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OBJECTIVE EVALUATION OF NASAL DIMENSIONS IN CHILDREN WITH ACOUSTIC RHINOMETRY

by

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To my family

ABSTRACT

Lotta Haavisto. **Objective evaluation of nasal dimensions in children with acoustic rhinometry.** The Department of Otorhinolaryngology – Head and Neck Surgery, University of Turku, Turku, Finland.

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Aims: This study was carried out to investigate the usefulness of acoustic rhinometry in the evaluation of intranasal dimensions in children. The aim was to define reference values for school children. In addition, the role of the VAS scale in the subjective evaluation of nasal obstruction in children was studied.

Materials and methods: Measurements were done with Acoustic Rhinometry A1. The values of special interest were the minimal cross-sectional area (MCA) and the anterior volume of the nose (VOL). The data for reference values included 124 voluntary school children with no permanent nasal symptoms, aged between 7 and 14 years. Data were collected at baseline and after decongestion of the nose; the VAS scale was filled in before measurements. The subjects in the follow-up study (n=74, age between 1 and 12 years) were receiving intranasal spray of insulin or placebo. The nasal symptoms were recorded and acoustic rhinometry was measured at each control visit.

Results: In school children, the mean total MCA was 0.752 cm^2 (SD 0.165), and the mean total VOL was 4.00 cm^3 (SD 0.63) at baseline. After decongestion, a significant increase in the mean TMCA and in the mean TVOL was found. A correlation was found between TMCA and age, and between TVOL and height of a child. There was no difference between boys and girls. A correlation was found between unilateral acoustic values and VAS at baseline, but not after decongestion. No difference was found in acoustic values or symptoms between the insulin and placebo group in the follow-up study of two years.

Conclusions: Acoustic rhinometry is a suitable objective method to examine intranasal dimensions in children. It is easy to perform and well tolerated. Reference values for children between 7 and 14 years were established.

Key words: Acoustic rhinometry, minimal cross-sectional area, children, reference values, visual analogue scale, VAS, follow-up

TIIVISTELMÄ

Lotta Haavisto. **Lasten nenän rakenteiden objektiivinen tutkiminen akustisella rinometrilla.** Korva-, nenä- ja kurkkutautioppi, Turun Yliopisto, Turku, Suomi.

Annales Universitatis Turkuensis, Medica-Odontologica, Painosalama Oy 2011, Turku, Suomi.

Tavoite: Tutkimuksen tarkoituksena oli selvittää akustisen rinometrin käyttökelpoisuutta lasten nenän rakenteiden tutkimisessa. Tavoitteena oli asettaa vertailuarvot kouluikäisille lapsille. Lisäksi tutkittiin, miten VAS-jana soveltuu lasten nenän tukkoisuuden subjektiiviseen arviointiin.

Aineisto ja menetelmät: Mittaukset tehtiin Acoustic Rhinometry A1 -laitteella. Arvioinnin kohteena olivat erityisesti nenän etuosan minimipinta-ala ja tilavuus. Tutkimukseen osallistui 124 vapaaehtoista 7-14 -vuotiasta koululaista, joilla ei ollut jatkuvia nenäoireita. Mittaukset tehtiin sekä perustilanteessa että limakalvojen supistuksen jälkeen. Lapset täyttivät VAS-janan ennen jokaista mittausta. Seurantatutkimukseen osallistuneet lapset (n=74, ikä 1-12 vuotta) käyttivät nenään suihkutettavaa insuliinia tai lumelääkettä. Kontrollikäyntien yhteydessä kartoitettiin mahdollisten nenäoireiden esiintyminen ja tehtiin nenämittaus akustisella rinometrilla.

Tulokset: Kouluikäisten lasten sierainten yhteenlaskettu minimipinta-ala oli 0.752 cm^2 (SD 0.165) ja tilavuus 4.00 cm^3 (SD 0.63). Arvot suurenivat merkitsevästi limakalvojen supistuksen jälkeen. Lasten iän ja sierainten minimipinta-alan välillä todettiin merkitsevä korrelaatio, samoin kuin lasten pituuden ja nenän tilavuuden välillä. Poikien ja tyttöjen välillä ei ollut eroa. Perustilanteessa mitatut yhden sieraimen arvot korreloivat VAS-janalla tehtyyn arvioon, mutta yhteyttä ei voitu osoittaa limakalvojen supistamisen jälkeen. Seurantatutkimuksessa ei havaittu eroa nenäoireissa tai mittaustuloksissa insuliini- ja lumelääkeryhmien välillä kahden vuoden seurannan aikana.

Johtopäätökset: Akustinen rinometri sopii lasten nenän rakenteiden arviointiin. Mittaus on hyvin siedetty ja vaivaton suorittaa. Tutkimuksen perusteella voitiin asettaa 7-14 -vuotiaille lapsille käyttökelpoiset vertailuarvot.

Avainsanat: Akustinen rinometri, minimipinta-ala, lapset, vertailuarvot, VAS-jana, seuranta

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ABBREVATIONS

BMI	body mass index
BSA	body surface area
dB	decibel
CT	computed tomography
DIPP	Type I Diabetes Prediction and Prevention Study
DMCA	distance of the minimal cross-sectional area from the nostril
DMCAl	distance of the minimal cross-sectional area from the nostril on the left side
DMCAr	distance of the minimal cross-sectional area from the nostril on the right side
MCA	minimal cross-sectional area
MCAl	minimal cross-sectional area on the left side
MCAr	minimal cross-sectional area on the right side
MRI	magnetic resonance imaging
NCI	Nasal Congestion Index
nCPAP	nasal continuous positive airway pressure
NOSE	Nasal Obstruction Symptom Evaluation scale
NPIF	nasal peak inspiratory flow
OSA	obstructive sleep apnea
SNOT-20	Sino-Nasal Outcome Test 20
SNOT-22	Sino-Nasal Outcome Test 22
TMCA	total minimal cross-sectional area as the sum of left and right side
TVOL	total nasal volume as the sum of left and right side
VAS	visual analogue scale
VOL	nasal volume
VOLl	volume between 0 and 3 cm from the nostril on the left side
VOLr	volume between 0 and 3 cm from the nostril on the right side

LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following publications, which are referred to in the text by their Roman numerals I-IV. The original communications have been reproduced with the kind permission of the copyright holders.

I Haavisto LE, Sipilä JI. Acoustic rhinometry in children: some practical aspects and influence of age and body surface area on results. Am J Rhinol 2008; 22(4): 416-419.

II Haavisto L, Vahlberg T, Sipilä J. A follow-up study with acoustic rhinometry in children using nasal insulin. Rhinology 2010; 48: 95-99.

III Haavisto LE, Vahlberg TE, Sipilä JI. Reference values for acoustic rhinometry in children at baseline and after decongestion. Rhinology 2011; 49: 243-247.

IV Haavisto LE, Vahlberg TJ, Sipilä JI. Correlation between acoustic rhinometry and visual analogue scale in children with no nasal symptoms: A prospective cohort study. Clin Otolaryngol 2011; 36: 129–133.

1 INTRODUCTION

The development of acoustic rhinometry started in 1977 when Jackson et al published their study on measuring airway geometry by analysis of acoustic pulse response. The method was based on a sophisticated algorithm presented by Ware and Aki in 1969. Sound reflection was first applied to the lower respiratory tract (Jackson et al 1977, Hilberg et al 1989, Fisher 1997) and was used to measure lungs, trachea and later pharynx and supraglottal oral cavity.

The Aarhus group was the first to use the method to evaluate the nose (Hilberg et al 1989). They stated that acoustic rhinometry provides an accurate and easy-to-use method for measuring nasal geometry. Since then, acoustic rhinometry has been under intense development.

During these decades, there has been a need for guidelines for optimal application of the method. In 2000, the Standardisation Committee on Acoustic Rhinometry proposed preliminary recommendations for standard operating procedures (Hilberg and Pedersen 2000), and finally, in 2005, the Consensus report on acoustic rhinometry was published (Clement and Gordts 2005).

Many reference values for a normal adult population have been established in the literature for acoustic rhinometry (Grymer et al 1991, Hilberg et al 1995, Grymer et al 1997, Corey et al 1998, Millqvist et al 1998, Straszek et al 2007). In addition, efforts have also been made to find normal values for children, and to establish the role of age, sex, body size, or other specific factor, for optimal clinical use of the method in children (Ho et al 1999, Jurlina et al 2002, Millqvist and Bende 2006, Qian 2007, Straszek et al 2007, Straszek et al 2008). However, no complete consensus has been found so far.

2 REVIEW OF THE LITERATURE

2.1 Acoustic rhinometry

2.1.1 Principles of the method

The method is based on acoustic reflections that arise with changes in the local acoustic impedance (Jackson 1977 et al, Hilberg et al 1989, Fisher 1997, Clement and Gordts 2005). The changes in impedance result from the changes in the cross-sectional area of the nasal cavity. The area can be calculated at any point by using the data of reflections. It is possible to determine the distance of a certain change in cross-sectional area by taking into account the time interval between the incident and reflected waves (see Figure 1).

The audible sound pulse (150 to 10 000 Hz) is generated by a spark. The pulse passes through a wave tube and a nosepiece into the nose and is reflected by changes in acoustic impedance in the narrowing and widening of the nasal cavity. The reflected and incident sound travels back along the wave tube and is acquisitioned by a microphone. The analogue signal is then low-pass filtered, amplified, digitized and analysed by a computer over time. Delay, frequency and amplitude of reflected sound are analysed as explained above. The measurement lasts 8 ms.

Theoretically, there are some hypotheses to be fulfilled for optimal results (Hilberg et al 1989, Fisher 1997). First of all, it is assumed that sound waves propagate as plane ones, which is probably true in the nasal cavities. The second assumption is that walls are rigid and non-compliant. The nasal cavity is covered by a soft mucosa, but the walls consist of firm bone and cartilage. Thirdly, it is assumed that the loss of sound energy is minimal. This may be a problem in the narrowest part of the nasal cavity at the anterior valve area, and can be responsible for the underestimation of areas beyond it. This issue is further discussed later. Finally, the mathematical model presumes symmetrical and regular branching of the airway, but this is neither completely fulfilled in the nose.

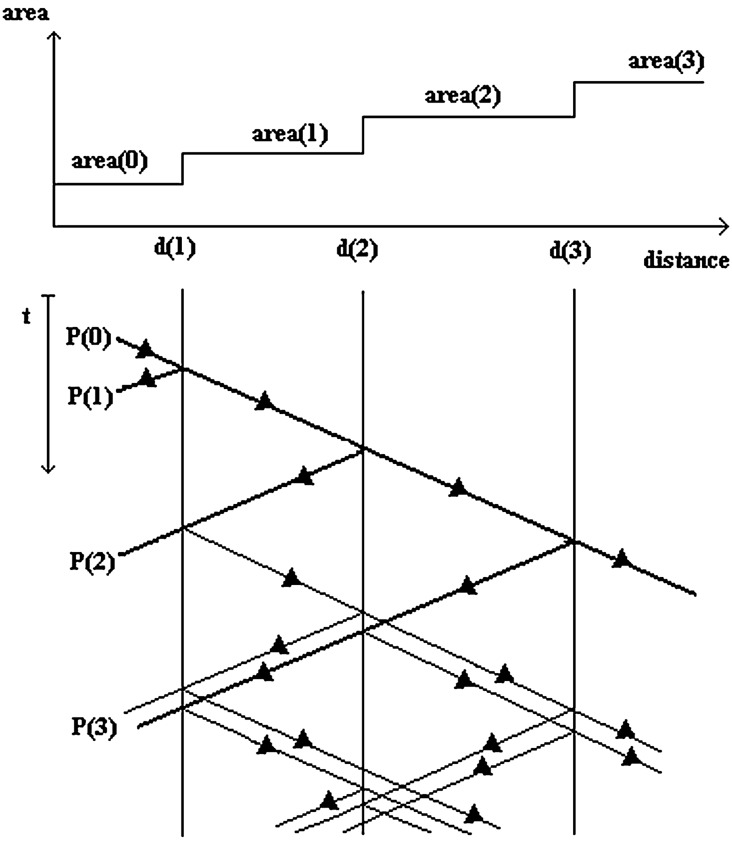


Figure 1. The characteristic impedance of the hypothetical acoustic transmission line as a function of distance and reflections resulting from the incident wave. P(0) = incident pressure wave; P(1) = first reflected pressure wave; P(2), P(3) = next reflected pressure waves; d = distance of impedance discontinuity; t = time. *Modified from Jackson et al. Airway geometry by analysis of acoustic pulse response measurements. J Appl Physiol 1977; 43(3): 523-536.*

The resolution of acoustic rhinometry is determined by the sampling frequency of the equipment. Resolution means the ability to discriminate between areas along the distance axis (Hilberg and Pedersen 2000). Fisher et al (1994) demonstrated that a sphere of 7.0 mm diameter (corresponding to volume change of 1.44 cm^3 and area change of 1.54 cm^2) is measurable by acoustic rhinometry with an impulse technique. In a nose model the resolution has been as good as 3 mm (Hilberg et al 1989), but such a good resolution has not been achieved in a living nose (Fisher et al 1994).

The original technique is based on short-pulsed clicks. Later on, a technique with continuous wide-band noise generated by a digital signal processor instead of pulsed emissions was introduced (Djupesland and Lyholm 1997). The new technique improves the repeatability and accuracy of the measurements. In addition, it is faster and more suitable for infants with small dimensions, especially when used with a miniprobe (Djupesland and Lyholm 1997).

2.1.2 Sources of error

Different types of factors influence the reliability of acoustic rhinometry. Some of the limitations result from the mathematical background, and some are technical or environmental in origin (Table 1).

Table 1. Possible sources of error.

Instrumentation and measuring procedure	
	Shape and size of the nosepiece
	Use of gel
	Distortion of the nose
	Insertion of the nosepiece
	Angle of the tube
Patient	Acclimatisation
	Breathing
	Swallowing
	Lack of co-operation
Operator	Training
	Curve selection procedure
Environmental	Background noise
	Room temperature

The theoretical model assumes that the loss of sound energy is minimal. Nevertheless, the narrowest part of the nose usually lies within the first 3 cm (Clement and Gordts 2005) and this may cause viscous losses. It has been shown that if the narrowing in the nose is less than 0.6-0.7 cm^2, or if the narrowing is less than 30-40 % of the internal cross-sectional area of the probe, it can cause underestimation of the more distal areas and volumes (Hilberg et al 1989, Fisher 1997, Djupesland and Lyholm 1998a, Cakmak et al 2005). On the other hand, this underestimation also depends on the shape of the obstruction (Hilberg et al 1989, Hilberg 2002).

In children, it has been estimated that a minimal area less than 0.2 cm^2 can cause underestimation of the distal areas (Riechelmann et al 1993). This underestimation of area because of energy loss was confirmed by Buenting et al (1994b). In addition, they found an oscillation artefact beyond small cross-sectional areas. These oscillations actually grew in magnitude as the area decreased.

The accuracy of acoustic rhinometry diminishes with distance from the nostril (Hilberg et al 1989, Hilberg et al 1993, Fisher 1997, Hilberg and Pedersen 2000, Numminen et al 2003b). This has been explained by the nature of the algorithm used in calculations, and the reflection of sound to the contralateral cavity in the nasopharynx. Recently, it has been argued that the low accuracy of the posterior region beyond the maxillary sinus ostium is due to interaction between the nasal cavity and paranasal sinuses instead of energy loss into the sinuses (Cakmak et al 2005, Tarhan et al 2005). In the study of Tarhan et al (2005), areas beyond the sinus ostia were overestimated when the nasal valve was within normal range and sinus ostium diameter was larger than 0.10 cm. In conclusion, the areas within the first 6 cm are more accurate than the areas beyond.

Acoustic rhinometry is very sensitive to sound leaks which cause massive overestimation of the nasal area (Hamilton et al 1997). Using gel between the nose and the adapter helps to prevent sound leakage, diminishes the overestimation of the area (Hamilton et al 1997, Parvez et al 2000), and also improves the reliability and speed of measurements (Parvez et al 2000).

Distortion of the nostril may affect the anterior part of the nose and cause errors in the area of the valve region (Hilberg and Pedersen 2000). On the other hand, the forced insertion of the nosepiece may cause an error if conical nosepieces are used instead of anatomical nosepieces (Hamilton et al 1997). The deformation of the vestibulum is shown to be less when using the anatomical nosepiece instead of the conical nosepiece (Fisher et al 1995a, Cole 2000*)*.

The spatial alignment of the wave tube has been considered to be one possible cause of error and previously chin supports or stands were used (Grymer et al 1991, Cole 2000, Djupesland and Pedersen 2000). The most appropriate angle seems to be 45^o in the vertical plane and $8\text{-}10^o$ in the horizontal plane (Parvez et al 2000), but the role of the exact angle is minor in comparison to the proper fit with the nostril (Hilberg et al 1977, Djupesland and Pedersen 2000). It is acceptable to handhold the wave tube for more flexible use, and to avoid distortion of the nose (Fisher et al 1995a, Cole 2000, Parvez et al 2000, Clement and Gordts 2005). The use of anatomical nosepieces helps to maintain a stable angle between the sound tube and the nose (Djupesland and Pedersen 2000).

External noise results in a higher coefficient of variation in area distance curves (Parvez et al 2000). It is recommended to keep the ambient noise level below 60 dB (Djupesland and Lyholm 1998a, Parvez et al 2000). Temperature changes will change the sound velocity and the recorded distance (Djupesland and Lyholm 1998a), so a period of acclimatization is recommended before measurements (Sipilä et al 1996).

Breathing during the measurements can cause overestimation of the nasal volumes. A brief pause in breathing also makes the measuring session faster (Parvez et al 2000). In the study of Tomkinson and Eccles (1995a), the minimal cross-sectional area increased during expiration, and decreased during inspiration, especially if the opposite nostril is obstructed. In the same way, it is assumed that swallowing can induce pressure changes by the motion of the soft palate (Hilberg et al 1977, Hilberg and Pedersen 2000).

Training of the operator reduces the measurement time, along with the number of curves needed, and makes it easier to carry out repeated measurements of good quality (Parvez et al 2000). In order to eliminate false curves, training is also crucial for curve selection procedures. To fulfil a standard, at least three acceptable curves are needed for calculations (Djupesland and Pedersen 2000).

Buenting et al (1994b) concluded that an acoustic rhinometry system suitable for adults may yield errors in a pediatric population. Similarly, Riechelmann et al (1993) found that artefacts are more common in children than in adults. It is recommended to use smaller wave tubes and special nosepieces for children, especially for infants, in order to avoid underestimation of distal areas and overestimation of the nasal valve area (Buenting el al 1994b, Djupesland and Lyholm 1997, Djupesland and Lyholm 1998b, Hilberg and Pedersen 2000, Baczek et al 2001, Liukkonen et al 2006). One possibility is to use continuous wide-band noise for better resolution in small children (Djupesland and Lyholm 1997, Djupesland and Pedersen 2000). The collaboration with children seems to be most difficult in age group three-to-four-year-olds (Riechelmann et al 1993, Liukkonen et al 2006).

2.1.3 Standardisation of the measurements

The guidelines for standardisation of acoustic rhinometry were presented by the Standardisation Committee on Acoustic Rhinometry in 2000 (Hilberg and Pedersen 2000), and further specified in 2005 in a Consensus Report (Clements and Gordts 2005). The standardisation procedure is essential in order to enhance the validity of the measurements, and to compare results between different centres and equipment (Hilberg and Pedersen 2000). The guidelines for optimal application are also needed because of some important causes of error as described above.

Some specific definitions are used to determine the quality of measurements. Repeatability of the measurements means that results are constant when the same operator uses the same instrument in the same way over a short period of time in constant conditions. The mean coefficient of variation in repeated measurements has varied between 2 % and 15 % (Hilberg et al 1989, Sipilä et al 1996, Hilberg and Pedersen 2000).

