the worldwide average natural dose is about 2.4 mSv per year. A lateral neck X-ray requires minimal radiation with an average of 0.2 millisievert (mSv) (reported variation in the literature ranges between 0.07 and 0.3 mSv) [24–26].

The obtained lateral neck radiography shows the vertebrae, the oral and nasal airways, the nasopharynx, part of the trachea, the epiglottis, the soft tissue in front of the vertebrae, and the adenoids and tonsils. Some ratios can be determined using different methods, the most frequently analyzed radiographic parameter in studies is the adenoidal-nasopharyngeal (AN) ratio (Fig. 16.1) [2, 3, 27–35]. However, a systematic review concluded that there are conflicting outcomes because of methodological problems that limit the applicability of these results to clinical decision-making [36]. A cohort study evaluated the ability of lateral radiography to assess adenoid hypertrophy in 72 children

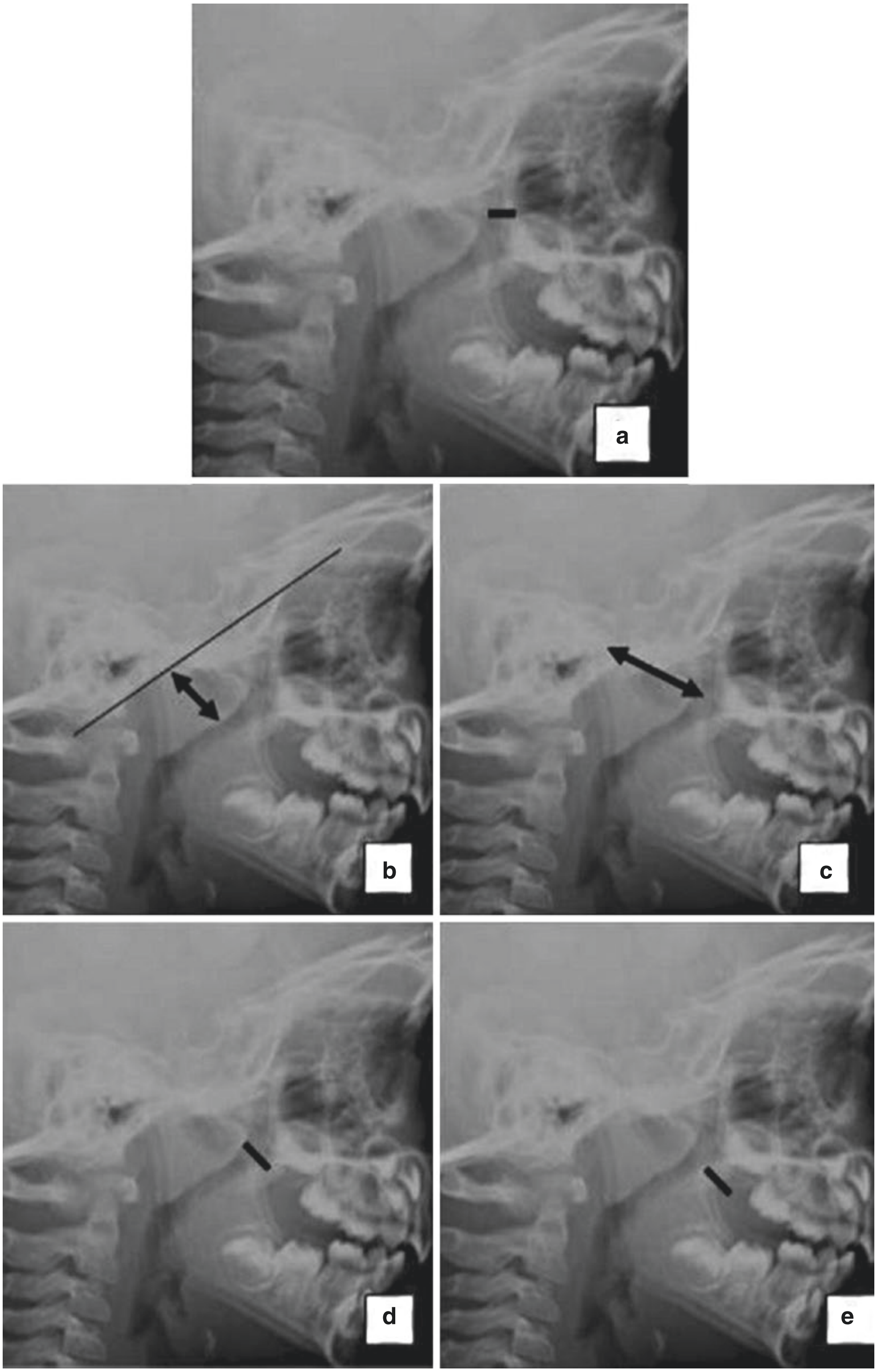

Fig. 16.1 (**a**–**e**) Lateral X-ray. (**a**) Hibbert's method: the distance from the anterior adenoid to the post-maxillary antrum. (**b**) The distance along a perpendicular line from the pharyngeal tubercle on the base of the skull to the adenoidal convexity (maximal adenoidal thickness). (**c**) Distance measured along a line from the posterior–superior edge of the hard palate to the spheno- occipital synchondrosis on the base of the skull. (**d**) Minimal width of the airway immediately behind the soft palate at (e). (**e**) Width of the supero-anterior soft palate 1 cm below the hard palate (half a centimeter in children younger than 3 years old). (From Waters et al. [37]. Reprinted with permission from John Wiley and Sons)

using four different methods [37]. Twenty-six children (36.1%) without OSA and only nine children (12.5%) with severe OSA were studied. The best correlations between OSA severity and radiography were found using the anterior airway measurement (the distance from the anterior adenoid to the post-maxillary antrum; method by Hibbert et al.) [33]. Using the definition of obstructive apnea/hypoapnea index (oAHI) >1 with adjustment for sex, age, body-mass index (BMI), the method of e (presented in Fig. 16.1) provided the largest receiver operating characteristic (ROC) area (0.775) for predicting OSA, with a sensitivity of 86.7% and a specificity of 55.6%.

