Children with cleft lip and palate

van der Heijden, Perry

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Capita selecta

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Children with cleft lip and palate

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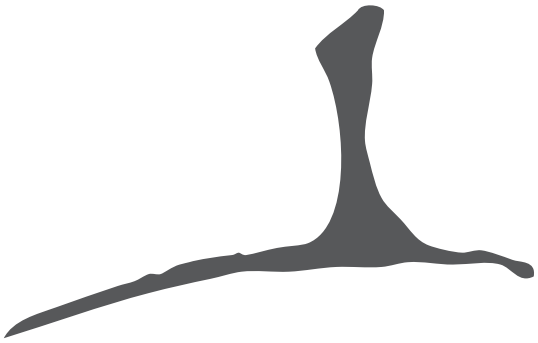
Contents

Chapter 1

General introduction



This thesis is about several aspects of cleft care. Cleft is the most common congenital facial malformation, approximately with an incidence of 1 in 600 born children. An older term is harelip, based on the similarity to the cleft in the lip of a hare. The defect is caused by an abnormal development during the sixth till the twelfth week of gestation.[1] Despite the finding of multiple genes and environmental factors to be related to cleft, the exact aetiology is still not clear.[2] It is safe to consider the cause as heterogeneous.

A cleft can appear in multiple variants. The upper lip, upper jaw and palate can be affected solely or in combination with each other. Furthermore, a cleft lip, jaw and palate can be separated completely or incompletely. Defects of lip and jaw can be unilateral or bilateral. Every combination is possible and has its own consequences on facial esthetics for example lip scar, nasal deviation, retracted maxilla. Functional aspects, such as speech, hearing, chewing and nasal respiration, might be influenced as well. Especially cleft of the lip and jaw can disfigure a face quite striking, as can be seen in figures 1 and 2. For the reason of multiple variants of cleft in combination with various personalities every patient has its own variation of complaints, troubles and wishes. Treatment should be tailored to the type of cleft, possibilities and desires of patient and his or her parents. The challenge is to find a treatment which fits the patient as a whole. Therefore, cleft care requires a multidisciplinary team to cover all the expected issues. The team includes at least a plastic surgeon, dentist, speech therapist, otolaryngologist, paediatrician, child psychologist, orthodontic therapist and maxillofacial surgeon. All have care for different aspects, but have to chase the same goal. This should be a satisfied patient, who can have a life, possibilities and health like their counterparts without cleft. The cooperation between the practitioners with different specialities with different issues at stake means that concessions have to be made. For example, early palatal closure is considered to be beneficial for the development of speech,[3] but might affect growth of the maxilla.[3, 4] Choices have to be made in favour of the most important aspect in relation to age and critical periods of development. Multiple aspects of cleft care are prone to discussion and subject of research. Some aspects are highlighted in the following sections and investigated in the following chapters.

Facial Growth

Growth of the middle part of the face, the midface, is a complex development with vectors of push and traction in and around the nose. It is evident what happens, but little is known how it happens.[5, 6] Growth of the midface might be affected by interruptions of the palate, nasal septum, nasal bones and facial muscles. For example a patient with complete unilateral cleft of lip, jaw and palate (UCLP) has typically an ala implanted more laterally, inferiorly and posteriorly, see figure 1 for the newborn and figure 2 for the adolescent. The cause is traction from both ends of the cleft by the interrupted circle of the oral orbicularis muscle. The usually underdeveloped maxilla on the cleft side contributes to this particular anatomy.[5, 7, 8] For this reason the plastic surgeon has to take care to repair not only the skin of the upper lip, but the orbicularis muscle as well. By this means the nostril is reshaped and the vectors of traction become more natural.[9] However, next to the interrupted anatomy, trauma and scars from surgery can affect growth as well.[10, 11] Numerous examples of disturbed growth of the midface after trauma or nasal surgery have been published.[10, 12-14] It remains unclear whether surgery or the malformation itself has the most important role in growth disturbances. For this reason the dogma stating not to perform surgery in a growing nose is under question, but still valid.[15] However, some adolescent cleft patients are

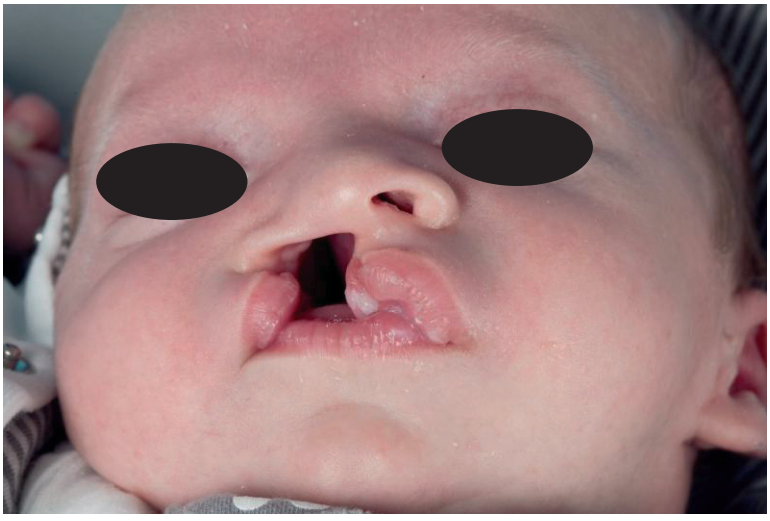


Figure 1: A two weeks old patient with unilateral cleft of lip, jaw and palate.