Accuracy means the difference between the measured and the true area (Hilberg and Pedersen 2000). A standard nose can be used to test the accuracy and repeatability of acoustic measurements (Djupesland and Lyholm 1997, Hilberg and Pedersen 2000). A standard nose is a circular tube with an area-distance function equivalent to that of a normal nose. It should be delivered by the manufacturer and used daily before any measurements. The accuracy seems to decrease as the distance from the nostril increases (Jackson et al 1977, Fisher 1997, Hilberg and Pedersen 2000, Tarhan et al 2005). The accuracy has been tested by comparing the results with other methods to evaluate area and volume. The correlation has been good with CT scans in cadavers (Hilberg et al 1989, Mayhew and O'Flynn 1993), with CT scans in subjects (Cakmak et al 2003, Tarhan et al 2005, Cankurtaran et al 2007, Muñoz-Cano 2010), and with the water displacement method in subjects (Hilberg et al 1989). The correlation was also reasonable with MRI in non-decongested noses, but the acoustic method seemed to overestimate volumes by 15 % in comparison to MRI (Hilberg et al 1993). Additionally, in the study of Corey et al (1999), the anatomic accuracy was confirmed by comparing acoustic rhinometry with endoscopic findings.

Reproducibility of the measurements describes the consistency of the results with changing conditions. The reproducibility has varied between 1 % and 10 % (Grymer et al 1991, Djupesland and Lyholm 1998a, Silkoff et al 1999, Cole 2000). To control changing conditions and other sources of error, a Standard operating procedure described by Hilberg and Pedersen (2000) should be followed. The procedure pays attention to acclimatisation to room temperature, breathing pause, actual room temperature, external noise, avoidance of acoustic leak and distortion of the nose, and training of the operator, as well as curve selection procedures.

2.1.4 Acoustic values and anatomic relations

The best way to evaluate the results is to consider the entire curve prior to single values (Hilberg and Pedersen 2000). The typical shape of a normal curve is schematically illustrated in Figure 2.

The most used value in literature is the minimal cross-sectional area (MCA), mostly located within the first 5 cm (Hilberg and Pedersen 2000, Clement and Gordts 2005). Another value of interest is the distance of the MCA from the nostril (DMCA). This value helps to determine the anatomical location of the MCA.

Usually, in the normal nose, the anterior part includes two minima of the cross-sectional area (Grymer et al 1991, Cole 2000, Hilberg and Pedersen 2000, Clement and Gordts 2005). The first notch corresponds to the nasal valve and is by some authors called the *I-notch* (isthmus area) or CSA1 (cross-sectional area 1). The second notch which corresponds to the anterior part of the inferior turbinate is often called the *C-notch* (concha as head of the inferior turbinate), or in some cases CSA2 (cross-sectional area 2) (Lenders and Pirsig 1990, Corey et al 1999, Cole 2000, Hilberg and Pedersen 2000, Clement and Gordts 2005, Eduardo Nigro et al 2009). Direct and endoscopic measurements have been used to confirm the actual distance between columella and inferior turbinate (Grymer et al 1991, Corey et al 1999). The site of the nasal valve has been confirmed by comparing acoustic values with CT scans (Cankurtaran et al 2007).

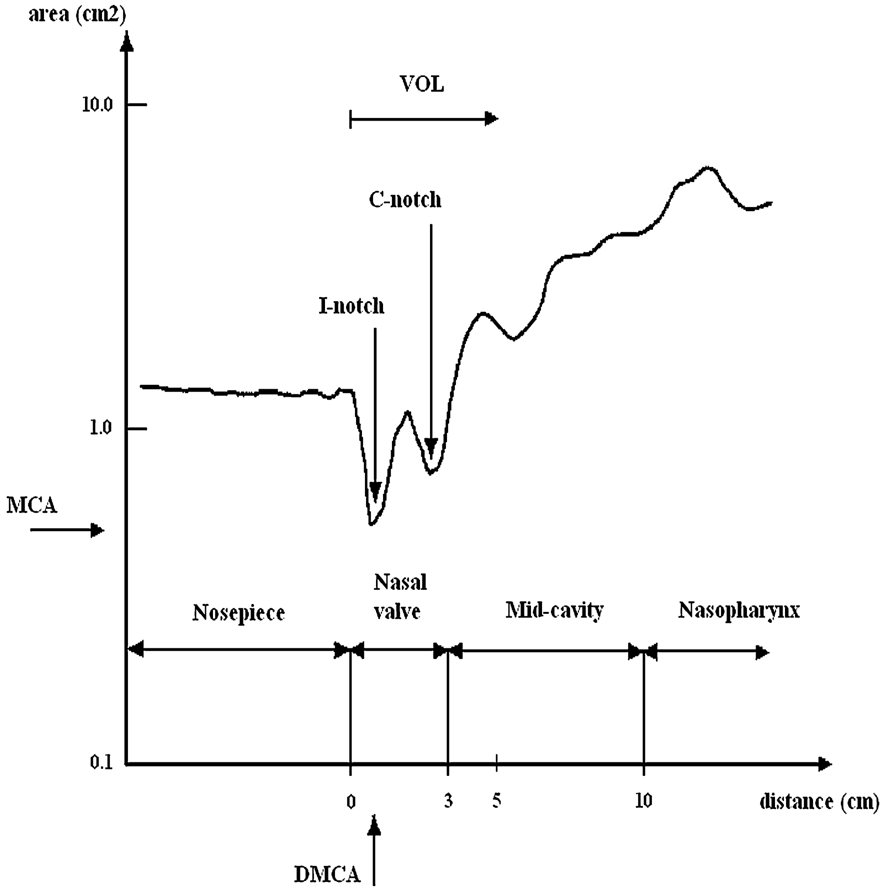


Figure 2. A schematic drawing of a normal curve of acoustic rhinometry. I-notch = isthmus area; C-notch = concha, anterior part of the inferior turbinate; MCA = minimal cross-sectional area; DMCA = distance of the minimal cross-sectional area; VOL = volume between 0 and 5 cm from the nostril. *Modified from Fisher EW. Acoustic rhinomanometry. Clin Otolaryngol 1997; 22: 307-17.*

It has been suggested that the first notch might be an artefact caused by a nosepiece or might rather correspond to the nostril (Clement and Gordts 2005, Tikanto and Pirilä 2007, Gomes et al 2008, Eduaro Nigro et al 2009). In that case, the second notch in the curve is called *I-notch* and corresponds to the nasal valve. This alternative interpretation of the curve is illustrated in Figure 3. Even more surprisingly, it has been claimed that the second, third and fourth notches may all be caused by acoustic resonances and do not correspond to any anatomical structures (Cankurtaran et al 2007). This may be true in the posterior part of the nasal cavity (beyond 6 cm) and in the nasopharynx due to interaction between nasal cavity and paranasal sinuses, as described above (Cakmak et al 2005, Tarhan et al 2005).

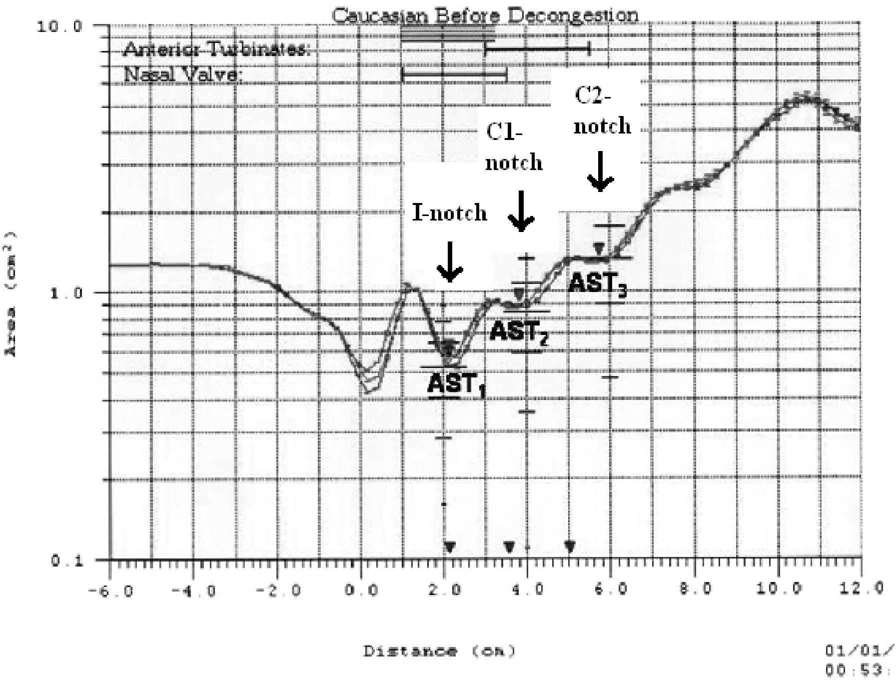


Figure 3. An alternative interpretation of a normal curve of acoustic rhinometry. The first notch corresponds to the nostril. I-notch = isthmus area; C1-notch = concha, anterior part of the turbinates; C2-notch = concha, posterior part of the turbinates. *From Gomes AO, Sampaio-Teixeira AC, Trindade SH, Trindade IE. Nasal cavity geometry of healthy adults assessed using acoustic rhinometry. Braz J Otorhinolaryngol 2008; 74: 746-754.*

On the contrary to older children and adults, infants seem to have only one minimum instead of two (Buenting et al 1994a, Djupesland and Lyholm 1997, Baczek et al 2001). This is considered to be a true difference in nasal geometry and can be detected using a mini-probe designed for infants (Djupesland and Lyholm 1997).

In addition to MCA, it is recommended that nasal cavity volume (VOL) at the distance from 0 to 5 cm should be given (Hilberg and Pedersen 2000, Clement and Gordts 2005). For mucosal changes the volume between 2 and 5 cm may be more appropriate, because the most anterior part of the nose does not include erectile tissue responsible for decongestion of the mucosa (Hilberg and Pedersen 2000, Clement and Gordts 2005, Straszek et al 2007).

Sometimes, total values of the areas and volumes as a sum of left and right sides are used to describe the status of the whole nose or to avoid the effect of the nasal cycle. In the same way, these values (MCA, DMCA and VOL) can be measured before and after decongestion of nasal mucosa to determine the role of mucosal swelling (Hilberg et al 1995a, Corey et al 1997, Clement and Gordts 2005, Straszek et al 2007). Decongestion of the mucosa can be achieved with locally administered ephedrine, xylometazoline hydrochloride, or with a combination of both (Grymer et al 1997).

2.1.5 Reference values

2.1.5.1 Adults

Many reference values of acoustic rhinometry for a normal adult population have been established in the literature (Grymer et al 1991, Hilberg et al 1995, Grymer et al 1997, Corey et al 1998, Millqvist et al 1998, Straszek et al 2007). The unilateral MCA in the non-decongested nose has varied between 0.50 cm^2 (SD 0.02) and 0.98 cm^2 (SD 0.18), and after decongestion between 0.64 cm^2 (SD 0.12) and 0.92 cm^2 (SD 0.02). Hilberg and Pedersen (2000) performed a meta-analysis of an adult population of 1756 subjects. They found the average unilateral MCA to be 0.60 cm^2 +/- 0.18 (SD).

Reference values of volume between 0 and 7 cm from the nostril have varied between 20.5 cm^3 and 22.6 cm^3 before decongestion, and between 27.7 cm^3 and 31.0 cm^3 after decongestion (Grymer et al 1991, Hilberg et al 1995, Straszek et al 2007).

Grymer et al (1997) suggested that a MCA of 0.50 cm^2 in a non-decongested nose and a large effect of decongestion could be the best variables to separate obstructed noses from normal ones. Later on, the same group further concluded that a MCA less than 0.35 cm^2 could indicate a feeling of obstruction (Hilberg and Pedersen 2000). In a recent review, a MCA less than 0.40 cm^2 after decongestion indicated obstruction that might be corrected by surgery (Holmström 2010).

To make the discussion of normal values more interesting, some groups have suggested that normal values are not useful in a single patient because of large inter-individual variations (Larsson et al 2001, Millqvist and Bende 2006, Andre et al 2009). However, the situation may be different after decongestion of the mucosa (Holmström 2010).

2.1.5.2 Children

Efforts have also been made to find normal values for children in different age groups. Values published so far for infants, pre-school children, and school children are summarized in Appendix 1. In these studies, subjects under 17 years are considered to be children. In fact, it has been concluded that the growth of the nose is usually completed by the age of 16 years (Samolinski et al 2007).

The acoustic values most commonly used in a pediatric population are MCA and total MCA (TMCA). In addition, values for nasal cavity volumes are also used. It may be difficult to compare results of different studies because of large variations in the ways establishing nasal volume (see Appendix 1). Only a few groups give values after decongestion in children.

The first values for infants were introduced by two groups in 1994 (Buenting et al 1994a, Pedersen et al 1994). The unilateral MCA for term infants has been reported to be between 0.08 cm^2 and 0.114 cm^2 (Buenting et al 1994a, Pedersen et al 1994, Djupesland and Lyholm 1997, Baczek et al 2001). Most neonates seem to have only one minimum in contrast to adults or older children with two minima (Djupesland an Lyholm 1997, Bazek et al 2001). No decongestants have been used in infants.

The nasal airway geometry changes significantly during the first year of life. Djupesland and Lyholm (1998b) found an increase of 67% in TMCA, from 0.21 cm^2 to 0.35 cm^2, during the first year. The increase in the volume between 0 and 4 cm was 36% during the same period. On the other hand, the distance of the MCA increased by only 19%. Hence, it may be concluded that the height of the nasal cavity increases more than the depth of the nasal cavity during the first year of life.

In a study of pre-school children, Liukkonen et al (2006) found baseline MCA values in children between one and two years to be 0.32 cm^2 (SD 0.1), in children between three and four years 0.36 cm^2 (SD 0.1) and in children between five and six years 0.40 cm^2 (SD 0.1). They also introduced values after decongestion of the nose. Likewise, Riechelmann et al (1993) found the mean MCA for children between three and six years to be 0.29 cm^2 (SD 0.06), and Ho et al (1999) 0.32 cm^2 (SD 0.12) in the same age group. Qian et al (2007) demonstrated normal values for bilateral nasal cavity volume (from 1.5 to 3.5 cm) in a four-year-old group and a five-year-old group to be 2.0 cm^3 (SD 0.4) and 2.05 cm^3 (SD 0.4), respectively.

In the group of children aged six and seven years, Jurlina et al (2002) found TMCA in the isthmus area to be 1.01 cm^2 (SD 0.09). In their study of Japanese school children between seven and eight years of age, Miyamoto et al (2009) found the mean MCA to be 0.389 cm^2, whereas Millqvist and Bende (2006) found the mean TMCA to be 0.99 cm^2 in the same age group of school children.

The non-decongested values of MCA in school children have varied between 0.33 cm^2 and 0.52 cm^2, and the values of TMCA between 0.95 cm^2 and 1.24 cm^2, depending on the age of the children (Larsson et al 2001, Jurlina et al 2002, Millqvist and Bende 2006, Samolinski et al 2007, Straszek et al 2007, Straszek et al 2008). Ho et al (1999) studied normal values among children between one and 11 years (mean age five years). They found the mean MCA to be 0.32 cm^2 (SD 0.13) in the whole group.

In most cases no decongestant has been used in school children. The only study until now with both baseline and decongested values was published by Straszek et al in 2007. They found an increase in MCA from 0.33 cm^2 to 0.36 cm^2 after decongestion in children between nine and 11 years. A significant increase in the nasal volume at the anterior part of the nose was also detected.

2.1.5.3 Predictive factors

Although most publications give values for acoustic rhinometry in a certain age group there has been some debate about other factors influencing the values. Efforts have been made to establish normative values for nasal airway dimensions in relation to age, sex, body size, or some other specific factor, for optimal clinical use of the method (Ho et al 1999, Jurlina et al 2002, Millqvist and Bende 2006, Qian 2007, Straszek et al 2007, Straszek et al 2008).

2.1.5.3.1 Sex

In infants, some groups have not found any difference between boys and girls (Pedersen et al 1994, Baczek et al 2001). Instead, Djupesland and Lyholm (1997) found that boys had a higher TMCA than girls among healthy term infants.

Larsson et al (2001) found that men had larger noses than women, but no difference was found between boys and girls aged between seven and 17 years. This conclusion is in accordance with the findings of other groups (Riechelmann et al 1993, Millqvist and Bende 1998, Millqvist and Bende 2006, Qian et al 2007, Straszek et al 2007, Straszek et al 2008, Paiva et al 2010).

Miyamoto et al (2009) found that MCA was larger in boys than in girls in children between seven and eight years. On the contrary, Samolinski et al (2007) found that girls had slightly larger nasal cavities than boys up to the age of 11 years, but *vice versa* after the age of 11 years. Thus, the growth rate of the nasal cavities seemed different in boys than in girls in that study.

2.1.5.3.2 Age

The increase in acoustic values during the first year of life is discussed above. A positive correlation between age and acoustic values in children over one year has been found by many groups (Riechelmann et al 1993, Millqvist and Bende 1998, Ho et al 1999, Samolinski et al 2007). In addition, Riechelmann et al (1993) found that MCA increased by 0.024 cm^2 per year in children between three and six years. Samolinski et al (2007) concluded that the growth of the nose is usually completed by age of 16 years, but nasal cavities may slowly continue to increase in size after that.

On the contrary, other groups have not found any significant correlation between age and the MCA (Jurlina et al 2002, Straszek et al 2008). Millqvist and Bende (2006) found large variations among individuals in their follow-up study, and no correlation between increasing age and growth of nasal geometry during a period of two years. Qian et al (2007) found no difference between the volumes of four-year-old and five-year-old children.

2.1.5.3.3 Height, weight, BSA, and BMI

In a large group of children (age 4 to 13 years) Straszek et al (2008) found height to be a significant predictor for all acoustic variables measured. In the same way, a correlation between height and MCA, and height and anterior nasal volume in children has been found by other groups (Millqvist and Bende 1998, Millqvist and Bende 2006). On the other hand, some groups have found a correlation between height and volume, but no correlation between height and MCA (Ho et al 1999, Miyamoto et al 2009). No correlation has been found between height and acoustic values in adults (Tomkinson and Eccles 1995b, Corey et al 1998).

Many groups have found a correlation between acoustic values and weight in children (Millqvist and Bende 1998, Straszek et al 2008, Miyamoto et al 2009), but again, Ho et al (1999) could not find any correlation. In the same way, no correlation has been found in adults between acoustic values and weight (Tomkinson and Eccles 1995b, Corey et al 1998). The same difference in opinions is also related to the birth weight of term infants (Pedersen et al 1994, Baczek et al 2001).

Body surface area (BSA) and body mass index (BMI) can be calculated using the data on height and weight. BSA is mostly used in children, and BMI in adults, but some groups have used BMI in children.

Jurlina et al (2002) found a significant correlation between BSA and MCA in healthy subjects over six years of age. They even suggested that the expected value of each subject’s MCA could be calculated from his/her height and weight with a corrective factor. Also Miyamoto et al (2009) found a weak correlation between MCA and BMI in children. On the contrary, no correlation has been found in adults between acoustic values and BMI (Numminen et al 2002, Kemppainen et al 2008).

2.1.5.3.4 Other

Previously it was assumed that race has a significant effect on acoustic rhinometry measurements (Morgan et al 1995, Corey et al 1998). A recent review including data of 78 references concludes that significant differences in the nasal dimensions exist between ethnic groups, but no differences in nasal physiology can be demonstrated (Leong and Eccles 2009). The article recommends the use of a nasal index calculated from the width and height of the nose instead of any ethnic or racial categories, and states that no method exists for predicting internal nasal dimensions from other external characteristics. In the same way, Tomkinson and Eccles (1995b) found that TMCA showed a good correlation with the alar breadth and the nasal triangular area, but no correlation with other facial or body dimensions in adults.

In infants, there is a controversy about the influence of head circumference on acoustic values. Some groups have not found any predictive value of head circumference on acoustic values (Pedersen et al 1994, Baczek et al 2001), while Djupesland and Lyholm (1998b) found a high correlation between the increase in anterior narrowing of the nasal cavity and head circumference in term infants.