Additionally, there are a few more studies that show correlations between lateral X-ray findings and OSA severity while one study failed to show a correlation [2, 3, 28, 29, 35]. Brooks et al. reported a correlation between obstructive apneas and AN ratio (according to the method described by Fujioka) in a study of 33 children. Children with OSA had a larger AN ratio (0.83 ± 0.3 vs. 0.69 ± 0.03; $p < 0.003$), resulting in reasonable, although suboptimal, positive and negative predictive values of 71% and 75%, respectively [28]. Li et al. investigated the value of tonsillar–pharyngeal (TP) ratio as a measure of tonsillar enlargement in 35 children (mean age of 6.2 (4–10) years old) with suspected OSA. There was a significant correlation between the TP ratio and the AHI ($r = 0.8$; $p < 0.001$) and oxygen desaturation index ($r = 0.51$; $p = 0.002$). However, there was no correlation between tonsil size and the TP ratio. The ROC curve analysis revealed that a TP ratio cut off of 0.5 was optimal for predicting severe OSA, with the area under the curve being 1.0. The corresponding sensitivity and specificity were 95.8% and 81.8%, respectively, while the positive and negative predictive values were 92.0% and 90.0%, respectively [3]. Xu et al. determined whether parents' observation, clinical examination, and lateral upper airway radio- graph were useful in diagnosing OSA in 50 children (OSA group; $n = 31$, mean age 7.8 ± 3.2 years old and primary snoring group; $n = 19$, mean age 8.1 ± 3.7 years old). There was a sensitivity of 81% and specificity of 58% for UA narrowing on lateral X-ray by AN ratio for predicting OSA. Secondly, combining UA narrowing with mouth breathing, nocturnal enuresis, observed apnea during sleep, intrusive naps, mouth breathing, enlarged tonsils, and radiologic features of narrowing increased the positive predictive value to 73% and the negative predictive value to 80% [2].

Currently, there are no studies that have investigated whether lateral neck radiography can predict the effect of treatment.

In summary, this technique has relatively good predictive values for the diagnosis of OSA. In view of the advantages associated with this technique, further studies in other and larger populations are warranted. Furthermore, the predictive value can be improved by incorporating certain clinical predictors such as obesity, mouth breathing, nocturnal enuresis, observed apnea during sleep, intrusive naps, and enlarged tonsils on clinical examination.

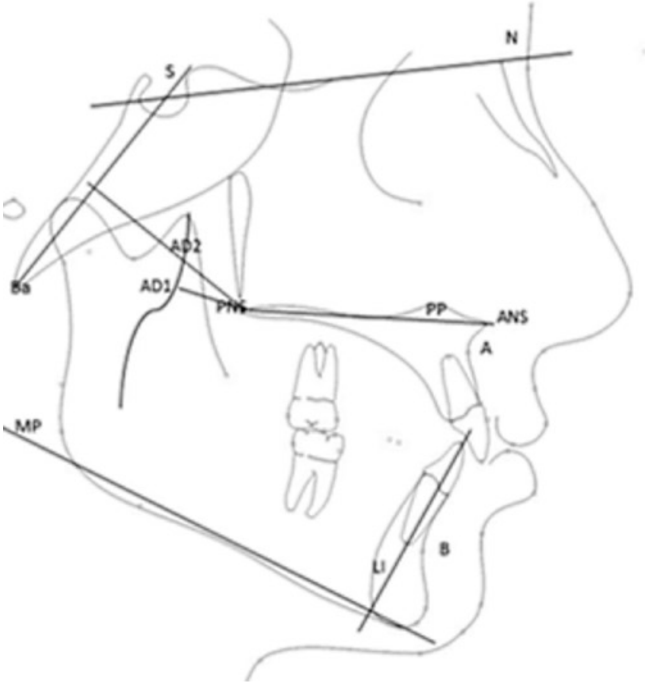

Fig. 16.2 Cephalometric references and landmarks used in the meta-analysis. S Sella, N nasion, Ba basion, ANS anterior nasal spine, PNS posterior nasal spine, PP palatal plane, A A-point, B B-point, MP mandibular plane (gonion-menton), PNS-AD1 distance from PNS to the nearest adenoid tissue measured along the line PNS- Ba, PNS-AD2 distance from PNS to the nearest adenoid tissue measured along the line perpendicular to S-Ba, LI, long axis of the mandibular incisor. (From Katyal et al. [48]. Copyright © 2013 American Association of Orthodontists. Published by Mosby, Inc. All rights reserved. Reprinted with permission from Elsevier)

Cephalometry

Cephalometry involves a standardized lateral radiographic view of the head and neck with more calculations of markers, distances, and ratios (Fig. 16.2). Therefore, there is a need for an experienced radiologist. The method shows skeletal (including mandibular and hyoid position) and soft-tissue (tongue and soft palate) UA structures. The advantages and disadvantages are comparable to lateral neck X-ray. Due to several measurements, the position of the head is critical. The following angles are commonly described in cephalometric studies: maxillary protrusion is expressed by the sella, nasion, and A-point (SNA) angle, the mandibular protrusion is expressed by the sella, nasion, and B-point (SNB) and point A nasion to B (ANB) angle is the difference of the SNA and SNB angles. In sagittal direction, an increase of the ANB angle describes a skeletal Class II malocclusion and in the vertical direction it shows a mandibular clockward rotation [38–40].