2.1.6 Clinical applications

Acoustic rhinometry is a useful objective method in many clinical situations because it gives practical information on the place and degree of nasal obstruction. In addition, it provides values before and after decongestion of the nasal mucosa. This makes acoustic rhinometry a multipurpose tool for diagnosis and follow-up of treatment in both rhinology and rhinosurgery (Grymer 2000, Corey 2006, Uzzaman et al 2006).

Most clinical studies carried out so far deal with an adult population. However, acoustic rhinometry is a very suitable method for children because it is rapid, non-invasive, with no side-effects, and minimal co-operation is required (Djupesland and Pedersen 2000, Clement and Gordts 2005).

2.1.6.1 Nasal cycle

The nasal cycle is a physiologic phenomenon with cyclic congestion and decongestion in the two nasal cavities. The nasal cycle can be detected with acoustic rhinometry (Fisher et al 1993, Lang et al 2003).

Fisher et al (1995b) found that 80 % of children aged between three and ten years had a classical reciprocal nasal cycle, whereas Gallego et al (2006) found an irregular pattern to be the most prevalent (50%) in the same age group. On the other hand, it has been shown that most infants have no significant fluctuations in nasal patency (Baczek et al 2001).

2.1.6.2 Mucosal changes and nasal challenge

Acoustic rhinometry is a sensitive way to study mucosal changes, and the ability to distinguish reversible and irreversible swelling of nasal mucosa is very important (Corey 2006). The method has been used to observe spontaneous variability and responsiveness to topical decongestants and exercise in allergic and non-allergic persons (Hilberg et al 1995b, Corey et al 1997, Clement and Gordts 2005). Acoustic rhinometry is also sensitive enough to recognize intranasal mucosal changes during common cold (Numminen et al 2003a).

Because of the ability to detect mucosal changes, acoustic rhinometry has been used as an objective tool to measure nasal reaction in nasal provocation tests with histamine, different allergens, and other environmental agents (Scadding et al 1994, Hilberg et al

1995a, Kesavanathan et al 1996, Lane et al 1996, Fisher 1997, Pirilä and Nuutinen 1998, Gosepath et al 2005, Uzzman et al 2006).

The MCA appears to be the most sensitive value in detecting a positive reaction during nasal challenge, but the limitations of the method must be understood (Wang et al 2004). The optimal threshold for a positive test has been suggested to be a 15 % decrease in the MCA during the observation period of 30 min, and a decrease of 30 % for a 60-min observation period (Pirilä and Nuutinen 1998). It should be noted that the variations in the change of the MCA after nasal challenge may be large, and spontaneous variations can be more pronounced in allergic than in non-allergic subjects (Hilberg et al 1995a, Lane et al 1996).

Acoustic rhinometry has been used to study nasal patency and mucosal changes also in children. Chawes et al (2009) found that allergic rhinitis was associated with irreversible nasal airway obstruction in children at the age of six years, whilst children with non-allergic rhinitis had nasal airway patency similar to that of healthy controls. On the contrary, no difference was found in acoustic values between asthmatic and control children aged between two and five years (Steinsvåg et al 2007).

2.1.6.3 Surgery

Acoustic rhinometry can be used before nasal operation to confirm the diagnosis, and after the surgery to evaluate the outcome of the operation. Most commonly, acoustic rhinometry has been used to evaluate the need for surgery of nasal septum and turbinates in adults (Lenders and Pirsig 1990, Grymer et al 1993, Kemker et al 1999, Grymer 2000, Pirilä and Tikanto 2001, Holmström 2010), and even in children (Can et al 2005).

It is recommended to perform some objective measurement before septoplasty because subjective sensation of obstruction can be misleading (Roithmann et al 1994, Sipilä et al 1995, Sipilä and Suonpää 1997, Pirilä and Tikanto 2001, Mlynski 2006), and acoustic rhinometry has been proven to be one of the choices.

In a recent review, MCA less than 0.40 cm^2 after decongestion indicated obstruction that might be corrected by surgery (Holmström 2010).This is in line with the earlier criteria suggested by Grymer (2000). Their group determined the inclusive criteria for surgery on the deviated side to be less than 0.40 cm^2 before decongestion, and less than 0.50 cm^2 after decongestion (Grymer et al 1993). Acoustic rhinometry has also been used to evaluate the results of septoplasty in children (Can et al 2005), but no limit values have been established.

Some efforts have been made to determine the role of acoustic rhinometry in evaluating hypertrophy of the adenoids, but the results remain inconsistent (Cho et al 1999, Riechelmann et al 1999, Marques and Anselmo-Lima 2004). In the same way, the acoustic pharyngometer has failed to assess pharyngeal volumes in a pediatric population

(Hatzakis et al 2003). Nevertheless, Brinckmann et al (2008) found improvement in nasal turbinate region volume after adenoidectomy in children aged five to 11 years.

Even though some groups have found acoustic rhinometry suitable for detecting congenital choanal malformations (Djupesland et al 1997), others state that the method is not useful in posterior nasal conditions such as choanal atresia in adults (Leclerc et al 2008).

Other surgical situations studied with acoustic rhinometry include nasal polypectomy (O'Flynn 1993), and orthodontic procedures such as rapid maxillary expansion (Compradetti et al 2006, Gordon et al 2009). No congruity has been achieved in these fields either.

2.1.6.4 Follow-up

Acoustic rhinometry has been successfully used for a follow-up after nasal surgery for obstruction to measure the objective outcome of the operation (Grymer et al 1993, Pirilä and Tikanto 2001, Ho et al 2004, Can et al 2005, Brinckmann et al 2008). However, acoustic rhinometry is not helpful in the postoperative evaluation of sinus surgery or paranasal sinus ostia (Marais and Maran 1994, Fisher 1997, Tarhan et al 2005).

Larsson et al (2001) concluded that acoustic rhinometry is a suitable tool for following changes in mucosal swelling with time. Furthermore, acoustic rhinometry has potential as an objective method to monitor the effectiveness of medical therapy (Chan et al 2003, Valero et al 2009).

In the follow-up of children, some special aspects must be taken into account. In the study of Millqvist and Bende (2006), a statistically non-significant increase in nasal geometry was found in the follow-up of two years. Nevertheless, they recommended that the normal development of height should be taken into account in long-term studies with acoustic rhinometry in children over seven years of age, but this argument still remains to be proven. Similarly, in a recent study of Paiva et al (2010), no significant change in total MCA was found in a follow-up of children between six and twelve years in the time course of 36-48 months.

2.1.6.5 Sleep apnea and snoring

The role of nasal obstruction in obstructive sleep apnea (OSA) and snoring has been evaluated with acoustic rhinometry (Virkkula et al 2003, Corey 2006, Moris et al 2006). Lower volumes have been found in habitual snorers than in healthy individuals (Yahyavi et al 2008). Similarly, a correlation has been found between nasal volume and the severity of OSA in a supine position but not in a seated position or in decongested values

(Virkkula et al 2003). In addition, Lam et al (2006) found that MCA and nasal volume were significantly lower in the supine than in the upright position.

Even though patients with severe OSA tend to have smaller nasal areas, it seems to be hard to predict from acoustic rhinometry examinations whether patients have sleeping problems (Liu et al 2006). Still, acoustic rhinometry may be helpful in improving the intervention of OSA. Morris et al (2006) found that MCA less than 0.60 cm^2 may indicate intolerance for nasal continuous positive airway pressure (nCPAP) management, and in this situation nasal surgery could improve compliance.

In a recent pilot study in children, Okun et al (2010) found that upright nasal and nasopharyngeal volumes were significantly larger in children with obstructive sleep apnea as compared to primary snorers, while no difference in values was seen in the supine position. The positional changes in nasal volume were strongly predictive of the diagnosis of sleep apnea in children between four and nine years.

2.1.6.6 Other applications

Nasal obstruction may cause severe respiratory distress in infants because they are unable to switch to oral breathing (Holinger and Weese-Mayer 1997, Djupesland and Pedersen 2000). It has been proposed that acoustic rhinometry may assist in determining the role of nasal obstruction as a contributing factor in sudden infant death syndrome because measurements can be performed during sleep and while awake (Djupesland and Pedersen 2000). As a matter of fact, Olarinde et al (2006) have found a significant decrease in total MCA when sleeping newborns were turned from a supine to a lateral position.

2.2 Other objective methods to evaluate nasal patency

In addition to acoustic rhinometry, there are several other usable techniques to test nasal airway patency, or nasal flow. Most of them are also used in clinical practice. The correlation between the different methods has been questionable (Naito et al 2001, Numminen et al 2002, Nathan et al 2005, Lam 2006), although correlations have been found during nasal challenge (Holmström et al 1990, Scadding et al 1994, Pirilä and Nuutinen 1998), and in obstructed noses (Zhang 2008).

In conclusion, many groups recommend the concomitant use of different objective methods and find these methods as complementary to each other rather than alternatives (Pirilä and Nuutinen 1998, Passali et al 1999, Cole 2000, Schumacher 2002, Numminen et al 2002, Lang et al 2003, Numminen et al 2003a, Lam et al 2006, Zhang 2008, Holmström 2010).

2.2.1 Rhinomanometry

Rhinomanometry is generally accepted as a standard technique for assessing the patency of the nose (Nathan et al 2005). Rhinomanometry is based on the simultaneous registration of nasal airflow and pressure difference between the anterior and the posterior parts of the nose. The nasal resistance is further calculated from these values (Clement 1984, Clement 1997, Cole 2000, Hilberg 2002, Clement and Gordts 2005).

The guidelines for optimal use of rhinomanometry are published by the International Standardisation Committee and should be followed (Clement 1984, Clement and Gordts 2005). Because of its functional character, rhinomanometry can be defined as a dynamic method (Naito et al 2001, Pirilä and Tikanto 2001, Schumacher 2002).

Active anterior rhinomanometry is one of the most commonly used methods in clinical practice. It means that the patient is actively breathing through one nostril while the pressure difference is assessed on the contralateral side. Active posterior rhinomanometry means that the postnasal pressure is measured with a catheter placed inside the oral cavity. In passive rhinomanometry, an artificial flow is blown through the nose and the resulting pressure difference is measured.

The latest development of rhinomanometry is the four-phase active anterior rhinomanometry. This method provides supplementary information about inspiration and expiration, but the clinical role of the method is still unclear (Clement and Gordts 2005).

Another development of active anterior rhinomanometry is rhinoresistometry which provides information about the transition from laminar to turbulent flow in the nasal cavity, and is a measure of functional nasal width and wall configuration triggering turbulence (Lang et al 2003, Clement and Gordts 2005).

2.2.2 Nasal peak inspiratory flow

Nasal peak inspiratory flow (NPIF) is the simplest way to measure the maximum nasal airflow (Hilberg 2002, Holmström 2010). It is easy to perform, suitable for serial measures and for home use. In the same way as rhinomanometry, NPIF can be considered as a dynamic method measuring nasal air flow (Lam et al 2006).

With this method only bilateral values are available and the condition of the lower airways has an influence on the results (Hilberg 2002). Sometimes, instead of NPIF, nasal peak expiratory flow (NPEF) is used because the technique is easier for the patient, but NPIF has better reproducibility (Numminen et al 2003a, Nathan et al 2005).

2.2.3 Other rhinological methods

Rhinohygrometry is the oldest method to study the nasal airway (Zwaardemaker 1894). The method is based on the misting of a cold shiny metal surface by warm airflow. This simple method has been used in adults and children, but the clinical use of it is history (Fisher et al 1995b).

Rhinostereometry has been described by Juto and Lundberg (1982), but only a few groups use this method regularly (Ellegård 2003). The method uses a microscope to measure the distance between the medial (septal) and lateral wall of the nasal cavity.

2.2.4 Imaging

In a recent study of Landa et al (2010), a very strong correlation was found between MCA and volume measured with acoustic rhinometry and the anterior cross-sectional area calculated from panoramic and cephalometric radiographs taken by dentists. The patients were children aged between six and nine years under consideration for orthodontic treatment.

Computed tomography (CT) and magnetic resonance imaging (MRI) are objective methods to evaluate the nasal passages and paranasal sinuses. A correlation has been found between CT and acoustic rhinometry (Hilberg at al 1989, Cakmak 2003, Numminen et al 2003b). CT is especially used for evaluation of paranasal sinuses, but the role of CT alone as an objective method to evaluate nasal obstruction remains uncertain (Hilberg 2002, Fraser and Kelly 2009, Holmström 2010).

In a study of Hilberg et al (1993), a reasonable correlation between anterior nasal cavity areas and MRI was found, but the areas with acoustic rhinometry were 15 % larger than those measured with MRI. Nevertheless, MRI is mainly used in the case of suspicion of malignancy in the nasal cavity or paranasal sinuses (Hilberg 2002).

2.3 Subjective evaluation of nasal patency

2.3.1 VAS

The visual analogue scale (VAS) is used in social and behavioural sciences to measure a variety of subjective phenomena (Wewers and Lowe 1990). The method is commonly used as a subjective tool to measure nasal obstruction in adults in either a bilateral or a unilateral manner with the anchors indicating “no obstruction” and “total obstruction” (Sipilä et al 1995, Simola and Malmberg 1997, Numminen et al 2003a, Ho et al 2004, Clarke et al 2005, Clarke et al 2006, Lam et al 2006, Kjaergaard et al 2008, Kjaergaard et al 2009). In order to get more information about the obstruction, VAS can be used before and after decongestion of the nose as well. Sometimes VAS scores are used for further classification of patients into different groups (Lim et al 2007, Kjaergaard et al 2008, Kjaergaard et al 2009).

VAS is used among children too, but mostly to evaluate pain. Some modifications of VAS for children using different colours or laughing and crying faces have been introduced to evaluate pain and nausea (McGrath 1989, Hamunen et al 2008, Klemetti et al 2009). It has been stated that children under seven years of age can not complete VAS accurately; they mainly use only the endpoints or the endpoints and middle of the scale (Shields et al 2003, Bayer et al 2009). On the other hand, it is stated that children over five years old could use VAS in a reliable and valid manner (McGrath 1989, Hamunen et al 2008). Shields et al (2003) concluded that the cognitive ability of a child, combined with chronological age, was the best predictor of a child's accurate use of VAS.

Only few studies have been published on the evaluation of nasal symptoms with VAS in children (McGrath 1989, Shields et al 2003, Hamunen 2008). Instead, for subjective evaluation of the nose in children, symptom scores or a general sensation of obstruction have been used (Öztürk et al 2004, Miyamoto et al 2009).

Often VAS is not completed by a child, but by parents or someone else. Steinsvåg et al (2007) studied asthmatic children and controls aged from two to five years, and VAS was completed by parents for nasal signs. Similarly, in the study of Datema et al (2008), parents filled in VAS, as well as a standard questionnaire. They found that VAS completed by parents for ear symptoms is a reliable and fast method to evaluate the effect of surgical treatment in children with chronic otitis media with effusion. In the study of Klemetti et al (2009), both children and parents filled in VAS for pain and nausea before and after tonsillectomy.

2.3.2 Other subjective methods

The Nasal Obstruction Symptom Evaluation (NOSE) scale was developed for the assessment of nasal obstruction and its impact on quality of life (Stewart et al 2004). The five items in the questionnaire are: nasal congestion or stuffiness, nasal blockage or obstruction, trouble breathing through the nose, trouble sleeping, and unable to get enough air through the nose during exercise or exertion. Patients score every symptom from 0 (not a problem) to 4 (severe problem), as they have experienced them over the past month (Stewart et al 2004).

The Sino-Nasal Outcome Test 22 (SNOT-22) is a modification of a former Sino-Nasal Outcome Test 20 (SNOT-20), and includes 22 different symptoms related to both nasal and general health (Piccirillo et al 2002, Buckland et al 2003, Hopkins et al 2009). Patients score every symptom from 0 (no problem) to 5 (problem as bad as it can be), as they have experienced them during the past two weeks. In addition, they choose up to the five most important items affecting their health (Buckland et al 2003).

Even though the SNOT-22 was originally developed and validated to measure rhinosinusitis, it can also be used in other rhinological procedures (Buckland et al 2003, Hopkins et al 2009). The SNOT-22 score questions can also be divided into nasal-related problems and more general health issues, or even into four domains (psychological function, sleep function, rhinological symptoms, and ear and facial symptoms), to be more helpful in rhinological evaluation (Buckland et al 2003, Pynnonen et al 2009).

Besides these validated tools to evaluate obstructions, many researchers simply ask if there is obstruction or not, or ask the patient to grade nasal obstruction as mild, moderate or severe (Grymer et al 1997, Larsson et al 2001, Naito et al 2001, Öztürk et al 2004, Miyamoto et al 2009). These kinds of questionnaires are commonly used in clinical practice, but make the comparison between studies more difficult.

2.3.3 Correlations between objective and subjective methods

Recently, Andre et al (2009) made a meta-analysis of correlations between objective and subjective analysis of nasal patency. They consistently found that it may be difficult to find a correlation between subjective and objective measurements in individuals with no nasal symptoms. However, several groups have concluded that a correlation between an objective and subjective method is easier to discover in an obstructed nose, when each nasal passage is assessed individually, or when there is a sufficient difference between the two nostrils (Sipilä et al 1995, Simola and Malmberg 1997, Larsson et al 2001, Pirilä and Tikanto 2001, Numminen et al 2003a, Clarke et al 2006, Kjaergaard et al 2009).

Numminen et al (2003a) found a statistical correlation between VAS and acoustic values in adults, but estimated that there was no clinical significance ($r < 0.40$). They used total values instead of unilateral ones before and during acute viral rhinitis. Correlation between bilateral acoustic values and subjective evaluation of the obstruction has not been found by other groups (Kim et al 1998, Passali et al 2000, Pirilä and Tikanto 2001, Öztürk et al 2003, Ho et al 2004). Moreover, similar results have been achieved between bilateral measurements with rhinomanometry and subjective evaluation of the nose (Szucs et al 1995, Kim et al 1998, Passali et al 2000, Pirilä and Tikanto 2001, Clarke et al 2005).

On the contrary, correlations between unilateral values of objective measurements and subjective evaluation have been found by many groups (Sipilä et al 1995, Pirilä and Tikanto 2001, Clarke et al 2005, Miyamoto et al 2009). In the study of Lam et al (2006), VAS correlated with MCA, but not with volume or nasal flow measured with a nasal peak inspiratory flow meter. They used unilateral values of acoustic rhinometry, but VAS for total nose obstruction.

Kjaergaard et al (2008) found a correlation between total VAS and total MCA, and between VAS and total nasal cavity volume in the non-decongested nose. Later on, they introduced a Nasal Congestion Index (NCI) calculated from MCA, nasal volume, and peak nasal inspiratory flow, to quantify the reversible congestion of nasal mucosa (Kjaergaard et al 2009). This index was associated with a subjective sensation of nasal obstruction. Naito et al (2001) found a correlation between volume and subjective nasal obstruction, but no correlation between MCA and subjective evaluation in the nose as a whole.

In a study of children with allergic rhinitis, Öztürk et al (2004) found no correlation between patient-recorded symptom scores of nasal obstruction (none, mild, moderate, severe) and total MCA or total volume. In another study of children aged between seven and eight years, the general sensation of obstruction correlated with the cross-sectional areas in the posterior part of the nose (Miyamoto et al 2009). No correlative study between VAS and acoustic values has been published in children.

3 AIMS OF THE PRESENT STUDY

The purpose of the present study was

1. To investigate the usefulness of acoustic rhinometry for objective evaluation of intranasal dimensions in children.
2. To establish a standard way of measuring children with acoustic rhinometry for clinical practice, and to clarify the role of the most important sources of error.
3. To define reference values for acoustic rhinometry in school children at baseline and after decongestion of the nose.
4. To find the predictive value of age, sex, height, and BSA on acoustic values in children, if any.
5. To investigate the usefulness of acoustic rhinometry in follow-up of nasal reactions in children.
6. To study the use of VAS as a subjective method to evaluate the sensation of nasal obstruction in children, and to find a possible correlation between acoustic values and VAS in children with no nasal symptoms.