Some case-control studies in adults investigated the usefulness of cephalometric measurements in OSA patients. A meta-analysis in adults has shown a strong correlation between OSA severity and mandibular plane hyperdivergence. However, this correlation was not strong enough to indicate that craniofacial morphology had a direct causal effect in the development of OSA in adults [41].

Several case series investigated the influence of skeletal abnormality in children and suggested that children with mouth breathing, adenotonsillar hypertrophy, or sleep-disordered breathing have a retropositioned mandible, narrow maxilla, increased lower anterior face height, increased mandibular plane angle, inferior position of the hyoid bone, and smaller airway space [42–46]. Several studies have also investigated whether cephalometry could predict the diagnosis of Obstructive Sleep Apnea Syndrome (OSAS). Two systematic reviews investigated the association between maxillomandibular discrepancy and OSA. They suggested that children with OSA have more skeletal Class II mandibular growth direction compared to normal children. However, an increased ANB angle of less than 2° in children with OSA and primary snoring, compared with the controls, might not be clinically significant. Evidence for a direct causal relationship between craniofacial structure and OSA could not be supported by these meta-analyses [47, 48].

Galeotti et al. analyzed the correlation between cephalometric variables and OSA severity in 62 children. They reported a correlation between increased oAHI and skeletal discrepancy expressed by ANB angle. Therefore, one could hypothesize that more severe OSA leads to an increased mouth-breathing pattern that in turn strongly affects skeletal growth with Class II skeletal malocclusion and hyperdivergent growth pattern in children [49]. Pirila-Parkkinen et al. investigated the capability of 2D lateral cephalography in recognizing pharyngeal obstruction compared to 3D MRI and clinical observation in 36 children with OSA. The study showed an association between the cephalometric nasopharyngeal and retropalatal airway measurements and MRI findings. However, retroglossal pharyngeal measurements by cephalography did not correlate with MRI variables. Palatal tonsils mainly are situated in the retroglossal region and because of their lateral position; enlarged tonsils can cause the transversal narrowing of the retroglossal airway, which is not detectable on the anteroposterior view of the cephalogram [50].

Similar as for the lateral neck radiography, there are currently no studies which used cephalometry to predict the effect of treatment in pediatric OSA.

In summary, it remains unclear if cephalometry can be a valid diagnostic tool and there are no studies using cephalometry to predict treatment outcome.

Magnetic Resonance Imaging (MRI)

MRI is another method to localize and diagnose the site of UA obstruction (Fig. 16.3). It is accurate, reproducible, and there is no need for radiation. Furthermore, it is possible to have moving images during sleep by cine MRI. However, MRI is expensive, and requires a long examination time, resulting in a higher probability of motion artifacts. That is why it often requires sedation that puts the patient in a state of mimicking physiological sleep as closely as possible, but this also makes it more invasive. Children with OSA are sensitive to the respiratory depressant effects of sedative and hypnotic drugs that affect the UA dynamics, including the possibility of increasing UA obstruction. Dexmedetomidine provides an acceptable level of sedation and less need for airway support during MRI studies [51–55].

Fig. 16.3 UA imaging by MRI. Several studies have investigated the relationship between UA anatomy assessed by MRI and OSA severity

Normal-Weight Children

A case-control study investigated anatomical risk factors involved in the development of pediatric OSA in 40 normal-weight children (20 with OSA and 20 controls) by MRI. MRI performed in supine position, without sedation. Volumetric measurements were made from T1-weighted images and T2-weigthed images and were used to evaluate the lymphoid tissues. This study showed a significantly smaller UA volume (1.4 ± 0.7 cm^3 versus 1.6 ± 0.7 cm^3) and midsagittal nasopharyngeal airway (0.7 ± 0.2 cm^3 versus 1.2 ± 0.4 cm^3) in OSA patients. The axial cross-sectional area of the oropharyngeal airway was also smaller (0.5 ± 0.3 cm^3 versus 0.8 ± 0.5 cm^3). Thereby, children with OSA also had a significantly lager soft palate volume and midsagittal palate volume. Additionally, the adenoids and tonsils were considerably larger in the OSA group. Concerning skeletal structure, the study showed that the OSA group had a smaller mandibular volume and a lower vertical position of the hyoid bone [56]. Another study investigated the UA in sedated children with OSA by MRI. In a first study, they compared the UA structure in 18 young children with OSA (mean age

4.8 years) and 18 controls (mean age 4.9 years). They showed a correlation between increased tonsil and adenoid volume and AHI in sedated children [57]. Another study investigated 10 children with adenotonsillar hypertrophy and OSA and 10 controls. Children with OSA had a smaller UA volume, particularly during inspiration, whereas dilatation occurred during expiration. The OSA group had larger adenoid and tonsils in comparison with the control group. The volumes of both mandible and tongue were similar in both groups. The study concluded that the adenoid and tonsils in children with moderate OSA restrict the UA. Additionally, the study found that further UA restriction in OSA patients could be caused by enlargement of the soft palate [58].

Obese Children

Arens et al. investigated the body fat composition and UA structure in 44 obese children (22 with OSA and 20 controls). UA lymphoid hypertrophy, parapharyngeal fat pads, and abdominal visceral fat were significantly increased in obese children with OSA. In regression analysis, only lymphoid tissue correlated with OSA severity [20]. Another study evaluated the frequency of enlarged lingual tonsils in 71 obese children with sagittal fast spin-echo inversion recovery imaging. They concluded that obese children had a high frequency of enlargement of the lingual tonsils with a significantly higher prevalence in those who had previously undergone tonsillectomy. Enlarged lingual tonsils may thus play a role in the pathogenesis of persistent obstructive sleep apnea in obese children [59].

Nandalike et al. evaluated how ATE affects anatomical factors of airway obstruction in 27 obese children with OSA. All underwent polysomnography (PSG) and MRI during wakefulness before and after ATE. ATE was associated with a significant increase in soft palate volume, tongue size, and head and neck subcutaneous fat tissue. A complete resolution of OSA only occurred in 44% of cases and complete resolution was achieved in only 22% of children with severe OSA. Residual OSA was associated with substantial residual adenoid tissue, an increase in the volume of the soft palate and, to a lesser extent, the increased volume of the tongue [60].

Children with DS

Children with DS have certain anatomical factors that predispose for a higher risk of OSA: underdeveloped midface and mandibular hypoplasia, macroglossia, posterior-placed tongue, hypotonia, smaller upper airway, lymphoid hyperplasia, and obesity [51, 61–63].

Two studies used imaging in children with DS to investigate UA morphology. Uong et al. investigated the anatomical differences by MRI (size and shape of the upper airway in relation to surrounding tissue) between 11 children with DS without OSA and 14 controls without DS and OSA (mean age of 3 years old). Adenoid and tonsil volume were significantly smaller in the DS children. However, tongue, soft-palate, pterygoid, and parapharyngeal fat pads were similar. There was a smaller upper airway size in DS children, the authors suggested that this was caused by soft tissue crowding within a smaller mid- and lower face skeleton [63]. Another imaging study investigated the stiffness of the airway wall from MRI by a noninvasive method in 21 children with DS and OSA. Airway changes were evaluated by continuous positive airway pressure (CPAP). The localized airway and tissue elasticity were found to increase with increasing OSA severity. They concluded that elasticity-based patient phenotyping could potentially assist clinicians in decision making concerning the needed CPAP pressure [64].

Donnelly et al. concluded that persistent OSA in DS has multiple causes. The most common causes include macroglossia, glossoptosis, recurrent enlargement of the adenoids, and enlarged lingual tonsils [17].

Cine MRI

Cine MRI is a high-resolution imaging method that captures the dynamic movement of the UA in a sedated child. These dynamic images can show both the degree and the direction of airway collapse (anterior-posterior or circumferential). Thereby, it can sometimes show compensating of the tongue or jaw thrusting during the period of obstruction. It is performed for approximately 30 seconds at each level with a rate of imaging of about three images per second [65–69].

Donnelly et al. investigated 16 young patients with OSA and 16 without airway problems or airway diseases. These researchers showed several differences concerning dynamic airway motion [67]. OSA patients were much more likely to demonstrate intermittent collapses of the nasopharynx and exclusively demonstrated intermittent collapse of the hypopharynx. The mean change in diameter of the nasopharynx and hypopharynx, implicating a more compliant UA, was also significantly greater in the OSA group. Abbott et al. investigated 31 children (mean age of 11.3 years) with OSA and 21 control children (mean age of 3.5 years). They included OSA subjects with the following predispositions to obstruction: craniofacial anomalies, DS, persistent OSA, and pre-operative evaluation to complex airway surgery. All children underwent transverse phase gradient-echo cine MRI imaging of the hypopharynx with sedation. The airway volumes were obtained by a k-means clustering algorithm and the airway wall motion was described. The study showed airway distention and airway collapse in children with OSA. Airway volume oscillated in both groups, but the amplitude was much larger in the OSA group. A clear limitation of this study is the fact that the mean age of the control group was much lower than the mean age of the OSA patients. A concern about the large difference in age is that UA size may increase by age. Interestingly, the size of UA volume in some of the youngest subjects with OSA had volumes as large as some of the oldest in the control group. In this study, airway volume did not correlate significantly with age in either the control group or the children with OSA [70].

In summary, MRI gives a better insight into UA anatomy because it provides a detailed assessment of the UA as the pharyngeal size and soft tissue anatomy (including adipose tissue). Several studies involving MRI have shown detailed correlations with OSA severity or the identification of critical anatomical sites. However, more research is needed for sensitivity or specificity for diagnosis and prediction of treatment outcome.

Computerized Tomography (CT)

CT is a fast, noninvasive technique to visualize the UA and is available in the majority of institutions (Fig. 16.4). CT images can be taken during wakefulness and sleep. A major disadvantage of CT is radiation. The radiation dose for a neck CT is approximately 3 mSv for adults [24, 71, 72]. Recently, cine CT or ultra-fast CT has been used more frequently and can obtain multiple images with a lower radiation dose. Fleck et al. evaluated the cine (dynamic 3D) CT technique for the UA in six children with OSA and compared the required radiation dose between these children. The radiation from a low-dose CT scan was between 0.08 and 0.27 mSv [73].

Fig. 16.4 CT image of the UA

The UA from nares to trachea can be reconstructed into three-dimensional (3D) models and subdivided into five zones for measuring volumes of different parts in the UA and CSA (Figs. 16.5 and 16.6).