4 MATERIALS AND METHODS

4.1 Patients

4.1.1 Pilot study (Study I)

The subjects in the Pilot study (I) were a subcohort of the Type I Diabetes Prediction and Prevention study (DIPP). The study comprised three phases: genetic screening, immunological screening for the appearance of autoantibodies, and intervention. Children over one year of age, at genetic risk for type 1 diabetes, with at least two types of autoantibodies, indicating an increased risk for type 1 diabetes, were invited to participate in the randomised double-blinded intervention trial comparing intranasal insulin with placebo. The study design is described in more detail in the publication by Näntö-Salonen et al (2008). Participants for the Pilot study of acoustic rhinometry in children were selected from the DIPP study before they started the prevention trial with intranasal insulin.

The criterion for exclusion was any permanent nasal obstruction or septal deviation detected by anterior rhinoscopy. A standard questionnaire of nasal symptoms was filled in with the children or their parents.

The study cohort in the Pilot study (I) included 74 children. The mean age was 4.25 years (SD 2.39, range 1.39 to 12.7 years), and the mean BSA was 0.701 m^2 (SD 0.279).

4.1.2 Follow-up study (Study II)

Similarly, the subjects in the Follow-up study (II) were a subcohort of the DIPP study. They received either recombinant human short-acting insulin (Actrapid®) in regular buffer or the buffer alone (called placebo group), in the form of a nasal spray, once a day. The randomisation was performed by the Turku University Hospital Pharmacy according to the schema of the DIPP study.

The criterion for exclusion was any permanent nasal obstruction or septal deviation detected by anterior rhinoscopy at the first visit.

In the Follow-up study (II), data were available from the baseline visit, before starting any treatment, for 72 children, aged between 1.39 and 12.7 years. There were 35 children in the insulin group (mean age 4.35 years, SD 2.52, range 1.39-12.7 years) and 37 children in the placebo group (mean age 3.87 years, SD 1.97, range 1.47-8.32 years).

4.1.3 Reference data and VAS study (Studies III and IV)

The subjects were recruited on a voluntary basis from two primary schools in south-western Finland. Information of the study was sent to the parents of every pupil in the both schools, and every willing child was considered to take part in the study. The criteria for exclusion were any permanent nasal symptoms or acute upper respiratory infection within two weeks. Anterior rhinoscopy was performed to rule out prominent septal deviations and remarkable mucosal swelling.

The study included 124 children aged between 6.90 and 13.84 years (mean 10.38 years, SD 1.68). There were 59 boys (47.6%) and 65 girls (52.4 %) in the study group. All the measurements were carried out between November 2009 and January 2010, outside the pollen season, by the researcher (LH) during the school day.

4.2 Acoustic rhinometry

4.2.1 Equipment and software

Acoustic rhinometry was performed on each subject according to the recommendations of the Committee on Standardisation of Acoustic Rhinometry (Clement and Gordts 2005). The equipment used was delivered by GM Instruments (Acoustic Rhinometer A1, GM Instruments Ltd., Kilwinning, United Kingdom), and is part of the permanent hardware in the Rhinolaboratory of Turku University Hospital.

The software used was delivered by the manufacturer. When the study started in 1999 (Studies I and II), the A1child version 2.1.0.2 was used. The software was updated in 2003, and the Naris version 5.2 was used after that. For reference values (Studies III and IV), the Naris version 5.2 was used.

4.2.2 Measurement procedure

The measurements in the Pilot study (I) and the Follow-up study (II) were carried out in the Rhinolaboratory of Turku university Hospital by the same trained nurse. Before any further calculations, the researcher (LH) reviewed the whole data to ensure that curves were acceptable and acoustic values were correctly collected from the curves.

In the studies of reference data (III) and VAS (IV) all the measurements were carried out by the researcher herself (LH) with an ambulatory unit of acoustic rhinometry and a laptop at school (Figure 4). The equipment was checked with an artificial nose delivered by the manufacturer every day before the first measurement.

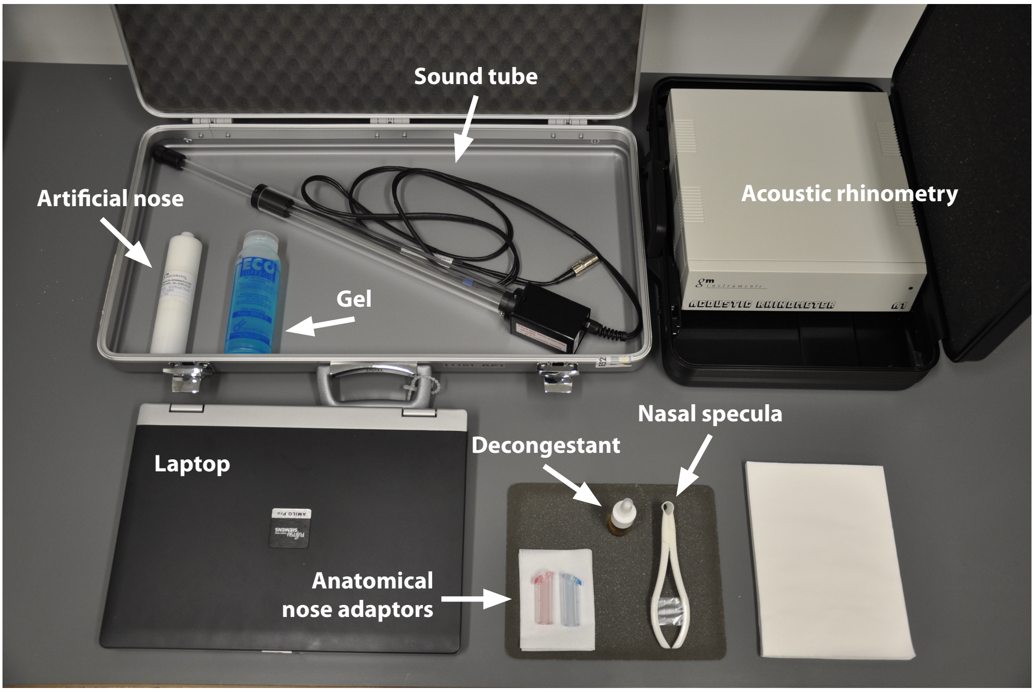


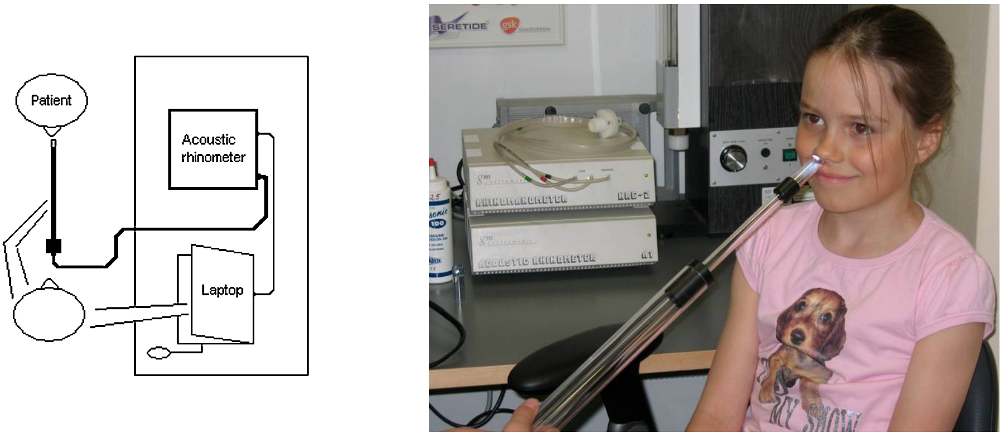
Figure 4. The ambulatory unit of acoustic rhinometry.

Children were asked to blow their nose before all measurements. The baseline measurement was performed after acclimatisation to the room temperature of 10 minutes. All the measurements took place in a quiet room with no other people than the researcher and a child (Studies III and IV), or a child with his/her parent (Studies I and II). Measurements were obtained while children were in a sitting position (Figure 5). The atmosphere during the measurements was relaxed.

At least three measurements were performed on each side. The mean values of the three acceptable curves were used for calculations. Curves with significant deviation were excluded, and the measurement was repeated if necessary.

Special soft nosepieces for children or medium-size anatomical nose adaptors for adults were used. On principal, medium-size anatomical nose adaptors were used for children aged five years or more. The length of the adapter used was 5 cm. If necessary, ultrasound gel (ECO Supergel, Ceracarta S.p.A., Forli, Italy) between adapter and nostril was used to prevent acoustic leakage. Special efforts were made to avoid distortion of the nostril. Children were asked to hold their breath, or allowed to breathe quietly through the mouth.

No stands or chin supports were used. The spatial alignment was not fixed. Instead, the sound tube was handheld by the researcher for more flexible use and for better adaptation of the nose adaptor. The approximate vertical angel of the sound tube was about 45°.



A. **B.**

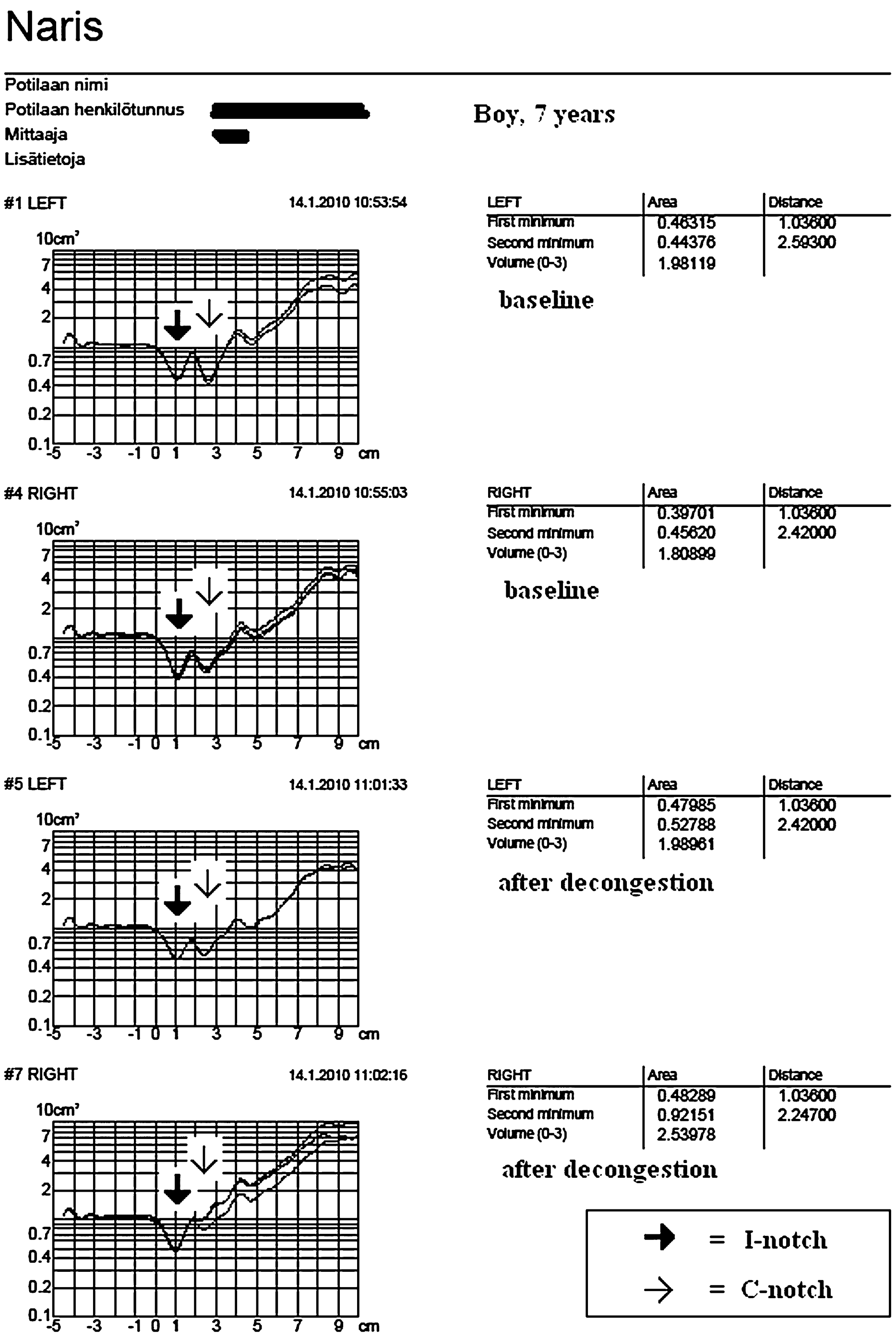
Figure 5. A. The arrangement of the measurement procedure with the ambulatory unit (Studies III and IV). **B.** Measuring a nine-year-old girl with acoustic rhinometry in the Rhinolaboratory.

4.2.3 Acoustic values of interest

The acoustic values of special interest in the Pilot study (I) and in the study of correlations between acoustic values and VAS (IV), were the unilateral minimal cross-sectional areas (MCAl on the left side and MCAr on the right side), and the unilateral nasal cavity volume between 0 and 3 cm from the nostril, measured from the left and right cavities separately (VOLl and VOLr, respectively). In addition, in the Pilot study (I) the distance of the unilateral minimal cross-sectional area from the nostril (DMCAl and DMCAr on the left and right sides, respectively), and total volume as the sum of the left and right sides (TVOL) were also calculated.

In the Follow-up study (II), and in the study of reference data (III), the acoustic values of special interest were the total minimal cross-sectional area (TMCA, calculated as the sum of the left and right sides), and the total nasal cavity volume at a distance of 0-3 cm from the nostril, calculated as the sum of the right and left sides (TVOL).

The location of the minimal cross-sectional area (MCA) was determined from the curve as illustrated in the Figure 6. In some occasions, the MCA was located at the area of nasal valve. In other cases, especially at baseline before decongestion of the nose, the MCA was located at the anterior head of the inferior turbinate.



Naris

Potilaan nimi
Potilaan henkilötunnus [redacted]
Mittaaja [redacted]
Lisätietoja

Boy, 7 years

#1 LEFT 14.1.2010 10:53:54

LEFT	Area	Distance
First minimum	0.46315	1.03600
Second minimum	0.44376	2.59300
Volume (0-3)	1.98119	

baseline

#4 RIGHT 14.1.2010 10:55:03

RIGHT	Area	Distance
First minimum	0.39701	1.03600
Second minimum	0.45620	2.42000
Volume (0-3)	1.80899	

baseline

#5 LEFT 14.1.2010 11:01:33

LEFT	Area	Distance
First minimum	0.47985	1.03600
Second minimum	0.52788	2.42000
Volume (0-3)	1.98961	

after decongestion

#7 RIGHT 14.1.2010 11:02:16

RIGHT	Area	Distance
First minimum	0.48289	1.03600
Second minimum	0.92151	2.24700
Volume (0-3)	2.53978	

after decongestion

➜ = I-notch
→ = C-notch

Figure 6. An example of the interpretation of the curve of a seven-year-old boy. I-notch = isthmus area; C-notch = concha, anterior part of the inferior turbinate.

4.2.4 Decongestion

In the studies of reference data and VAS (Studies III and IV), measurements were carried out with acoustic rhinometry both at baseline and after decongestion of the nose. After baseline measurements, the nose was decongested with two puffs of xylometazoline spray (Nasolin 0.5 mg/ml, Orion Oyj, Espoo, Finland) in each nostril. The measurements were repeated 10 min after the decongestion was delivered into the nose.

At baseline, the data of 124 children were available (Studies III and IV). However, after decongestion, data were available for only 106 children, because permission to use a decongestant (Nasolin spay) was specially asked from children and parents, and some of them refused.

4.3 Other values of interest

4.3.1 Visual analogue scale

In the study of correlations between acoustic rhinometry and VAS (IV), prior to any measurement, the child was asked to evaluate the level of the obstruction of his/ her nose using a 10-cm-long visual analogue scale (VAS). Each nostril was evaluated separately and the child was advised to gently close the opposite nostril with a finger. The left anchor of the scale was defined as “my nostril is completely obstructed” (VAS = 0), and the right anchor as “my nostril is totally open” (VAS = 10). The self-evaluation was repeated after decongestion before the measurement in the same way.

4.3.2 Body surface area

Instead of body mass index (BMI), body surface area (BSA) was used because it is more suitable for children (Jastaniah and Aseeri 2010). BSA was determined using the data on height and weight of each child. There are many ways of calculating BSA, and the formula used in this study was the Mosteller formula because it seems to be the most precise, reliable, and easy to use (Mosteller 1987, Jastaniah and Aseeri 2010). BSA based on the Mosteller method is calculated by the formula:

$\mathrm{BSA}\ (\mathrm{m}^2) = ([\mathrm{height}\ (\mathrm{cm}) * \mathrm{weight}\ (\mathrm{kg})]/\ 3600)^{1/2}$

4.4 The follow-up schema

In the Follow-up study (II), the baseline measurement was carried out before the child started the prevention trial. Each child was then randomised either to the insulin or the placebo group and started the nasal spray according to the DIPP Study protocol (see above).

The points of special interest in the follow-up were at 3 months, 6 months, 12 months, and 24 months. After that point, the measurements were carried out once a year (Table 2). At every control visit to the rhinolaboratory, a standard questionnaire concerning nasal symptoms was filled in with the children or their parents, and acoustic rhinometry was performed.

All the measurements were performed between 1999 and 2007. There was a continuous intake of children into the study until it was terminated in 2007. The follow-up time was up to 72 months. In the course of the study, each child had 1-9 visits to the rhinolaboratory; some of the children were measured only once (baseline visit). A total of 247 bilateral measurements were performed.

Table 2. Number of children at control points during the follow-up.

Control Point	Insulin Group	Placebo Group	Total
Baseline	35	37	72
3 Months	24	25	49
6 Months	20	20	40
12 Months	19	15	34
24 Months	12	12	24
36 Months	7	6	13
48 Months	3	5	8
50 Months	1	0	1
60 Months	1	2	3
72 Months	1	2	3
Total	123	124	247

4.5 Statistics

The software used for statistical calculation was SAS for Windows 9.2 (in the Pilot study (I) version 8.0). P-values less than 0.05 were considered statistically significant.

4.5.1 *Pilot study (I)*

The distributions of the acoustic variables were not normally distributed according to the Shapiro-Wilk test. Spearman correlation coefficients were used to calculate the correlations of the acoustic values with age and BSA. Fisher`s Exact test was used to compare age, BSA, and amount of the nasal symptoms between accepted and rejected measurements.

Because of the large variation in age in this material, children were grouped into three subgroups. The mean values for each subgroup (0-2 years, 3-5 years, more than 6 years) were calculated separately.

4.5.2 *Follow-up study (II)*

For the statistical analysis at baseline, values in the insulin and placebo groups were compared for age, BSA, nasal symptoms, TMCA, and TVOL. Since the continuous variables were not normally distributed, the non-parametric Mann-Whitney U-test was used.

For the follow-up of symptoms, logistical regression analysis with random intercept (PROC GLIMMIX) was used to compare changes within each group and between the groups during the follow-up of 3, 6, 12, and 24 months.

For the follow-up of BSA and the acoustic values, TMCA and TVOL, the Wilcoxon signed rank test was used to compare changes within both groups during the follow-up of 3, 6, 12 and 24 months. To compare changes between the two groups at the control points the Mann-Whitney U-test was used.

4.5.3 *Reference values (III)*

The variables, TMCA and TVOL, were normally distributed according to the Shapiro-Wilk test. Pearson correlation coefficients were used to calculate the correlations between the acoustic values, (TMCA and TVOL) and age, height, and BSA, as constant predictors.

On the other hand, the distribution of DMCA was not normally distributed, and Spearman correlation coefficients were used for calculations of correlations. To test the difference in acoustic values between boys and girls a two-sample t-test was used for TMCA and TVOL, and the Mann-Whitney U-test for DMCA. In the comparison of values between baseline and after decongestion a paired t-test and the Wilcoxon Signed Rank test were used.