Only three studies investigated the utility of CT in pediatric OSA. Van Holsbeke et al. investigated whether anatomical and functional properties of the airway were correlated with OSA severity in 33 children with OSA. The study concluded that children with OSA had a lower volume of UA zone 3, the overlap region of adenoids and tonsils, and a lower mean CSA of the UA. No correlation was found between the clinical scores of UA patency (Brodsky and Mallampati scoring system) and OSA severity indicating that imaging might be more powerful in the assessment of UA patency [74]. Slaats et al. further investigated whether functional respiratory imaging (FRI) by CT could provide more information about UA characteristics in 91 normal-weight children with OSA mainly to predict treatment outcome. They concluded, comparable with Van Holsbeke et al., which a smaller overlap region and a more concave shape of the UA correlated with more severe OSA. There was also no correlation with clinical examination and OSA severity. UA volumes could not predict treatment outcome in this study [75].

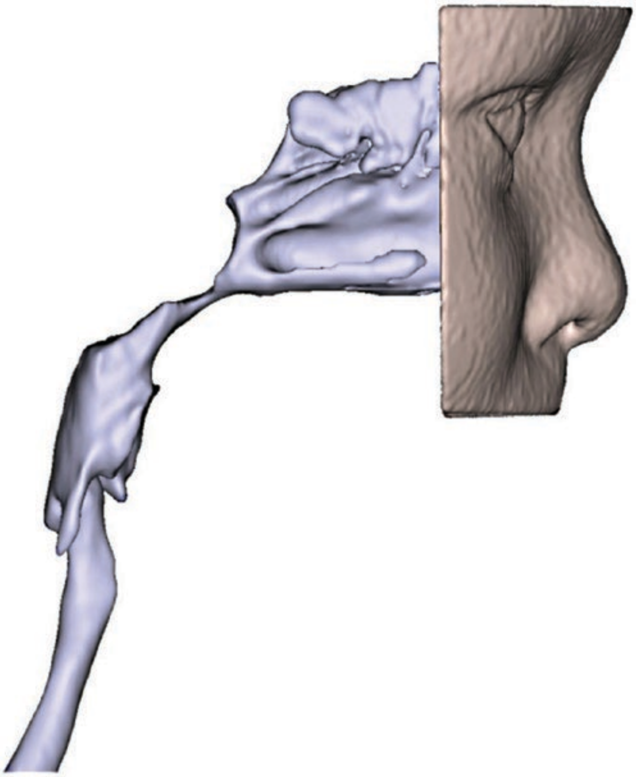

Fig. 16.5 Reconstructed into 3D model of the upper airway. (From Slaats et al. [75]. Reprinted with permission from John Wiley and Sons)

Another study about CT images and pediatric OSA was performed in children with DS. Slaats et al. characterized treatment outcome after ATE in 33 young children with DS and OSA by UA imaging (CT images). At baseline, children with more severe OSA had a smaller minimal passage through the upper airway. After treatment, persistent OSA was seen in 79% of the children; however, 79% had a decrease of >50% in oAHI after treatment. Children with less favorable response had a smaller volume of the zones below the tonsils, which is probably due to enlargement of the lingual tonsils, glossoptosis, or macroglossia that is not treated by ATE (Fig. 16.7). In conclusion, this study suggests that UA imaging could have an influence in treatment selection in children with DS and OSA. Exact cut-off values are needed to be confirmed by larger studies [76].

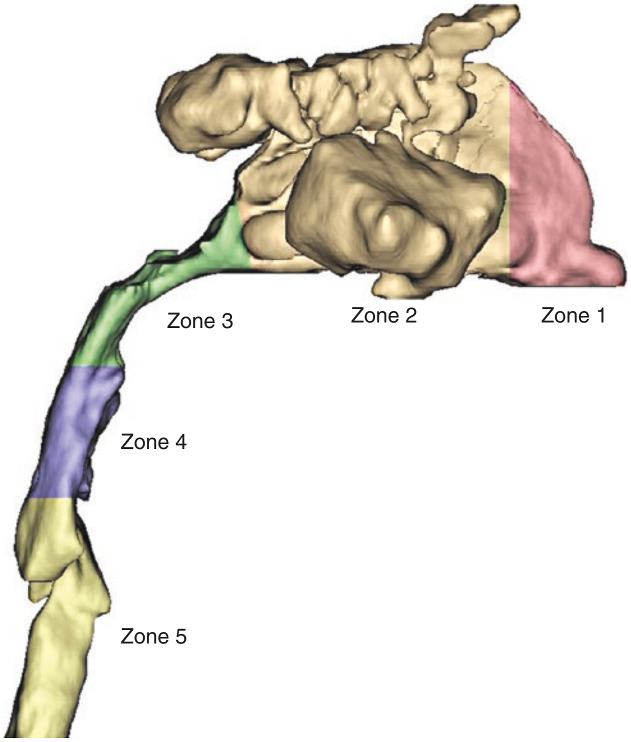

Fig. 16.6 3D model of the upper airway divided into five zones. Zone 1 = nostril to bottom of inferior turbinate; Zone 2 = bottom of inferior turbinate to choanae; Zone 3 = choanae to tip of uvula; Zone 4 = uvula to epiglottis; Zone 5 = epiglottis to the first vertebra. (From Slaats et al. [75]. Reprinted with permission from John Wiley and Sons)

In conclusion, CT also provides a detailed analysis of the anatomy. CT studies have shown detailed correlations with OSA severity or the identification of critical anatomical sites without sensitivity or specificity reported. One study indicates that UA imaging could have a role in treatment selection in children with DS and OSA. However, this was a very small study group and exact cut-off values are needed to be confirmed by larger studies. More research is needed in this group because DS is an important risk factor for OSA with a high incidence of residual OSA.

Cone Beam CT (CBCT)

Cone beam computed tomography (CBCT) is a low-dose radiation 3D imaging technique. A disadvantage is that it shows limited differentiation of soft tissue. CBCT is not available in all hospitals. However, it is widely available in dental and oral medicine. For example, it has been used for many maxillofacial applications such as for implant site imaging and treatment planning for craniofacial surgery and orthodontics [77].

The radiation dose is lower compared to normal CT and is more like that of low dose protocol CT. When used in maxillofacial imaging, CBCT produces an eight- to tenfold lower effective dose than a conventional CT examination using standard protocols [78–80].

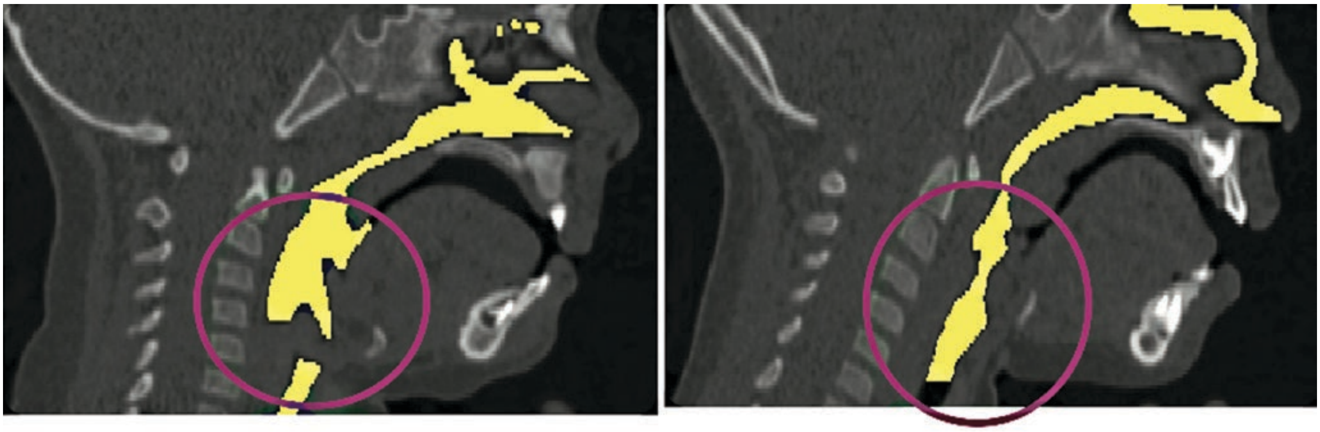

Fig. 16.7 Left: image of a child's UA with a decrease of more than 50% in oAHI after ATE Right: decrease of less than 50% in oAHI after ATE. (From Slaats et al. [76]. Copyright © 2018 American Academy of Sleep Medicine, reprinted with permission)

Some studies in adults have demonstrated that CBCT produces extremely accurate anatomical representations [81–83]. A review of the use of CBCT in adult patients with OSA concluded that there is a need for more research, but that the use of CBCT for both pre-operative planning and for postoperative evaluation of therapeutic interventions is likely to become increasingly important [84]. There are only a few studies in pediatric OSA. Eimar et al. investigated in 96 children diagnosed with or at risk of SDB, particularly OSA, whether these children had a reduced bone density estimated by mandibular cortical width (MCW) on CBCT images [85]. MCW demonstrates the highest sensitivity and specificity for detection of reduced bone density [86]. It represents the distance, in millimeters, between the lower borders of the mandible to the superior margin of the mandible cortex. MCW values were significantly lower in OSA children (MCW = 2.9 ± 0.6 mm) compared to control children (MCW = 3.5 ± 0.6 mm; $P = 0.002$). This finding may reflect alterations in bone homeostasis [85].

A case–control study verified the differences in the volume and areas of the UA between 27 children with persistent OSA after AT and a 20 sex-age matched healthy control group by CBCT. Children with OSA had a significant narrowing in the nasopharynx and in the lower portion of the UA. This result demonstrated that other factors than adenotonsillar hypertrophy, such as craniofacial abnormalities, could play a role in the pathogenesis of OSA [87]. Alsufyani et al. evaluated with a clinical pilot study the anatomical changes that occur in the UA before and after AT using CBCT in 12 children. Secondly, they evaluated whether changes in airway reflects in the quality of life [88]. Quality of life was tested by the OSA-18 questionnaire. Only UA constriction and patency correlated with changes in OSA-18. Airway patency gained by at least 150% and constriction relief by at least 15% showed marked improvement in OSA-18 by 40–55%. A limitation of this study was the method for diagnosis of OSA. This was based on history of nocturnal symptoms, physical examination, overnight pulse oximetry, and pediatric sleep questionnaire (PSQ-22) instead of the gold-standard polysomnography [7, 89]. Another limitation of this study was that the analysis did not include other OSA parameters such as saturation and a sleep study after treatment [89].

In conclusion, CBCT provides a detailed analysis of the anatomy by low dose protocol. Unfortunately, there are only a few studies in children that make it unclear if CBCT can be a diagnostic tool or predict treatment outcome.