For further evaluation of the role of height in the acoustic values, four subgroups were formulated according to height (111-130 cm, 131-140 cm, 141-150 cm and 151-170 cm). The differences between subgroups were tested with one-way ANOVA using Tukey's post-hoc comparisons. DMCA values were compared with the Kruskal-Wallis test.

4.5.4 VAS study (IV)

In the study of correlations between acoustic values and VAS, the unilateral MCA and VOL were normally distributed according to the Shapiro-Wilk test. On the contrary, the distribution of VAS was not normal, and Spearman correlation coefficients were used for calculations of correlations between acoustic values (MCA and VOL) and VAS. To test the difference between left and right sides a paired t-test was used.

4.6 Ethical considerations

Studies I-IV were approved by the Joint Ethical Committees of Turku University and Turku University Hospital. Written informed consent was elicited from the parents of the participants (Study I and II). In Studies III and IV, written informed consent was elicited from every child and from his/her parents. All the subjects were recruited on a voluntary basis.

5 RESULTS

5.1 Reference data (I, III)

5.1.1 Total values at baseline and after decongestion (III)

In the study of reference data (III), total values of acoustic rhinometry were available for 124 children at baseline. The mean TMCA calculated as the sum of left and right sides was 0.752 cm^2 (SD 0.165), the mean DMCA 1.168 cm (SD 0.399), and the mean total volume between 0 and 3 cm from the nostril (TVOL) 4.00 cm^3 (SD 0.63).

After decongestion, acoustic data for 106 children were available, because some of the children or their parents refused the use of the decongestant spray. In this material the mean TMCA was 0.794 cm^2 (SD 0.162), the mean DMCA 1.066 cm (SD 0.278), and the mean TVOL 4.38 cm^3 (SD 0.75).

The change in total acoustic values between baseline and decongestion was significant. The mean change in the TMCA was 0.04 cm^2 ($p < 0.01$), in the DMCA -0.12 cm ($p < 0.01$), and in the TVOL 0.41 cm^3 ($p < 0.001$). The total values of TMCA and TVOL at baseline and after decongestion are summarised in Table 3. A significant change in values after decongestion is pointed out if present.

Table 3. The reference values for acoustic rhinometry at baseline and after decongestion in children between 7 and 14 years.

Minimal cross-sectional area			**Volume between 0 and 3 cm**		
	Baseline	**Decongestion**		**Baseline**	**Decongestion**
TMCA (cm^2)			**TVOL (cm^3)**		
N	119	105	**N**	119	104
Mean	0.752	0.794 *	**Mean**	4.00	4.38 *
SD	0.165	0.162	**SD**	0.63	0.75
MCAr (cm^2)			**VOLr (cm^3)**		
N	120	105	**N**	120	105
Mean	0.392	0.421 *	**Mean**	2.05	2.28 *
SD	0.094	0.087	**SD**	0.39	0.46
MCAl (cm^2)			**VOLl (cm^3)**		
N	120	106	**N**	119	104
Mean	0.360	0.373	**Mean**	1.96	2.11 *
SD	0.093	0.106	**SD**	0.37	0.47

TMCA = total minimal cross-sectional area as a sum of left and right sides: MCAr = minimal cross-sectional area on the right side; MCAl = minimal cross-sectional area on the left side; TVOL = volume between 0 and 3 cm from the nostril as the sum of left and right sides; VOLr = volume on the right side; VOLl = volume on the left side; * = a significant change between baseline and decongestion.

5.1.2 Unilateral values at baseline and after decongestion (I, III)

Like total values, unilateral acoustic values were also available for 124 children at baseline and for 106 children after decongestion (Study III). At baseline, the mean MCA on the right side was 0.392 cm^2 (SD 0.094), and on the left side 0.360 cm^2 (SD 0.093). The values were significantly higher on the right side compared to the left side ($p < 0.001$).

The mean volume between 0 and 3 cm from the nostril on the right side was 2.05 cm^3 (SD 0.39), and on the left side 1.96 cm^3 (SD 0.37). Again, the values were significantly higher on the right side compared to the left side ($p < 0.05$).

After decongestion, the mean MCA on the right and left side was 0.421 cm^2 (SD 0.087) and 0.373 cm^2 (SD 0.106), respectively. The mean VOL on the right and left side was 2.28 cm^3 (SD 0.46) and 2.11 cm^3 (SD 0.47), respectively. After decongestion, the difference in acoustic values between right and left sides remained (for MCA $p < 0.001$ and for VOL $p < 0.005$).

The change in unilateral MCA between baseline and decongested nose was significant on the right side (mean change 0.029 cm^2, $p < 0.001$), but not on the left side (mean change 0.012 cm^2, NS). Instead, the change in unilateral VOL between baseline and decongested nose was significant on both sides of the nose. The mean change in VOLr was 0.24 cm^3 ($p < 0.0001$), and in VOLl 0.17 cm^3 ($p < 0.001$).

The unilateral values of MCA and VOL on both sides of the nose in the reference data are summarised in Table 3. A significant change in values after decongestion is pointed out if present.

In the Pilot study of 74 children (I), unilateral areas and volumes were also calculated. For statistical analysis, acceptable results were available for 38 children (mean age 4.17 years, SD 1.98), while the results of 36 children had to be rejected (mean age 4.36 years, SD 2.82) because of inappropriate data. The statistical analysis showed no difference in age or BSA between the accepted and the rejected group. In this material, the mean MCA on the left side was 0.227 cm^2 (SD 0.042), and the mean MCA on the right side was 0.216 cm^2 (SD 0.052). The mean unilateral volumes between 0 and 3 cm from the nostril on the left and right side were 1.125 cm^3 (SD 0.373) and 1.048 cm^3 (SD 0.321), respectively.

5.1.3 Influence of predictive factors

5.1.3.1 Age

In the Pilot study (I) of 38 acceptable measurements, a positive correlation was found between age as a constant predictor and MCA on the right side, and unilateral nasal cavity volume on the left side. Age correlated negatively with DMCA on the left side.

Because of the large variation in age, children were grouped into three subgroups. The values for each subgroup (0-2 years, 3-5 years, more than 6 years) together with values of the whole data are summarised in Table 4. There is a tendency towards larger areas and volumes in older children, but the groups were too small for further calculations.

Table 4. The acoustic values for subgroups according to age and for total group of the Pilot study (I).

	Age group 1-2 years [(a)]			**Age group 3-5 years** [(b)]		
Variable	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age (years)	29	2.122	0.46	26	4.185	0.83
BSA (m^2)	26	0.567	0.06	25	0.753	0.13
MCAl (cm^2)	13	0.220	0.05	14	0.227	0.02
MCAr (cm^2)	16	0.189	0.07	16	0.227	0.03
DMCA (cm)	13	1.020	0.75	14	0.693	0.50
VOLl (cm^3)	10	0.944	0.23	13	1.161	0.32
VOLr (cm^3)	11	0.884	0.27	15	1.131	0.33
TVOL (cm^3)	9	1.890	0.39	13	2.295	0.52

	Age group >6 years [(c)]			**Total group 1-13 years**		
Variable	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age (years)	19	7.574	1.71	74	4.247	2.39
BSA (m^2)	18	1.016	0.16	69	0.751	0.21
MCAl (cm^2)	12	0.233	0.05	39	0.227	0.04
MCAr (cm^2)	12	0.237	0.04	44	0.216	0.05
DMCA (cm)	11	0.591	0.69	38	0.775	0.66
VOLl (cm^3)	11	1.246	0.49	34	1.125	0.37
VOLr (cm^3)	11	1.098	0.32	37	1.048	0.32
TVOL (cm^3)	10	2.346	0.80	32	2.197	0.61

(a) = Age between 1.39 and 2.98 years; (b) = Age between 3.02 and 5.52 years; (c) = Age between 6.01 and 12.7 years; BSA = body surface area; MCAl = minimal cross-sectional area on the left side; MCAr = minimal cross-sectional area on the right side; DMCA = distance of unilateral minimal cross-sectional area from the nostril; VOLl (cm^3) = volume between 0 and 3 cm from the nostril on the left side; VOLr (cm^3) = volume between 0 and 3 cm from the nostril on the right side; TVOL = total volume between 0 and 3 cm from the nostril as the sum of left and right side.

In a larger study (n=124) of reference data (III), there was a significant correlation between age and TMCA at baseline and after decongestion. On the contrary, no correlation was found between age and DMCA or TVOL at any point. The correlations between age and acoustic values based on the reference data can be seen in Table 5.

Table 5. The correlations between acoustic values (TMCA, DMCA and TVOL) and age, height, and BSA, at baseline and after decongestion.

	Acoustic Value					
	TMCA		**DMCA**		**TVOL**	
	Baseline	**Decong.**	**Baseline**	**Decong.**	**Baseline**	**Decong.**
Predictive Value						
Age						
Corr.*	0.19984	0.23442	- 0.05240	- 0.12941	0.16945	0.18338
p	*< 0.05*	*<0.02*	*NS*	*NS*	*NS*	*NS*
N	119	105	118	105	119	104
Height						
Corr.*	0.21736	0.16963	- 0.05751	- 0.16266	0.18697	0.22074
p	*< 0.02*	*NS*	*NS*	*NS*	*< 0.05*	*< 0.05*
N	115	102	114	102	115	101
BSA						
Corr.*	0.24765	0.17585	- 0.06600	- 0.21233	0.19501	0.22553
p	*< 0.01*	*NS*	*NS*	*< 0.05*	*< 0.05*	*< 0.05*
N	108	95	107	95	108	94

TMCA = total minimal cross-sectional area as a sum of left and right sides; DMCA = distance of the minimal cross-sectional area from the nostril; TVOL = total volume between 0 and 3 cm from the nostril as a sum of left and right sides; BSA = body surface area; Corr.* = Pearson Correlation Coefficient in MCA and VOL, Spearman Correlation Coefficient in DMCA.

5.1.3.2 Height

The height of the children in the study of reference data (III) ranged from 117 cm to 170 cm (mean 142.4 cm, SD 11.4). Height correlated with TVOL at baseline and after decongestion. The correlation was also found between height and TMCA at baseline, but not after decongestion. The correlation coefficients are shown in Table 5.

For further calculations, children were divided into subgroups according to height (111-130 cm, 131-140 cm, 141-150 cm, and 151-170 cm). The mean TMCA, DMCA, and TVOL before and after decongestion in the different subgroups of height are presented in Table 6. There was no statistical difference between the different subgroups in the TMCA and DMCA values. However, TVOL was higher in the subgroup 141-150 cm compared to subgroup 111-130 cm ($p<0.05$) at baseline. After decongestion, TVOL was higher in the subgroup 131-140 cm compared to subgroup 111-130cm ($p<0.05$).

Table 6. The acoustic values in the different subgroups of height.

	Variable **TMCA (cm^2)**			**DMCA (cm)**			**TVOL (cm^3)**		
Subgroup	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
111-130 cm									
Baseline	21	0.72	0.15	21	1.31	0.47	22	3.67	0.50
Decongestion	19	0.75	0.14	19	1.13	0.31	20	3.96	0.59
131-140 cm									
Baseline	25	0.70	0.17	25	1.13	0.36	25	4.04	0.65
Decongestion	20	0.78	0.21	20	1.06	0.20	19	4.60	1.07
141-150 cm									
Baseline	46	0.76	0.16	45	1.08	0.32	45	4.16	0.62
Decongestion	38	0.80	0.15	38	1.07	0.30	37	4.38	0.57
151-170 cm									
Baseline	23	0.80	0.18	23	1.28	0.49	23	3.92	0.70
Decongestion	25	0.83	0.16	25	1.02	0.29	25	4.51	0.72

TMCA = total minimal cross-sectional area as a sum of left and right sides; DMCA = distance of the minimal cross-sectional area from the nostril; TVOL = total volume between 0 and 3 cm from the nostril as the sum of left and right sides.

5.1.3.3 BSA

In the Pilot study (I), the mean BSA was 0.701 m^2 (SD 0.279). For statistical analysis the rhinometric results of 38 children were acceptable (BSA 0.740 m^2, SD 0.194), while the results of 36 children had to be rejected because of inappropriate data (BSA 0.764 m^2, SD 0.233). The statistical analysis showed no difference in BSA between the accepted and the rejected group. BSA as a constant predictor correlated positively with MCA on the right side and negatively with DMCA on the left side.

In the study of reference values (III), the mean BSA was 1.22 m^2 (SD 0.20). A significant correlation was found between BSA and TVOL at baseline and after decongestion. In addition, a correlation was found between BSA and TMCA at baseline, and between BSA and DMCA after decongestion. The correlation coefficients based on the reference data are shown in Table 5.

5.1.3.4 Sex

There was no statistical difference in the acoustic values between boys and girls at baseline in children between 7 and 14 years on the bases of the reference data (III).

At baseline, the mean TMCA was 0.75 cm^2 (SD 0.16), the mean DMCA 1.21 cm (SD 0.42), and the mean total volume 4.00 cm^3 (SD 0.63) in boys. Correspondingly, the mean TMCA was 0.75 cm^2 (SD 0.17), the mean DMCA 1.13 cm (SD 0.38), and the mean total volume 4.00 cm^3 (SD 0.64) in girls.

After decongestion, the corresponding values were 0.79 cm^2 (SD 0.13), 1.13 cm (SD 0.33) and 4.28 cm^3 (SD 0.61) in boys, respectively, and 0.80 cm^2 (SD 0.19), 1.01 cm (SD 0.20) and 4.48 cm^3 (SD 0.85) in girls, respectively. Again, no difference between boys and girls was found.

5.2 Correlations between acoustic values and VAS (IV)

5.2.1 VAS values

On the visual analogue scale (VAS) used in this study, value 0 means “my nostril is completely obstructed” and value 10 means “my nostril is totally open”. VAS was determined on each side separately.

At baseline, the mean VAS on the right side was 7.43 (SD 2.50, range 0.2-10.0) and on the left side 6.81 (SD 3.01, range 0.1-10.0). After decongestion, the mean VAS on the right side was 8.77 (SD 2.02, range 0.1-10.0) and on the left side 8.54 (SD 2.14, range 1.0-10.0). The mean change in VAS between baseline and decongestion values was significant on both sides ($p< 0.001$).

5.2.2 Correlations

To study the correlations between acoustic values and VAS, unilateral values were used. The mean unilateral values of MCA and VOL at baseline and after decongestion are summarised in Table 3.

At baseline, a significant correlation was found between VAS and MCA on both sides, and between VAS and VOL on the right side. No correlation was found after decongestion between VAS and any of the acoustic values. The correlations are summarised in Table 7.

Table 7. The Correlations between VAS and acoustic values MCA and VOL on the left and right sides separately.

Acoustic Value	VAS left Baseline	Decongestion	VAS right Baseline	Decongestion
MCA left				
r*	0.21	0.038		
p	*< 0.05*	*NS*		
N	120	103		
MCA right				
r*			0.25	- 0.0067
p			*< 0.01*	*NS*
N			120	102
VOL left				
r*	0.089	0.080		
p	*NS*	*NS*		
N	119	101		
VOL right				
r*			0.20	0. 78
p			*< 0.05*	*NS*
N			120	102

VAS = visual analogue scale on left and right side separately; MCA = minimal cross-sectional area: left and right side separately; VOL = volume between 0 and 3 cm from the nostril: left and right side separately; * = Spearman Correlation Coefficient.

5.3 Follow-up (II)

The follow-up time was up to 72 months. In the course of the study each child had 1-9 visits to the rhinolaboratory. A total of 247 measurements were performed; 219 of them within the first 24 months of follow-up (Table 2).

5.3.1 Acoustic values and BSA

At baseline, the mean TMCA was 0.400 cm^2 (SD 0.12) in the insulin group and 0.420 cm^2 (SD 0.11) in the placebo group. Similarly, the mean TVOL at baseline was 1.94 cm^3 (SD 0.85) in the insulin group and 2.06 cm^3 (SD 0.61) in the placebo group. The mean values for BSA were 0.77 m^3 (SD 0.21) and 0.73 m^3 (SD 0.22), respectively (see Table 8). There was no statistical difference at baseline between the two groups with regard to age (p=0.510), BSA (p=0.210), TMCA (p=0.451) or TVOL (p=0.668).

Table 8. Acoustic values and BSA in the insulin and placebo groups during the follow-up of 24 months (Study II).

Variable	**BSA (m^2)**			**TMCA (cm^2)**			**TVOL (cm^3)**		
	N	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Baseline									
Insulin	34	0.77	0.21	25	0.40	0.12	23	1.94	0.85
Placebo	33	0.73	0.22	20	0.42	0.11	16	2.06	0.61
3 Months									
Insulin	24	0.87	0.31	19	0.39	0.08	17	1.75	0.41
Placebo	23	0.79	0.28	15	0.41	0.09	14	1.94	0.59
6 Months									
Insulin	20	0.90	0.28	16	0.46	0.15	16	2.14	0.77
Placebo	19	0.83	0.36	15	0.45	0.11	15	2.07	0.68
12 Months									
Insulin	19	0.89	0.29	10	0.38	0.10	9	1.71	0.74
Placebo	14	0.95	0.31	11	0.48	0.12	11	2.33	0.56
24 Months									
Insulin	12	1.01	0.38	8	0.45	0.08	7	2.36	0.77
Placebo	12	1.04	0.42	7	0.48	0.13	5	2.65	0.99

BSA = Body surface area; TMCA = total minimal cross-sectional area as the sum of right and left side; TVOL = total volume between 0 and 3 cm from the nostril as the sum of right and left side.

There was no significant increase in the acoustic values, TMCA and TVOL, during the follow-up period of two years. Instead, BSA increased significantly in the insulin ($p<0.001$) and placebo ($p<0.002$) groups during the follow-up, indicating the growth of the children. There was no significant difference between the two groups in the change in TMCA, TVOL, or BSA. The mean values during the first 24 months of the follow-up period in the insulin and placebo groups are shown in Table 8.

5.3.2 Symptoms

At baseline, 23 out of 72 children (32 %) mentioned some form of occasional nasal symptoms (occasional congestion, discharge or nosebleeds). There was no statistical difference at baseline between the insulin group and the placebo group with regard to nasal symptoms. Table 9 illustrates the percentages of all reported nasal symptoms in the insulin and placebo groups during the follow-up of 72 months.

Table 9. The number (percentage) of children reporting nasal symptoms during the follow-up of 72 months.

Group	**Insulin**		**Placebo**		**Total**	
	n/N	**(%)**	**n/N**	**(%)**	**n/N**	**(%)**
Control point						
Baseline	9/35	(26 %)	14/37	(38 %)	23/72	(32 %)
3 Months	13/24	(51 %)	15/25	(60 %)	28/49	(57 %)
6 Months	14/20	(70 %)	12/20	(60 %)	26/40	(65 %)
12 Months	8/19	(42 %)	11/15	(73 %)	19/34	(56%)
24 Months	6/12	(50%)	5/12	(42 %)	11/24	(46 %)
36 Months	5/7	(71 %)	3/6	(50 %)	8/13	(62 %)
48 Months	1/3	(33 %)	3/5	(60 %)	4/8	(50 %)
50 Months	1/1	(100 %)	-		1/1	(100 %)
60 Months	1/1	(100 %)	1/2	(50 %)	2/3	(67 %)
72 Months	0/1	(0 %)	1/2	(50 %)	1/3	(33%)

n = number of children who reported nasal symptoms; N = total number of children at each control point; % = percentage of children reporting nasal symptoms at each control point.

The main nasal symptom during the follow-up was an unpleasant sensation in the nose after administration of the nasal spray. Other irritating symptoms caused by the spray were itching, hurting, and sneezing. Occasionally, nasal obstruction, discharge, or bleeding was mentioned.

For closer review of the symptoms, each control point was specially evaluated. For statistical calculations, only those cases were accepted for which data were available at both the baseline visit and that particular control point. The insulin group showed a significant increase in the extent of symptoms at three months (OR = 4.87, 98% CI 1.23-19.32, p = 0.0262) and six months (OR = 9.034, 95% CI 1.83-44.72, p = 0.0096), but not at 12 or 24 months when compared to baseline.