Functional Respiratory Imaging (FRI)

FRI is a relatively new method that can simulate airflow dynamics and the resulting pressure distribution by anatomical narrowing by computational fluid dynamics (CFD). The 3D model (Fig. 16.6) is used for analysis of anatomical parameters, volume meshing (representation of interior volume), and CFD [74–76, 90]. Exact details about CFD are described in the article of Slaats et al. [75]. A few studies investigated the utility of CFD in children with OSA. Preliminary data showed that FRI could identify differences in the UA of children with residual OSA and correlates well with OSA severity than parameters obtained from physical examination [74].

Normal-Weight Children

One study compared CFD data in three children with OSA and three controls. The results suggested that pharyngeal airway shape in children with OSA significantly affects internal pressure distribution compared to nasal resistance [91]. A recent study investigated whether FRI by CT images could provide more information about UA characteristics in 91 normal-weight children with OSA without risk factors, mainly to predict treatment outcome. Imaging parameters correlated with OSA severity at baseline more than the tonsil score obtained by clinical assessment: a smaller overlap region of tonsils/adenoids, a higher resistance, and a more concave shape of the UA correlated with more severe OSA. Thereby, a less constricted airway, as characterized by both a higher conductance and a lower tonsil score, was associated with a less favorable response to (adeno)tonsillectomy. In conclusion, both UA conductance and the tonsil score predicted treatment response [75].

Obese Children

Mihaescu et al. evaluated computational simulation of pre- and post-AT by MRI in an obese child. A significant pressure drop was observed at the site of minimum CSA. There was an increase in airway CSA of the retropalatal pharynx. These findings indicate that ATE is associated with changes in flow characteristics [92]. A retrospective cohort study investigated whether CFD model endpoints correlated with treatment response of ATE in 10 obese children. MRI and CFD data before and after surgery were utilized to calculate the velocity and air pressure distribution. They reported more significant correlations between decreased OSA severity and CFD than with UA anatomical parameters [93].

Children with DS

Only one study investigated whether UA imaging combined with CFD could characterize treatment outcome in children with DS and OSA. They concluded that there was no extra value of CFD in prediction of treatment outcome. However, this was a relatively small study and further studies including larger samples of patients before treatment are needed to validate a model to predict treatment outcome [76].

In conclusion, FRI is a relatively new promising method that may can help in treatment selection. There are only a few studies in children; most of the studies are small. A prospective cohort study concluded that FRI and clinical assessment predicted treatment outcome in children without risk factors. More research is needed to investigate the predictive value in children with DS and obese children because the percentage of residual OSA is higher in these populations.

(Long-Range) Optical Coherence Tomography

Optical coherence tomography (OCT) is another new noninvasive imaging modality to image the UA [94]. This is a diagnostic evaluation without radiation and sedation. This tool utilizes a broadband light source to produce high-resolution cross-sectional images of tissue components with a resolution of 10 µm. The UA can be scanned in approximately 20–40 seconds. The produced images are similar in resolution to those of conventional microscopy. Ridgway et al. investigated the utility of OCT in characterizing the microanatomy of the UA in 15 children in vivo. They concluded that this technique identifies the epithelium and lamina propria [95]. Long-range OCT (LR-OCT) puts the emphasis on a longer range capture of airway wall location by a rotary fiber optic for helical scan to quantify size and shape of hollow organs such as the UA to generate accurate 3D reconstructions (Fig. 16.8). CFD simulations can be performed on these models [96–98].

Two studies investigated the value of OCT in children with OSA. Lazarow et al. investigated the feasibility of LR-OCT to identify airway narrowing in children who underwent ATE. They demonstrated that CSAs were measurably larger in 46 children after ATE [97]. Another study presented the first, airflow simulations by CFD in pediatric airways. They assessed the effect of three realistic airway curvatures in eight children on predicted airway resistance by CFD (before and after ATE). The LR-OCT imaging was incorporated into airway endoscopy exams conducted as part of the standard care before and after surgery. The imaging selection was based on the best signal-to-noise ratio, the best contrast between air and tissues, and the least loss of structure. The airway surface was subjected to a bending algorithm implemented in the software to cure the vertical reconstruction. The algorithm was based on planar curves to sagittal CT and MRI imaged of three normal children. CSA values were obtained by using the area calculation function in Mimics™. Minimal CSA (mCSA) values were calculated by averaging the areas of five consecutive CSAs corresponding to a 1- or 2- mm thick slab of the OCT data of the smallest CSA value. Steady-state, inspiratory airflow simulations were conducted under laminar conditions, along with turbulent simulations by CFD. In this study, CFD findings corroborated that postoperative airway resistance was significantly less compared to pre-operative data. The individual resistances did not vary for different curvatures. This suggests that airway curvature may not be predictive of surgical effects on airway resistance [98].

In summary, this is a novel noninvasive technique to create 3D reconstructions of the UA using OCT images from pre- and postoperative cases. These 3D models provide insight into its structure and shape and can help identify regions of obstruction without radiation. It can be feasibly

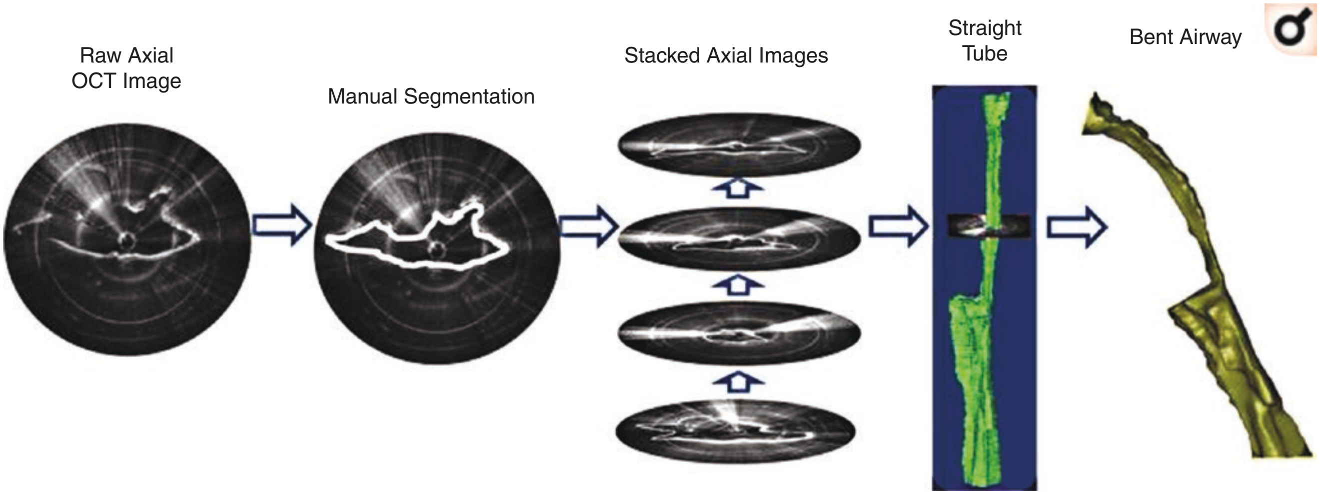

Fig. 16.8 Images converted to 3D model using Mimics software. (From Lazarow et al. [97]. Reprinted with permission from Elsevier)

obtained intraoperatively. Furthermore, more research needs to investigate the predictive value of these reconstructions for surgery selection and compare data in awake and sedated patients.

Drug-Induced Sleep (Sedation) Endoscopy (DISE)

DISE is another method to evaluate the level and degree of UA obstruction (Fig. 16.9). It allows UA visualization by flexible endoscopy or bronchoscope while the child is sedated. It is a promising technique in selecting the type of UA surgery because it provides live video of UA obstruction. There is no need for radiation; it is a simple, safe, and cost-effective technique [99]. However, its interpretation requires experience and the use of a standard protocol is recommended [99–111]. There are over 21 scoring methods described, of which six are in pediatric OSA. Only two studies reported a correlation between the scoring system and OSA severity [101, 102]. Another disadvantage is the utility of sedation during DISE as described earlier in MRI. A recent systematic review suggested that dexmedetomidine and ketamine do not lead to respiratory depression and are associated with less muscular relaxation, with a more sustained respiratory effort [53, 54]. Thereby, a disadvantage of DISE over cine MRI is that it is not possible to visualize multiple levels of obstruction at the same time. Besides, it is not possible to visualize the depth and thickness of abnormal tissues, such as enlarged lingual tonsils, what could be the cause of tongue base collapse [99].

The potential role for DISE prior to ATE and the effect on treatment outcome is not well defined and is subject of controversy. A review recommended not to systematically use DISE in otherwise healthy infants and children with OSA without prior UA surgery [105]. This recommendation contrasts with previous studies which have shown that DISE prior to ATE may change the surgical decision making, also in surgically naïve children [101, 104, 106–109].

Fig. 16.9 An image during the endoscopy

In conclusion, pre-operative assessment combining DISE could have better outcomes than routine Ear Nose and Throat (ENT) examinations in pediatric OSA. Currently, there is no universally accepted standard score system, this will be necessary in order to provide a more consistent method. More research is needed in all groups of risk factors to determine the role for predicting treatment outcome.

Future Developments

Virtual surgery based on 3D constructions would be the next logical research opportunity in choosing an effective surgical strategy [112]. Children with DS or obese children should be prioritized because the percentage of residual OSA is much higher in these populations. A recent pilot study of Mylavarapu et al. investigated the use of virtual surgery and compared virtual surgery with actual surgery. Virtual surgeries were performed on 10 patients with moderate-to-severe OSA. Changes in oAHI and upper airway resistance, as calculated by computational fluid dynamics for pre- and post-operative modeling, matched well for 8 of 10 patients. Limitations of this study were that the authors did not describe the influence of age and did not compare the virtual surgery with surgical changes in anatomy by MRI after treatment [113, 114]. More research is needed to confirm the clinical usability of this technique in surgical planning and studies that investigate the prediction of treatment outcome. Additionally, there is need for more research using imaging or DISE in children with persistent OSA after treatment. The aforementioned use of virtual surgery modeling could also be expanded beyond ATE surgery.

Summary

Many (surgical) options exist for treatment of pediatric (persistent) OSA. In the present era of personalized medicine, progress has been made in identifying the exact cause of OSA in children.

There are limited data on the usefulness of the different imaging techniques as a diagnostic tool in pediatric OSA and predictive value for treatment outcome. Most of the studies had small sample sizes with different inclusion and exclusion criteria. These simple techniques can already assist in predicting the severity of OSA and are minimally invasive. Thereby, there is a suggestion that functional imaging or virtual surgery could be of extra value in predicting treatment outcome. However, more research is needed to confirm the clinical utility of these techniques. Thereby, a comparison of the different imaging methods, including cost-effectiveness analysis, is warranted.

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