Similarly, the placebo group showed a significant increase in the extent of symptoms during the 12-month follow-up (OR = 5.67, 95% CI 1.00-32.10, p = 0.0496), but not at any of the other control points. In any case, there was no statistically significant difference between the insulin and placebo groups in the change in nasal symptoms at any of the control points (at 3 months p = 0.550, at 6 months p = 0.234, at 12 months p = 0.533, at 24 months p = 0.177).

5.4 Sources of error

In the Pilot study of 74 children (I), before any further calculations, the researcher reviewed the whole data to ensure that curves were acceptable and acoustic values were correctly collected from the curves. As a result, the data of only 38 children were available for statistical analysis, while the results of 36 children had to be rejected because of inappropriate data at the baseline visit. The same tendency was seen in the data of the Follow-up study (II).

The main reasons for rejection were obvious acoustic leakage determined visually by the shape of the curves (28.4 % of all measurements), other technical problems (13.5 %), and lack of co-operation of the child (6.8 %).

In the study on the reference data (III), the measurements were carried out in a more standard way and the data were more complete. Lubricant gel was used between nostril and nose adaptor to prevent acoustic leakage whenever necessary.

6 DISCUSSION

6.1 Methodological aspects

6.1.1 Acoustic rhinometry

Acoustic rhinometry is a commonly used method in clinical practice to evaluate nasal obstruction in adults, but in children it has been mainly used in research. Theoretically, acoustic rhinometry is a very suitable method for children because it is rapid, non-invasive, with no side-effects, and minimal co-operation is required (Djupesland and Pedersen 2000, Clement and Gordts 2005). This study confirms the usefulness of the method in children in clinical practice.

This study had two steps; it started with Pilot (I) and Follow-up (II) studies in order to get used to the equipment and to evaluate the process of measuring children. At that point, valuable information on the measurement process and practical aspect was achieved. In the second phase, reference data for children with no permanent nasal symptoms were collected in a more consistent way (Studies III and IV).

This study introduces a standard measurement procedure for children. The procedure aims to avoid the most significant sources of error, and makes the measurements more stable and reliable. The method was used in school children for reference data (Studies III and IV) and the outcome was good. In the Pilot study (I) and in the Follow-up study (II), a standard way of working was still under development, and the results were not so successful. This study emphasizes the need for strict technical care and a standard way of measuring children with acoustic rhinometry. The same kind of conclusion has been drawn in earlier recommendations for the use of the method in adults (Hilberg and Pedersen 2000, Schumacher 2002, Clement and Gordts 2005).

The collaboration with school children aged between seven and 14 years was easy and measuring was rapid. On the other hand, it must be stated that the children in the study on the reference data (Studies III and IV) were recruited on a voluntary basis and the measurements were done in a familiar environment during the school day. The situation might be different in the case of medical examination because of some disease or symptom, for example nasal obstruction. As a matter of fact, this was the case in studies I and II, where the children took part in the DIPP study for diabetes prevention, and used a nasal spray with insulin or placebo in a regular manner. The age of the children in this subgroup was between one and 12 years, so the mean age was younger than the mean age in the group of school children for the reference data. However, in that subgroup of younger children, only 6.8 % of the measurements had to be rejected because of lack of co-operation. Some groups have had more difficulties with co-operation; in the study of

Liukkonen et al (2006) as much as 30 % of children under two years of age refused to co-operate.

One of the most important sources of error in acoustic rhinometry is sound leakage between the nostril and the nosepiece. To avoid this leakage the use of appropriate equipment is crucial in children. Liukkonen et al (2006) evaluated the reasons for failed recordings and found that most nose adaptors for children are too small. The overall success rate of acoustic rhinometry was 60% in their group of 26 children. They found the most problematic age group to be three-to-four-year-olds. They stated that lack of adequate equipment, especially suitable nosepieces, induces artifacts in some children. In the same way, Djupesland and Pedersen (2000) recommended the use of a miniprobe for infants, a special probe for children over one year of age, and adult adapters for children more than six to ten years.

In this study, anatomical medium-size adult adapters were used in school children (Studies III and IV). Usually there was a good contact between the adapter and the nostril, and in addition, gel was used if necessary. In the Pilot and Follow-up studies (I and II), the use of nose adapters was more inconsistent, no gel was used, and the sound leakage was more common. As much as 28.4 % of the curves had to be rejected because of obvious sound leakage before statistical analysis in the Pilot study (I), but none in the reference data (Studies III and IV). Riechelmann et al (1993) found the same problem in their study of children aged between three and six years. They erased 25 % of the curves because of artifacts. In conclusion, the use of anatomical adapters, together with lubricant gel, seems to be a very easy and helpful way to prevent sound leakage, at least in school children.

Training of the operator diminishes the measurement time, along with the number of curves needed, and makes it easier to perform repeated measurements of good quality (Parvez et al 2000). In order to correctly and repeatable eliminate false curves, training is also crucial, because curve selection is always partly a subjective process. This study strongly confirms the need for adequate training and advice for the operating personnel.

The careful evaluation of the curve is crucial in order to select the accurate locations of the minima of the curve. As concluded in a recent review of the literature, there are different opinions regarding the anatomical correlation of the anterior part of the nose (Eduaro Nigro et al 2009). Because of this discrepancy, it is very important to define how the curve is measured and which point is considered as MCA. In this study, the first notch was considered as the nasal valve and the second notch as the anterior end of the inferior turbinate.

The environmental conditions must be stable in order to get correct results. In this study, measurements were performed after acclimatisation to room temperature in a quiet environment. A quiet breath through the mouth was allowed during the measurements, even though it is known that deep inspiration and expiration can cause artifacts in the acoustic curve (Tomkinson and Eccles 1995a). However, the situation for a child appears to be more relaxed if he/she is not asked to cease breathing, but is advised to breathe quietly through the mouth instead.

Unexpectedly, the unilateral acoustic values on the right side were significantly larger than on the left side (Study III). This is supposed to reflect some kind of systematic failure during the measurement process, because no side difference was found in unilateral VAS values. On the other hand, the same phenomenon has also been discussed by other groups (Parvez et al 2000, Paiva et al 2010). It has been concluded that readings on the right nostril are easier to carry out than readings on the left side, and this could be related to the placement of the sound tube by operators who are right-handed (Parvez et al 2000). In the same way, Paiva et al (2010) found a significant increase in the MCA on the right side, but not on the left side, in their follow-up study of children.

6.1.2 VAS

The visual analogue scale (VAS) is widely used in social and behavioural sciences to measure a variety of subjective phenomena (Wewers and Lowe 1990). VAS and its variations have been widely used to evaluate pain in children (McGrath 1989, Hamunen et al 2008, von Bayer et al 2009, Klemetti et al 2009). Some modifications of VAS for children with different colours or laughing and crying faces have been introduced (Hamunen et al 2008, Klemetti et al 2009). Cognitive ability, combined with chronological age, has been thought to be the best predictor of a child's accurate use of VAS; in general, the use of VAS in children under seven years of age may be uncertain (Shields et al 2003). Furthermore, it has been stated that children under seven years of age tend to use only the endpoints or the endpoints and middle of the VAS scale (Shields et al 2003, von Bayer et al 2009).

In rhinology, the most common way of using VAS is for subjective evaluation of the nasal obstruction in adults. On the contrary, only few studies have been published on the evaluation of nasal symptoms with VAS in children. Instead, symptom scores and a general sensation of obstruction have been used in children (Öztürk et al 2004, Miyamoto et al 2009). Sometimes VAS is not completed by a child, but by the parents or someone else (Steinsvåg et al 2007, Datema et al 2008).

This study is the first to use VAS as a subjective tool to evaluate nasal obstruction in children. A standard VAS was used in children aged between seven and 14 years with no permanent nasal obstruction. Children were asked to gently close the opposite side with a finger, and to evaluate the amount of nasal obstruction on the left and right side separately. Children found it quite easy to evaluate the obstruction of the nose and carefully completed the scale. In addition, they used the whole scale, not only the endpoints. It is concluded that children over seven years of age are able to correctly evaluate nasal obstruction with VAS when properly advised.

6.2 General discussion

6.2.1 Acoustic values

The use of acoustic rhinometry in children has increased during the last decade. However, only one group had published both baseline values and values after decongestion in school children before this study (Straszek et al 2007). Furthermore, this study provides both unilateral and total values of minimal cross-sectional areas (MCA) and anterior volumes of the nose.

In the study of children aged between seven and 14 years, the mean total MCA was 0.752 cm^2 (SD 0.165), and the mean total volume between 0 and 3 cm from the nostril was 4.00 cm^3 (SD 0.63) at baseline. Local decongestion (xylometazoline spray) was used to overcome mucosal swelling, and the total acoustic values after decongestion were 0.794 cm^2 (SD 0.162) and 4.38 cm^3 (SD 0.75), respectively. These total values before and after decongestion are in agreement with a similar study of school children aged between nine and 11 years (Straszek et al 2007). In the same way, the unilateral values of MCA and VOL on the right and left side are in concordance with those of the group of Straszek and co-workers (2007, 2008), but slightly narrower than in other studies of school children (Larsson et al 2001, Samolinski et al 2007, Miyamoto et al 2009).

The change in the acoustic values after decongestion was significant, indicating that the values are reliable and the change in mucosal swelling is detectable with acoustic rhinometry in children. This finding is especially remarkable because the children in this study had no permanent nasal symptoms, no chronic nasal obstruction, nor previous acute upper respiratory infection within the previous two weeks. Hence, the situation in the nasal mucosa may be considered quite stable at the time of the measurements. A significant change after decongestion was found in both unilateral and total values, and in both MCA and VOL values. It has been stated that the anterior volume could be the best value to use for studying changes in the mucosal swelling (Corey et al 1997, Hilberg and Pedersen 2000, Clement and Gordts 2005, Straszek et al 2007). On the other hand, MCA has been used to detect a positive mucosal reaction during nasal challenge (Pirilä and Nuutinen 1998, Wang et al 2004).

6.2.2 Predictive factors

Most studies have found no difference in acoustic values between boys and girls (Riechelmann et al 1993, Millqvist and Bende 1998, Millqvist and Bende 2006, Qian et al 2007, Straszek et al 2007, Straszek et al 2008, Paiva et al 2010). The same conclusion was drawn from these data; no difference between boys and girls was found at baseline or after decongestion of the nose.

Age seems to be one of the predictive factors of acoustic values (Riechelmann et al 1993, Millqvist and Bende 1998, Ho et al 1999, Samolinski et al 2007). In this study, a correlation between age and total MCA was found at baseline and after decongestion in school children (III). In the Pilot study (I), a similar correlation was found in unilateral values on the right side of the nose, but no difference was found between different age groups (0-2 years, 3-5 years, more than 6 years). Maybe these subgroups were too small to find any difference.

A correlation was found between the height of children and the total volume at baseline and after decongestion in children between seven and 14 years (Study III). Instead, no correlation was found between height and MCA. The same result has also been achieved by other groups (Ho et al 1999, Miyamoto et al 2009). In conclusion, height can be suggested as a predictor for acoustic values, especially for anterior volume of the nose.

Body surface area (BSA) is determined using the data of height and weight of a child. Thus, it is logical that a correlation was also found between BSA and volume. In addition, a correlation was found between BSA and total MCA at baseline, but not after decongestion. Based on the data of 83 children and 74 adults, Jurlina et al (2002) stated that an expected value of each subject's MCA could be calculated from his/her height and weight with a corrective factor. That conclusion sounds quite strong and straightforward. Furthermore, Eccles and co-workers found a correlation between total MCA and the width and height of the nose, but no correlation between acoustic values and any other body dimensions (Tomkinson and Eccles 1995b, Leong and Eccles 2009).

6.2.3 Follow-up

The set up of the Follow-up study (II) was very interesting. No follow-up study in children on intranasal medication has been published previously. The effect of the intranasal insulin was evaluated in adults with a short-term study prior to its use in children for safety reasons (Kupila et al 2003). No systemic or objective nasal side effects were detected, but some participants complained of transient nasal stinging. The actual DIPP study protocol allowed continuous intake of new children until year the 2007 (Näntö-Salonen et al 2008). The role of the rhinologist was to evaluate the possible local side effects of the nasal insulin spray during regular control visits.

The longest follow-up period was 72 months, even though the number of children at that control point was only three and allowed no further statistical analysis. Altogether, only minor side effects were reported during the follow-up (unpleasant feeling in the nose, itching, hurting and sneezing).The amount of irritation of the nose was similar in the insulin group compared to the placebo group during the first 24 months.

There was no difference in acoustic values between the insulin and placebo groups during the first two years. No increase was detected in total MCA or volume values during the follow-up period. Instead, BSA increased significantly in both the insulin and the placebo group, indicating the growth of children. It can be concluded that the growth of children does not significantly affect acoustic values in children between one and twelve years of age during the follow-up period of two years. Similar results in children with no nasal medication have been achieved by other groups (Millqvist and Bende 2006, Paiva et al 2010).

6.2.4 Correlations between objective and subjective evaluation

The correlation between acoustic rhinometry and VAS in adults has been conflicting (Sipilä et al 1995, Pirilä and Tikanto 2001, Clarke et al 2006, Andre et al 2009). Recently, Andre et al (2009) published a meta-analysis of correlations between objective and subjective analysis of nasal patency and concluded that it may be difficult to find a correlation in individuals with no nasal symptoms. They accepted sixteen studies for further analysis; all the patients in these studies were adults.

Similar difficulties in finding any correlation between objective and subjective methods has been found in children when using different symptom scores or a general sensation of obstruction as a subjective tool, and acoustic rhinometry as an objective tool (Öztürk et al 2004, Miyamoto et al 2009). No correlative study between VAS for nasal symptoms and any rhinometric measurement in children has been published earlier.

This study was able to find a correlation between unilateral VAS and acoustic values in children with no nasal symptoms (Study IV). The correlation was detectable at baseline with a variable amount of mucosal swelling, but not after decongestion of the nasal mucosa. This finding is in concordance with previous studies stating that a correlation between the objective and subjective method is easier to discover in an obstructed nose, when each nasal passage is assessed individually, or when there is a sufficient difference between the two nostrils (Sipilä et al 1995, Simola and Malmberg 1997, Larsson et al 2001, Pirilä and Tikanto 2001, Numminen et al 2003a, Clarke et al 2006, Kjaergaard et al 2009, Miyamoto et al 2009).

The correlations between objective and subjective evaluation of nasal obstruction found by different groups are usually weak (r-values between 0.12 and 0.32, if reported), even though statistically significant (Pirilä and Tikanto 2001, Kjaergaard et al 2008, Kjaergaard et al 2009). According to Burnand et al (1990), r-values greater than or equal to 0.32 mean a significant correlation for medical values. Similarly, Numminen et al (2003a) found a statistical correlation between VAS and acoustic values in adults, but estimated that there was no significance clinically ($r < 0.40$). In this study (Study IV), the r-values varied between 0.20 and 0.25, and were still considered significant. It is concluded that the existence of these correlations is remarkable, because the children in the study had no permanent nasal symptoms or acute infection. It can be assumed, on the bases of earlier studies, that a stronger correlation might be found in the case of nasal obstruction.

The subjective sensation of nasal obstruction is a complex issue. It has been clearly demonstrated that menthol inhalation causes subjective improvement in the nasal sensation of airflow without any objective decongestant action (Eccles 1992, Schumacher 2002, Eccles 2003). Furthermore, the sensation of nasal stuffiness has been demonstrated in atrophic rhinitis without any increase in nasal resistance (Schumacher 2002). This phenomenon is caused by the action of thermoreceptors in the skin and mucosal surfaces, and may partly explain the inconsistency in the correlations between subjective and objective methods.

As a conclusion to the discrepancy, Andre et al (2009) seriously questioned the need for objective measurements at all. On the contrary, just the opposite conclusion is drawn on the basis of these new results in children (Study IV). The use of both objective and subjective methods simultaneously is recommended to support the clinical decision. They reflect two different sides of the problem of nasal obstruction and should be considered together.

6.3 Implications for further studies

This study offers reference data for children aged between seven and 14 years with no permanent nasal problems. Further research is needed to evaluate the role of acoustic rhinometry in children with nasal obstruction. Clinically, one of the most interesting questions to be answered is the capability of acoustic rhinometry to distinguish between mucosal and structural stuffiness in children in the same way as it does in adults. This kind of information would help the clinician to plan the treatment of nasal obstruction in children, at least in the most problematic cases. In addition, it would help to evaluate the nose of children with asthma for the best possible nasal medication.

Furthermore, acoustic rhinometry could play a greater role in the follow-up of surgical or medical treatment of the nose in children than it does today. Acoustic rhinometry has potential as an objective method to monitor the effectiveness of medical therapy in adults (Chan et al 2003, Valero et al 2009). The Follow-up study (II) shows that the method has the same potential in children on nasal medication, as long as the growth of the child is taken into account in a long-term follow-up.

The study of children with nasal obstruction would provide us with more information about the role of objective and subjective tools in pediatric rhinology. The more extensive use of standard VAS in children would also improve the comparability of different studies.

In addition, it would be interesting to measure children less than seven years of age with acoustic rhinometry for reference values, and to determine the role of VAS in that age group as well. The usefulness of acoustic rhinometry in children under seven years, with or without nasal obstruction, remains to be proven.

7 CONCLUSIONS

1. Acoustic rhinometry is a suitable objective method to examine intranasal dimensions in children. It is easy to perform and well tolerated.
2. A standard way to measure children in clinical practice was achieved. The most important source of error is sound leakage when the nosepiece is not in good contact with the nostril. To avoid sound leakage and distortion of the nose, gel should be used if needed. Training of the personnel is the best way to avoid errors.
3. Reference values for children between seven and 14 years were established at baseline and after decongestion of the nose. The change in the acoustic values between baseline and decongestion was significant.
4. A significant correlation was found between MCA and age, height, and BSA of a child. Similarly, a significant correlation was found between the volume of the anterior part of the nose and height and BSA of a child. There was no difference between boys and girls.
5. Acoustic rhinometry is a suitable method for objective follow-up in children. In particular, it is useful to detect the changes in mucosal swelling. The increase in acoustic values caused by the growth of a child is not significant during a follow-up period of two years.
6. VAS is a suitable subjective method to evaluate the sensation of unilateral nasal obstruction in children over seven years of age. A correlation between VAS and acoustic values was found at baseline but not after decongestion of the nose in children with no nasal symptoms.

8 SUMMARY

Acoustic rhinometry is a useful objective method in many clinical situations to evaluate nasal obstruction. The method gives practical information about the place and degree of nasal obstruction, and in addition, it provides values before and after decongestion of the nasal mucosa. This makes acoustic rhinometry a multipurpose tool for the diagnosis and follow-up of treatment in both rhinology and rhinosurgery.

Acoustic rhinometry is nowadays widely used in adults. However, acoustic rhinometry seems to be a suitable method also for children because it is rapid, non-invasive, with no side-effects, and minimal co-operation is required. For proper use of the method, reference values are a necessity. So far, the information on normative values for children has been scattered. Furthermore, the correlation between objective and subjective instruments for nasal evaluation has been debated and the relevance of the correlation is still questioned by some rhinolologists.

The purpose of the present study was to evaluate the usefulness of acoustic rhinometry for objective evaluation of nasal dimensions in children. The aim was to define reference values for the method in school children at baseline and after decongestion of the nasal mucosa. Moreover, the role of the most probable predictors for the acoustic values (age, sex, height, and body surface area) was evaluated.

The study was carried out to establish a standard measurement procedure, and to clarify the strategies needed to avoid the most important sources of errors during the measurements. To determine the role of subjective and objective evaluation of the nose in children, the VAS scale was also used. Finally, to test the method in clinical practice, a follow-up study in children using nasal insulin or placebo was carried out.

For the reference values and VAS study (Studies III and IV), the subjects were recruited on a voluntary basis from two primary schools. The criteria for exclusion were any permanent nasal symptoms or acute upper respiratory infection within the previous two weeks. The study included 124 children aged between 6.90 and 13.84 years (mean 10.38 years). There were 59 boys (47.6%) and 65 girls (52.4 %) in the study group. All the measurements were carried out between November 2009 and January 2010, outside the pollen season, during the school day.

The subjects in the Pilot and Follow-up studies (Studies I an II) were a subcohort of the Type I Diabetes Prediction and Prevention study (DIPP). Children over one year of age, at risk of type 1 diabetes were invited to participate in the randomised double-blinded intervention trial comparing intranasal insulin with placebo. The study cohort included 74 children, with a mean age of 4.25 years (SD 2.39).

In the Follow-up study (II), there were 35 children in the insulin group and 37 children in the placebo group. The points of special interest were at three months, six months, 12 months and 24 months. After that, a control was arranged once a year, the longest follow-up time being 72 months. All the controls were carried out between 1999 and 2007, and in addition to acoustic measurements, nasal symptoms were also recorded.

The values of special interest were unilateral or bilateral minimal cross-sectional area (MCA) and anterior volume of the nostril between 0 and 3 cm (VOL). The age, sex, height, and weight of every child was recorded. The visual analogue scale (VAS) of 10 cm was filled in by children before any measurements in the VAS study (IV).

At baseline, the mean TMCA calculated as the sum of left and right sides was 0.752 cm^2 (SD 0.165), and the total volume between 0 and 3 cm from the nostril (TVOL) was 4.00 cm^3 (SD 0.63) in children aged between seven and 14 years. A significant increase in acoustic values was found after decongestion of the nose.

A significant correlation between TMCA and age, height, and BSA of the child was found at baseline. TVOL correlated with height and BSA at baseline and after decongestion. There was no difference between boys and girls. The unilateral VAS correlated with unilateral MCA and volume at baseline, but not after decongestion. In conclusion, VAS shows potential as a subjective method to evaluate the obstruction of the nose in school children.

This study introduces a standard measurement procedure for children. The procedure aims to avoid the most significant sources of error and makes the measurements more stable and reliable. The use of anatomical adapters, together with lubricant gel if needed, seems to be a very easy and beneficial way to prevent sound leakage, the most common sources of artifact. As a result, this study emphasizes the need for strict technical care and training of the operating personnel.

It can be concluded that acoustic rhinometry is a suitable objective method to examine nasal dimensions in children. It is easy and rapid to perform, and well tolerated. The method can be used in a follow-up of mucosal changes in children; the increase in values caused by growth is not significant during a two-year period.

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Lotta Haavisto

10 REFERENCES

Andre RF, Vuyk HD, Ahmed A, Graamans K, Nolst Trenite GJ. Correlation between subjective and objective evaluation of the nasal airway. A systematic review of the highest level of evidence. Clin Otolaryngol 2009; 34: 518-525.

Baczek M, Hassmann E, Alifier M, Iwaszko-Krawczuk W. Acoustic rhinometry assessment of the nasal cycle in neonates. Acta Otolaryngol 2001; 121: 301-304.

von Bayer CL, Spagrud LJ, McCormick JC, Choo E, Neville K, Connelly MA. Three new datasets supporting use of the Numerical Rating Scale (NRS-11) for children's self-reports of pain intensity. Pain 2009; 143: 223-227.

Brinckmann CAC, Scapin FP, Bernd LAG, Neto FL. Effect of improved nasal airflow after adenoidectomy on nasal erectile tissue. Arch Otolaryngol Head Neck Surg 2008; 134: 832-836.

Buckland JR, Thomas S, Harries PG. Can the sino-nasal outcome test (SNOT-22) be used as a reliable outcome measure for successful septal surgery? Clin Otolaryngol 2003; 28: 43-47.

Buenting JE, Dalston RM, Drake AF. Nasal cavity area in term infants determined by acoustic rhinometry. Laryngoscope 1994a; 104: 1439-1445.

Buenting JE, Dalston RM, Smith TL, Drake AF. Artifacts associated with acoustic rhinometry assessment of infants and young children: a model study. J Appl Physiol 1994b; 77: 2558-2563.

Burnand B, Kernan WN, Feinstein AR. Indexes and boundaries for "quantitative significance" in statistical decisions. J Clin Epidemiol 1990; 43: 1273-1284.

Cakmak O, Celik H, Cankurtaran M, Ozluoglu LN. Effects of anatomical variations of the nasal cavity on acoustic rhinometry measurements: a model study. Am J Rhinol 2005; 19: 262-268.

Cakmak O, Coşkun M, Celik H, Büyüklü F, Ozlüoğlu LN. Value of acoustic rhinometry for measuring nasal valve area. Laryngoscope 2003; 113: 295-302.

Can IH, Ceylan K, Bayiz U, Ölmez A, Samim E. Acoustic rhinometry in the objective evaluation of childhood septoplasties. Int J Pediatr Otorhinolaryngol 2005; 69: 445-448.

Cankurtaran M, Celik H, Coşkun M, Hizal E, Cakmak O. Acoustic rhinometry in healthy humans: accuracy of area estimates and ability to quantify certain anatomic structures in the nasal cavity. Ann Otol Rhinol Laryngol 2007; 116: 906-916.

Chan KO, Huang ZL, Wang DY. Acoustic rhinometric assessment of nasal obstruction after treatment with fluticasone propionate in patients with perennial rhinitis. Auris Nasus Larynx 2003; 30: 379-383.

Chawes BLK, Kreiner-Möller E, Bisgaard H. Objectice assessments of allergic and nonallergic rhinitis in young children. Allergy 2009; 64: 1547-1553.

Cho JH, Lee DH, Lee NS, Won YS, Yoon HR, Suh BD. Size assessment of adenoid and nasopharyngeal airway by acoustic rhinometry in children. J Laryngol Otol 1999; 113: 899-905.

Clarke JD, Hopkins ML, Eccles R. Evidence for correlation of objective and subjective measures of nasal airflow in patients with common cold. Clin Otolaryngol 2005; 30: 35–38.

Clarke JD, Hopkins ML, Eccles R. How good are patients at determining which side of the nose is more obstructed? A study on the limits of discrimination of the subjective assessment of unilateral nasal obstruction. Am J Rhinol 2006; 20: 20-24.

Clement PA. Committee report on standardization of rhinomanometry. Rhinology 1984; 22: 151-155.

Clement PA. Rhinomanometry. Allergy 1997; 52(Suppl 33): 26-27.

Clement PAR, Gordts F. Consensus report on acoustic rhinometry and rhinomanometry. Rhinology 2005; 43: 169-179.

Cole P. Acoustic rhinometry and rhinomanometry. Rhinology Suppl 2000; 16: 29-34.

Compadretti GC, Tasca I, Bonetti GA. Nasal airway measurements in children treated by rapid maxillary expansion. Am J Rhinol 2006; 20: 358-393.

Corey JP. Acoustic rhinometry: should we be using it? Curr Opin Otolaryngol Head Neck Surg 2006; 14: 29-34.

Corey JP, Gungor A, Nelson R, Liu X, Fredberg J. Normative standards for nasal cross-sectional areas by race as measured by acoustic rhinometry. Otolaryngol Head Neck Surg 1998; 119: 389-393.

Corey JP, Kemker BJ, Nelson R, Gungor A. Evaluation of the nasal cavity by acoustic rhinometry in normal and allergic subjects. Otolaryngol Head Neck Surg 1997; 117: 22-28.

Corey JP, Nalbone VP, Ng BA. Anatomic correlates of acoustic rhinometry as measured by rigid nasal endoscopy. Otolaryngol Head Neck Surg 1999; 121: 572-276.

Datema FR, Vemer-van den Hoek JG, Wieringa MH, Mulder PM, Baatenburg de Jong RJ, Blom HM. A visual analog scale can assess the effect of surgical treatment in children with chronic otitis media with effusion. Int J Pediatr Otorhinolaryngol 2008; 72: 461-467.

Djupesland P, Kaastad E, Franzén G. Acoustic rhinometry in the evaluation of congenital choanal malformations. Int J Pediatr Otorhinolaryngol 1997; 41: 319-337.

Djupesland PG, Lyholm B. Nasal airway dimensions in term neonates measured by continuous wide-band noise acoustic rhinometry. Acta Otolaryngol 1997; 117: 424-432.

Djupesland PG, Lyholm B. Changes in nasal airway dimensions in infancy. Acta Otolaryngol 1998a; 118: 852-858.

Djupesland PG, Lyholm B. Technical abilities and limitations of acoustic rhinometry optimised for infants. Rhinology 1998b; 36: 104-113.

Djupesland P, Pedersen OF. Acoustic rhinometry in infants and children. Rhinology Suppl 2000; 16: 52-58.

Eccles R. Nasal airway resistance and nasal sensation of airflow. Rhinol Suppl 1992; 14: 86-90.

Eccles R. Menthol: effects on nasal sensation of airflow and the drive to breathe. Curr Allergy Asthma Rep 2003; 3: 210-214.

Eduardo Nigro CE, Faria Aguar Nigro J, Mion O, Ferreira Mello J Jr, Louis Voegels R, Roithmann R. A systematic review to assess the anatomical correlates of the notches in acoustic rhinometry. Clin Otolaryngol 2009; 34: 431-7.

Ellegård E. Practical aspects on rhinostereometry. Rhinology 2002; 40: 115-117.

Fisher EW. Acoustic rhinomanometry. Clin Otolaryngol 1997; 22: 307-317.

Fisher EW, Daly NJ, Morris DP, Lund VJ. Experimental studies of the resolution of acoustic rhinometry in vivo. Acta Otolaryngol 1994; 114: 647-650.

Fisher EW, Morris DP, Biemans JAM, Palmer CR, Lund VJ. Practical aspects of acoustic rhinometry: Problems and solutions. Rhinology 1995a; 33: 219-223.

Fisher EW, Palmer CR, Lund VJ. Monitoring fluctuations in nasal patency in children: acoustic rhinometry versus rhinohygrometry. J Laryngol Otol 1995b; 109: 503-508.

Fisher EW, Scadding GK, Lund VJ. The role of acoustic rhinometry in studying the nasal cycle. Rhinology 1993; 31: 57-61.

Fraser L, Kelly G. An evidence-based approach to the management of the adult with nasal obstruction. Clin Otolaryngol 2009; 34: 151-155.

Gallego AJ, Cavallari FEM, Valera FCP, Demarco RC, Anselmo-Lima WT. Study of nasal cycles in children by acoustic rhinometry. Am J Rhinol 2006; 20: 560-562.

Gomes AO, Sampaio-Teixeira AC, Trindade SH, Trindade IE. Nasal cavity geometry of healthy adults assessed using acoustic rhinometry. Braz J Otorhinolaryngol 2008; 74: 746-754.

Gordon JM, Rosenblatt M, Witmans M, Carey JP, Heo G, Major PW, Flores-Mir C. Rapid palatal expansion effects on nasal airway dimensions as measured by acoustic rhinometry. A systematic review. Angle Orthod 2009; 79: 1000-1007.

Gosepath J, Amedee RG, Mann WJ. Nasal provocation testing as an international standard for evaluation of allergic and nonallergic rhinitis. Laryngoscope 2005; 115: 512-516.

Grymer LF. Clinical applications of acoustic rhinometry. Rhinology Suppl 2000; 16: 35-43.

Grymer LF, Hilberg O, Pedersen OF. Prediction of nasal obstruction based on clinical examination and acoustic rhinometry. Rhinology 1997; 35: 53-57.

Grymer LF, Illum P, Hilberg O. Septoplasty and compensatory inferior turbinate hypertrophy: a randomized study evaluated by acoustic rhinometry. J Laryngol Otol 1993; 107: 413-417.

Grymer LF, Hilberg O, Pedersen OF, Rasmussen TR. Acoustic rhinometry: Values from adults with subjective normal nasal patency. Rhinology 1991; 29: 35-47.

Hamilton JW, McRae RDR, Jones AS. The magnitude of random errors in acoustic rhinometry and re-interpretation of acoustic profile. Clin Otolaryngol 1997; 22: 408-413.

Hamunen K, Maunuksela E-L, Olkkola KT. Interpretation of the large red-and-white visual analog scale by children compared with adults. J Ped Nurs 2008; 23: 142-144.

Hatzakis GE, Karsan N, Cook J, Schloss M, Davis GM. Acoustic reflectance of pharyngeal structures in children. Int J Pediatr Otorhinolaryngol 2003; 67: 373-381.

Hilberg O. Objective measurement of nasal airway dimensions using acoustic rhinometry: methodological and clinical aspects. Allergy Suppl 2002; 57: 5-39.

Hilberg O, Grymer LF, Pedersen OF. Nasal histamine challenge in nonallergic and allergic subjects evaluated by acoustic rhinometry. Allergy 1995a; 50: 166-173.

Hilberg O, Grymer LF, Pedersen OF. Spontaneous variations in congestion of the nasal mucosa. Ann Allergy 1995b; 74: 516-521.

Hilberg O, Jackson AC, Swift DL, Pedersen OF. Acoustic rhinometry: evaluation of nasal cavity geometry by acoustic reflection. J Appl Physiol 1989; 66: 295-303.

Hilberg O, Jensen FT, Pedersen OF. Nasal airway geometry: comparison between acoustic reflections and magnetic resonance scanning. J Appl Physiol 1993; 75: 2811-2819.

Hilberg O, Pedersen OF. Acoustic rhinometry: recommendations for technical specifications and standard operating procedures. Rhinology Suppl 2000; 16: 3-17.

Ho WK, Wei WI, Yuen APW, Chan KL, Hui Y. Measurement of nasal geometry by acoustic rhinometry in normal-breathing Asian children. J Otolaryngol 1999; 28: 232-237.

Ho WK, Yuen APW, Tang KC, Wei WI, Lam PKY. Time course in the relief of nasal blockage after septal and turbinate surgery: a prospective study. Arch Otolaryngol Head Neck Surg 2004; 130: 324-328.

Holinger LD, Weese-Mayer DE. Apnea, apparent life-threatening events, and disorders of respiratory control. In Holinger LD, Lusk RP and Green CG eds. Pediatric Laryngology and Bronchoeosophagology, pp 337-347. Lippincott-Raven Publishers, Philadelphia 1997.

Holmström M. The use of objective measures in selecting patients for septal surgery. Rhinology 2010; 48: 387-393.

Holmström M, Scadding GK, Lund VJ, Darby YC. Assessment of nasal obstruction. A comparison between rhinomanometry and nasal inspiratory peak flow. Rhinology 1990; 28: 191-196.

Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item sinonasal outcome test. Clin Otolaryngol 2009; 34: 447-454.

Jackson AC, Butler JP, Millet EJ, Hoppin FG, Dawson SV. Airway geometry by analysis of acoustic pulse response measurements. J Appl Physiol 1977; 43: 523-536.

Jastaniah W, Aseeri M. A cross-sectional study comparing variation in body surface area and chemotherapy dosing in pediatric oncology using two different methods. J Oncol Pharm Pract 2010; 16: 189-193.

Jurlina M, Mladina R, Dawidowsky K, Ivanković D, Bumber Z, Subarić M. Correlation between the minimal cross-sectional area of the nasal cavity and body surface area: preliminary results in normal patients. Am J Rhinol 2002; 16: 209-213.

Juto JE, Lundberg C. An optical method for determining changes in mucosal congestion in the nose in man. Acta Otolaryngol 1982; 94: 149-156.

Kemker B, Liu X, Gungor A, Moinuddin R, Corey JP. Effect of nasal surgery on the nasal cavity as determined by acoustic rhinometry. Otolaryngol Head Neck Surg 1999; 121: 567-571.

Kemppainen T, Ruoppi P, Seppä J, Sahlman J, Peltonen M, Tukiainen H, Gylling H, Vanninen E, Tuomilehto H. Effect of weight reduction on rhinometric measurements in overweight patients with obstructive sleep apnea. Am J Rhinol 2008; 22: 410-415.

Kesavanathan J, Swift DL, Fitzgerald TK, Permutt T, Bascom R. Evaluation of acoustic rhinometry and posterior rhinomanometry as tools for inhalation challenge studies. J Toxicol Environ Health 1996; 48: 295-307.

Kim CS, Moon BK, Jung DH, Min YG. Correlation between nasal obstruction symptoms and objective parameters of acoustic rhinometry and rhinomanometry. Auris Nasus Larynx 1998; 25: 45-48.

Kjaergaard T, Cvancarova M, Steinsvåg SK. Does nasal obstruction mean that the nose is obstructed? Laryngoscope 2008; 118: 1476-1481.

Kjaergaard T, Cvancarova M, Steinsvåg SK. Nasal congestion index: A measure for nasal obstruction. Laryngoscope 2009; 119: 1628-1632.

Klemetti S, Kinnunen I, Suominen T, Antila H, Vahlberg T, Grenman R, Leino-Kilpi H. The effect of preoperative fasting on postoperative pain, nausea and vomiting in pediatric ambulatory tonsillectomy. Int J Pediatr Otorhinolaryngol 2009; 73: 263-273.

Kupila A, Sipilä J, Keskinen P, Simell T, Knip M, Pulkki K, Simell O. Intranasally administred insulin intended for prevention of type 1 diabetes – a safety study in healthy adults. Diabetes Metab Res Rev 2003; 19: 415-420.

Lam DJ, James KT, Weawer EM. Comparison of anatomic, physiological, and subjective measures of the nasal airway. Am J Rhinol 2006; 20: 465-470.

Landa J, Rich A, Finkelman M. Confirming nasal airway dimensions observed on panoramic and posterior-anterior cephalometric radiographs using an acoustic rhinometer. Eur Arch Paediatr Dent 2010; 11: 115-121.

Lane AP, Zweiman B, Lanza DC, Swift D, Doty R, Dhong HJ, Kennedy DW. Acoustic rhinometry in the study of the acute nasal allergic response. Ann Otol Rhinol Laryngol 1996; 105: 811-818.

Lang C, Grützenmacher S, Mlynski B, Plontke S, Mlynski G. Investigating the nasal cycle using endoscopy, rhinoresistometry, and acoustic rhinometry. Laryngoscope 2003; 113: 284-289.

Larsson C, Millqvist E, Bende M. Relationship between subjective nasal stuffiness and nasal patency measured by acoustic rhinometry. Am J Rhinol 2001; 15: 403-405.

Leclerc JE, Leclerc JT, Bernier K. Choanal atresia: long-term follow-up with objective evaluation of nasal airway and olfaction. Otolaryngol Head Neck Surg 2008; 138: 43-49.

Lenders H, Pirsig W. Diagnostic value of acoustic rhinometry: patients with allergic and vasomotor rhinitis compared with normal controls. Rhinology 1990; 28: 5-16.

Leong SC, Eccles R. A systematic review of the nasal index and the significance of the shape and size of the nose in Rhinology. Clin Otolaryngol 2009; 34: 191-198.

Lim M, Lew-Gor S, Darby Y, Brookes N, Scadding G, Lund VJ. The relationship between subjective assessment instruments in chronic rhinosinusitis. Rhinology 2007; 45: 144-147.

Liu SA, Su MC, Jiang RS. Nasal patency measured by acoustic rhinometry in East Asian patients with sleep-disordered breathing. Am J Rhinol 2006; 20: 274-277.

Liukkonen K, Virkkula P, Pitkäranta A. Acoustic rhinometry in small children. Rhinology 2006; 44: 160-163.

Marais J, Maran AG. Nasoantral window assessment by acoustic rhinometry. J Laryngol Otol 1994; 108: 567-568.

Marques VC, Anselmo-Lima WT. Pre- and postoperative evaluation by acoustic rhinometry of children submitted to adenoidectomy or adenotonsillectomy. Int J Pediatr Otorhinolaryngol 2004; 68: 311-316.

Mayhew TM, O'Flynn P. Validation of acoustic rhinometry by using the Cavalieri principle to estimate nasal cavity volume in cadavers. Clin Otolaryngol 1993; 18: 220-225.

McGrath PA. Evaluating a child's pain. J Pain Symptom Manage 1989; 4: 198-214.

Millqvist E, Bende M. Reference values for acoustic rhinometry in subjects without nasal symptoms. Am J Rhinol 1998; 12: 341-343.

Millqvist E, Bende M. Two-year follow-up with acoustic rhinometry in children. Am J Rhinol 2006; 20: 203-205.

Miyamoto Y, Takeuchi K, Majima Y. Measurement of nasal patency by acoustic rhinometry in Japanese school children. Auris Nasus Larynx 2009; 36: 406-410.

Mlynski G. Surgery of the nasal septum. Facial Plast Surg 2006; 22: 223-229.

Morgan NJ, MacGregor FB, Birchall MA, Lund VJ, Sittampalam Y. Racial differences in nasal fossa dimensions determined by acoustic rhinometry. Rhinology 1995; 33: 224-228.

Morris LG, Setlur J, Burschtin OE, Steward DL, Jacobs JB, Lee KC. Acoustic rhinometry predicts tolerance of nasal continuous positive airway pressure: a pilot study. Am J Rhinol 2006; 20: 133-137.

Mosteller RD. Simplified calculation of body-surface area. N Engl J Med 1987; 22: 1098

Muñoz-Cano R, Salvador R, Valero A, Berenguer J, Alobid I, Bartra J, Guilemany JM, Mullol J, Picado C. Accuracy of acoustic rhinometry versus computed tomography in the evaluation of nasal cavity in patients with nasal polyposis. Rhinology 2010; 48: 224-227.

Naito K, Miyata S, Saito S, Sakurai K, Takeuchi K. Comparison of perceptional nasal obstruction with rhinometric and acoustic rhinometric assessment. Eur Arch Otorhinolaryngol 2001; 258: 505-508.

Näntö-Salonen K, Kupila A, Simell S, Siljander H, Salonsaari T, Hekkala A, Korhonen S, Erkkola R, Sipilä JI, Haavisto L, Siltala M, Tuominen J, Hakalax J, Hyöty H, Ilonen J, Veijola R, Simell T, Knip M, Simell O. Nasal insulin to prevent type 1 diabetes in children with HLA genotypes and antibodies conferring increased risk of disease: a double-blind, randomised controlled trial. Lancet 2008; 372: 1756-1755.

Nathan RA, Eccles R, Howarth PH, Steinsvåg SK, Togias A. Objective monitoring of nasal patency and nasal physiology in rhinitis. J Allergy Clin Immunol 2005; 115: 442-459.

Numminen J, Ahtinen M, Huhtala H, Laranne J, Rautiainen M. Correlation between rhinometric measurement methods in healthy young adults. Am J Rhinol 2002; 16: 203-208.

Numminen J, Ahtinen M, Huhtala H, Rautiainen M. Comparison of rhinometric measurements methods in intranasal pathology. Rhinology 2003a; 41: 65-68.

Numminen J, Dastidar P, Heinonen T, Karhuketo T, Rautiainen M. Reliability of acoustic rhinometry. Respir Med 2003b; 97: 421-427.

O'Flynn P. Acoustic rhinometry: validation of volume changes following intra-nasal polypectomy. Clin Otolaryngol Allied Sci 1993; 18: 423-425.

Okun MN, Hadjiangelis N, Green D, Hedli LC, Lee KC, Krieger AC. Acoustic rhinometry in pediatric sleep apnea. Sleep Breath 2010; 14 : 43-49.

Olarinde O, Banerjee AR, O'Callaghan C. Effect of sleeping position on nasal patency in newborns. Arch Dis Child Fetal Neonatal Ed 2006; 91: 365-366.

Paiva JB, Freire-Maia BA, Rino Neto J, Di Francesco RC, Voegels RL. Evaluation of children nasal geometry, employing accoustic rhinometry. Braz J Otorhinolaryngol 2010; 76: 355-362.

Parvez L, Erasala G, Noronha A. Novel techniques, standardization tools to enhance reliability of acoustic rhinometry measurements. Rhinology Suppl 2000; 16: 18-28.

Passali D, Mezzedimi C, Passali DG, Bellussi L. Monitoring methods of nasal pathology. Int J Pediatr Otorhinolaryngol 1999; 49: 199-202.

Passali D, Mezzedimi C, Passali GC, Nuti D, Bellussi L. The role of rhinomanometry, acoustic rhinometry, and mucociliary transport time in the assessment of nasal patency. Ear Nose Throat 2000; 79: 397-400.

Pedersen OF, Berkowitz R, Yamagiwa M, Hilberg O. Nasal cavity dimensions in the newborn measured by acoustic reflections. Laryngoscope 1994; 104: 1023-1028.

Piccirillo JF, Merritt MG Jr, Richards ML. Psychometric and clinimetric validity of the 20-Item Sino-Nasal Outcome Test (SNOT-20). Otolaryngol Head Neck Surg 2002; 126: 41-47.

Pirilä T, Nuutinen J. Acoustic rhinometry, rhinomanometry and the amount of nasal secretion in the clinical monitoring of the nasal provocation test. Clin Exp Allergy 1998; 28: 468-477.

Pirilä T, Tikanto J. Unilateral and bilateral effect of nasal septum surgery demonstrated with acoustic rhinometry, rhinomanometry and subjective assessment. Am J Rhinol 2001; 15: 127-133.

Pynnonen MA, Kim HM, Terrell JE. Validation of the Sino-Nasal Outcome Test 20 (SNOT-20) domains in nonsurgical patients. Am J Rhinol Allergy 2009; 23: 40-45.

Qian W, Chen W, Chen JM, Haight J. Acoustic rhinometry in preschool children. Otolaryngol Head Neck Surg 2007; 137: 39-42.

Riechelmann H, O´Connel JM, Rheinheimer MC, Wolfensberger M, Mann WJ. The role of acoustic rhinometry in the diagnosis of adenoidal hypertrophy in pre-school children. Eur J Pediatr 1999; 158: 38-41.

Riechelmann H, Rheinheimer MC, Wolfensberger M. Acoustic rhinometry in pre-school children. Clin Otolaryngol 1993; 18: 272-277.

Roithmann R, Cole P, Chapnik J, Barreto SM, Szalai JP, Zamel N. Acoustic rhinometry, rhinomanometry, and the sensation of nasal patency: a correlative study. J Otolaryngol 1994; 23: 454-458.

Samolinski BK, Grzanka A, Gotlib T. Changes in nasal cavity dimensions in children and adults by gender and age. Laryngoscope 2007; 117: 1429-1433.

Scadding GK, Darby YC, Austin CE. Acoustic rhinometry compared with anterior rhinomanometry in the assessment of the response to nasal allergen challenge. Clin Otolaryngol 1994; 19: 451-454.

Schumacher MJ. Nasal congestion and airway obstruction: the validity of available objective and subjective measures. Curr Allergy Asthma Rep 2002; 2: 245-251.

Shields BJ, Palermo TM, Powers JD, Grewe SD, Smith GA. Predictors of a child's ability to use visual analogue scale. Child Care Health Dev 2003; 29: 281-290.

Silkoff PE, Chakravorty S, Chapnik J, Cole P, Zamel N. Reproducibility of acoustic rhinometry and rhinomanometry in normal subjects. Am J Rhinol 1999; 13: 131-135.

Simola M, Malmberg H. Sensation of nasal airflow compared with nasal airway resistance in patients with rhinitis. Clin Otolaryngol 1997; 22: 260-262.

Sipilä J, Nyberg-Simola S, Suonpää J, Laippala P. Some fundamental studies on clinical measurement conditions in acoustic rhinometry. Rhinology 1996; 34: 206-209.

Sipilä J, Suonpää J. A prospective study using rhinomanometry and patient clinical satisfaction to determine if objective measurements of nasal airway resistance can improve the quality of septoplasty. Eur Arch Otorhinolaryngol 1997; 254: 387-90.

Sipilä J, Suonpää J, Silvoniemi P, Laippala P. Correlations between subjective sensation of nasal patency and rhinomanometry in both unilateral and total nasal assessment. ORL J Otorhinolaryngol Relat Spec 1995; 57: 260-263.

Steinsvåg SK, Skadberg B, Bredesen K. Nasal symptoms and signs in children suffering from asthma. Int J Pediatr Otorhinolaryngol 2007; 71: 615-621.

Stewart MG, Witsell DL, Smith TL, Weaver EM, Yueh B, Hannley MT. Development and validation of the Nasal Obstruction Symptom Evaluation (NOSE) scale. Otolaryngol Head Neck Surg 2004; 130: 157-163.

Straszek SP, Moeller A, Hall GL, Zhang G, Stick SM, Franklin PJ. Reference values for acoustic rhinometry in children from 4 to 13 years old. Am J Rhinol 2008; 22: 285-229.

Straszek SP, Schlünssen V, Sigsgaard T, Pedersen OF. Reference values for acoustic rhinometry in decongested school children and adults: the most sensitive measurement for change in nasal patency. Rhinology 2007; 45: 36-39.

Szucs E, Kaufman L, Clement PAR. Nasal resistance - a reliable assessment of nasal patency? Clin Otolaryngol 1995; 20: 390-395.

Tarhan E, Coskun M, Cakmak O, Celik H, Cankurtaran M. Acoustic rhinometry in humans: accuracy of nasal passage area estimates, and ability to quantify paranasal sinus volume and ostium size. J Appl Physiol 2005; 99: 616-623.

Tomkinson A, Eccles R. Errors arising in cross-sectional area estimation by acoustic rhinometry produced by breathing during measurement. Rhinology 1995a; 33: 138-140.

Tomkinson A, Eccles R. External facial dimensions and minimum nasal cross-sectional area. Clin Otolaryngol 1995b; 20: 557-560.

Uzzman A, Metcalfe DD, Komarow HD. Acoustic rhinometry in the practice of allergy. Ann Allergy Asthma Immunol 2006; 97: 745-752.

Valero A, Serrano C, Bartrá J, Izquierdo I, Muñoz-Cano R, Mullol J, Picado C. Reduction of nasal volume after allergen-induced rhinitis in patients treated with rupatadine: a randomized, cross-over, double-blind, placebo-controlled study. J Investig Allergol Clin Immunol 2009; 19: 488-493.

Virkkula P, Maasilta P, Hytönen M, Salmi T, Malmberg H. Nasal obstruction and sleep-disordered breathing: the effect of supine body position on nasal measurements in snorers. Acta Otolaryngol 2003; 123: 648-654.

Wang DY, Raza MT, Goh DYT, Lee BW, Chan YH. Acoustic rhinometry in nasal allergen challenge study: which dimensional measures are meaningful? Clin Exp Allergy 2004; 34: 1093-1098.

Ware JA, Aki K. Continuous and discrete inverse-scattering problems in a stratified elastic medium. I. plane waves at normal incidence. J Acoust Soc Am 1969; 45: 911-921.

Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. Res Nurs Health 1990; 13: 227-236.

Yahyavi S, Parsa FM, Fereshtehnejad SM, Najimi N. Objective measurement of nasal airway dimensions and resistance using acoustic rhinometry and rhinomanometry in habitual snorers compared with non-snorers. Eur Arch Otorhinolaryngol 2008; 265: 1483-1487.

Zhang G, Solomon P, Rival R, Fenton RS, Cole P. Nasal airway volume and resistance to airflow. Am J Rhinol 2008; 22: 371-375.

Zwaardemaker H. Athembeschlag als Hulfmittel zur Diagnose der nasalen Stenose. Arciv fur Laryngologie und Rhinologie 1894; 1: 174-177.

Öztürk F, Türktaş I, Asal K, Ileri F, Münevver Pinar N. Effect of intranasal triamcinolone acetonide on bronchial hyper-responsiveness in children with seasonal allergic rhinitis and comparison of perceptional nasal obstruction with acoustic rhinometric assessment. Int J Pediatr Otorhinolaryngol 2004; 68: 1007-1015.

11 APPENDICES

Appendix 1. Reference values for acoustic rhinometry in children. MCA = unilateral minimal cross-sectional area, TMCA = total minimal cross-sectional area as the sum of left and right sides, VOL = unilateral volume, TVOL = total volume as the sum of left and right sides, SD = standard deviation.

Author Year	**Sample**		**Acoustic Values**					
			Non-decongested				**Decongested**	
Infants	**N**	**Age**	**MCA (cm²) (SD or +/- 95%)**	**TMCA (cm²) (SD or +/- 95%)**	**VOL (cm³) (SD or +/- 95%)**	**TVOL (cm³) (SD or +/- 95%)**	**MCA (cm²) (SD or +/- 95%)**	**VOL (cm³) (SD or +/- 95%)**
Buenting et al 1994a	10	Infants	0.096 (0.027)	0.192 (0.051)	-	0-3.64 cm 1.758 (0.527)	-	-
Pedersen et al 1994	27	36-42 weeks	0.114 (0.033)	0.229 (0.055)	-	0-4.5 cm 2.100 (0.390)	-	-
Djupesland and Lyholm 1997	94	37-42 weeks	0.102 (0.026)	0.204 (0.052)	-	0-4.5 cm 2.139 (0.388)	-	-
Djupesland and Lyholm 1998b	39	Infants	-	0.21 (0.06)	-	0-4 cm 1.80 (0.36)	-	-
Baczek et al 2001	67	37-42 weeks	0.08 (0.02)	0.16 (0.04)	0-4.5 cm 0.99 (0.15)	0-4.5 cm 1.98 (0.3)	-	-
Children 1 year or over	**N**	**Age**	**MCA (cm²) (SD or +/- 95%)**	**TMCA (cm²) (SD or +/- 95%)**	**VOL (cm³) (SD or +/- 95%)**	**TVOL (cm³) (SD or +/- 95%)**	**MCA (cm²) (SD or +/- 95%)**	**VOL (cm³) (SD or +/- 95%)**
Riechelmann et al 1993	35	3-6 years	0.29 (0.06)		-	-	-	-
Millqvist and Bende 1998	85$^{\#}$	< 9 years	-	1.05 (0.04) M 1.14 (0.05) F	-	-	-	-
# = estimated from figure	38$^{\#}$	10-14 years		1.19 (0.06) M 1.16 (0.07) F				
Djupesland and Lyholm 1998b	39	1 year	-	0.35 (0.01)	-	0-4 cm 2.44 (0.55)	-	-

Children 1 year or over	N	Age	MCA (cm^2) (SD or +/- 95%)	TMCA (cm^2) (SD or +/- 95%)	VOL (cm^3) (SD or +/- 95%)	TVOL (cm^3) (SD or +/- 95%)	MCA (cm^2) (SD or +/- 95%)	VOL (cm^3) (SD or +/- 95%)
Ho et al 1999	183	1-11 years 3-6 years	0.32 (0.13) 0.32 (0.12)	-	0-choana 3.69 (1.98)	-	-	-
Larsson et al 2001	98	7-17 years	0.52 (0.14)	-	-	-	-	-
Jurlina et al 2002 ** = includes baseline*	39	6-7 years	-	1.01(0.09) *	-	-	-	-
and decongested values	44	13-14 years		1.24 (0.19) *				
Liukkonen et al 2006	7	1-2 years	0.32 (0.1)	-	0-5 cm 3.22 (1.3)	-	0.37 (0.2)	0-5 cm 3.38 (1.2)
	4	3-4 years	0.36 (0.19)		0-5 cm 3.05 (0.7)		0.31 (0.05)	0-5 cm 3.34 (0.7)
	7	5-6 years	0.40 (0.1)		0-5 cm 3.21 (0.7)		0.38 (0.1)	0-5 cm 3.65 (0.7)
Millqvist and Bende 2006	8	5-6 years	-	0.98	-	2.2-5.4 cm 5.83	-	-
	20	7-8 years		0.99		2.2-5.4 cm 5.66		
	21	9-10 years		0.95		2.2-5.4 cm 5.70		
	21	11-12 years		0.98		2.2-5.4 cm 5.88		
	10	13-14 years		1.17		2.2-5.4 cm 9.97		
	8	15-16 years		1.22		2.2-5.4 cm 7.47		

Children 1 year or over	**N**	**Age**	**MCA (cm^2) (SD or +/- 95%)**	**TMCA (cm^2) (SD or +/- 95%)**	**VOL (cm^3) (SD or +/- 95%)**	**TVOL (cm^3) (SD or +/- 95%)**	**MCA (cm^2) (SD or +/- 95%)**	**VOL (cm^3) (SD or +/- 95%)**
Qian et al 2007	97	4 years	-	-	-	1.5-3.5 cm 2.0 (0.4)	-	-
	137	5 years				1.5-3.5 cm 2.05 (0.4)		
Samolinski et al 2007	42	9-16 years	0.445 F 0.496 M	-	-	-	-	-
Straszek et al 2007	53	9-11 years	0.33 (0.31-0.35)	-	0-5 cm 3.51 (3.36-3.66) 2-5 cm 2.48 (2.34-2.62)	-	0.36 (0.35-0.38)	0-5 cm 4.74 (4.61-4.89) 2-5 cm 3.71 (3.58-3.84)
Straszek et al 2008	171	4-13 years	0.36 (0.35-0.37)	-	0-5 cm 3.62 (3.50-3.73) 2-5 cm 2.59 (2.49-2-69)	-	-	-
Miyamoto et al 2009	46	7-8 years	A1 *(I-notch)* 0.389 (0.052) A2 *(C-notch)* 0.457 (0.142)	-	0-third notch (about 3.9 cm) 2.623 (0.735)	-	-	-

Appendix 2. Possible predictive factors for acoustic values in children and adults. BSA = body surface area; BMI = body mass index; VOL = nasal volume; MCA = minimal cross-sectional area; Yes = correlation between acoustic value and predictive factor found; No = no correlation between acoustic value and predictive factor found.

Author Year	**Age**	**Sex**	**Height**	**Weight**	**BSA**	**BMI**	**Race**	**Other**	**Subjects**
Riechelmann et al 1993	Yes	No	-	-	-	-	-	-	3-6 Years
Pedersen et al 1994	No	No	Yes	Yes	-	-	No	No: Head circumference	Infants
Tomkinson and Eccles 1995b	-	-	No	No	-	-	-	Yes: External facial dimensions	Adults
Morgan et al 1995	-	-	-	-	-	-	Yes	-	Adults
Djupesland and Lyholm 1997	-	Yes	-	-	-	-	-	-	Infants
Djupesland and Lyholm 1998b	-	-	-	-	-	-	-	Yes: Head circumference	Infants
Millqvist and Bende 1998	Yes	Yes (only in adults)	Yes	Yes	-	Yes	-	-	4-61 Years
Corey et al 1998	-	No	No	No	-	-	Yes	-	Adults
Ho et al 1999	Yes	-	Yes: VOL No: MCA	No	-	-	-	-	1-11 Years
Larsson et al 2001	-	Yes (only in adults)	-	-	-	-	-	-	7-52 Years
Baczek et al 2001	-	No	-	No	-	-	-	No: Head circumference	Infants

Author **Year**	**Age**	**Sex**	**Height**	**Weight**	**BSA**	**BMI**	**Race**	**Other**	**Subjects**
Jurlina et al 2002	No	-	-	-	Yes	-	-	-	6-7 Years 13-14 Years Adults
Numminen et al 2002	-	No	-	-	-	No	-	-	Adults
Millqvist and Bende 2006	No	No	Yes	-	-	-	-	-	5-16 Years
Qian et al 2007	No	No	-	-	-	-	-	-	4-5 Years
Samolinski et al 2007	Yes	Yes	-	-	-	-	-	-	9-74 Years
Straszek et al 2007	-	No	-	-	-	-	-	-	9-11 Years
Straszek et al 2008	No	No	Yes	Yes	No	-	-	-	4-13 Years
Kemppainen et al 2008	-	-	-	-	-	No	-	-	Over-weight adults with sleep apnoea
Miyamoto et al 2009	-	Yes	Yes: VOL No: MCA	Yes	-	Yes	-	-	7-8 Years
Leong and Eccles 2009	-	-	-	-	-	-	No	Yes: Shape and size of the nose	Review of the literature
Paiva et al 2010	-	No	-	-	-	-	-	-	6-12 Years Follow-up