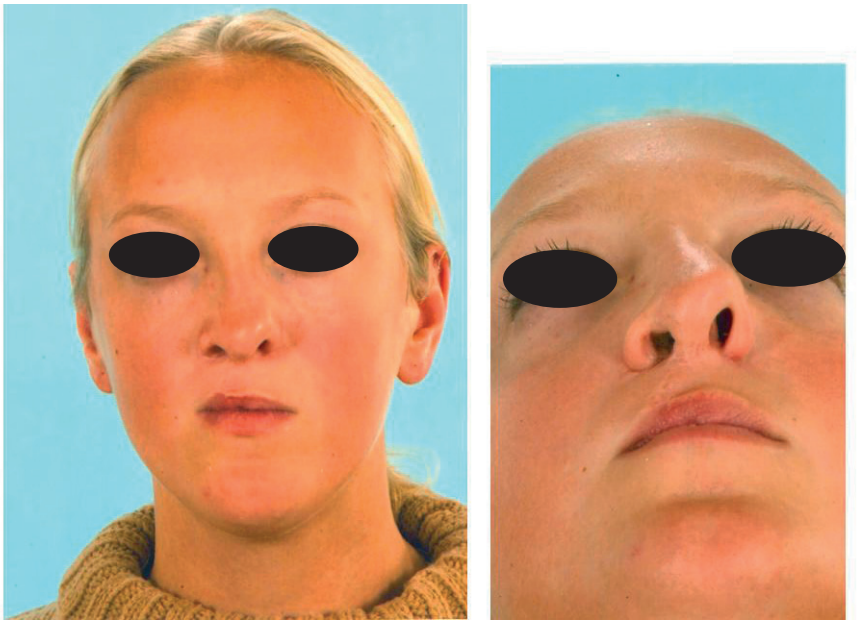


Figure 2: A 16 years old patient with unilateral cleft of lip, jaw and palate.

being teased with their facial appearance, which might cause a tremendous emotional burden.[16] These patients could benefit from a rhinoplasty at early age, thus on their still growing face. To deal with this dilemma it is essential to know when facial growth has ceased. **Chapter 2** is dealing with this issue. In here we define the age in normal boys and girls at which the growth is finished by means of a systematic review.

Influencing Growth

Enormous innovations en evolutions in the development of cleft care have passed over the years. Possibly the present state-of-the-art will be obsolete over centuries. In the last two decades nasoalveolar molding (NAM) has had its upcoming in many clinics over the world. NAM tries to tackle the disfigured cartilaginous structures of the nose, like the above described lower lateral cartilage. When analysing the lower lateral cartilage it looks as if the lower lateral nasal cartilage is stretched and twisted on the cleft side and pulling the tip of nose to the cleft side. Furthermore the columella has become oblique due to this stretching. The

aim of NAM is to correct these deviations as soon as possible in a nonsurgical way. The ultimate goal of NAM is to prevent rhinoplasty at adult age. In parallel with nonsurgical correcting congenital auricular deformities[17, 18] NAM makes use of the plasticity of neonatal tissue due to maternal hormones hyaluronic acid and estrogen.[19] The mother needs those hormones to weaken her pelvic cartilage to facilitate labour. The concept of NAM is to mould the cartilage in the right shape. The device is a custom made plate, which covers the palate, with a nasal extension like in figure 3. The extension supports the dome of the lower lateral cartilage and straightens the nose, see figure 4. In the first months after birth the

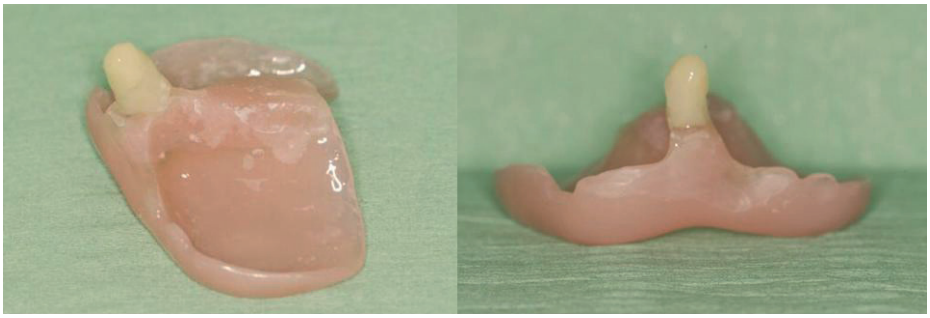


Figure 3: Nasoalveolar molding apparatus for a patient with unilateral cleft lip, jaw and palate. Palatal plate in pink, with a nasal extension in white to support the dome of the nose.

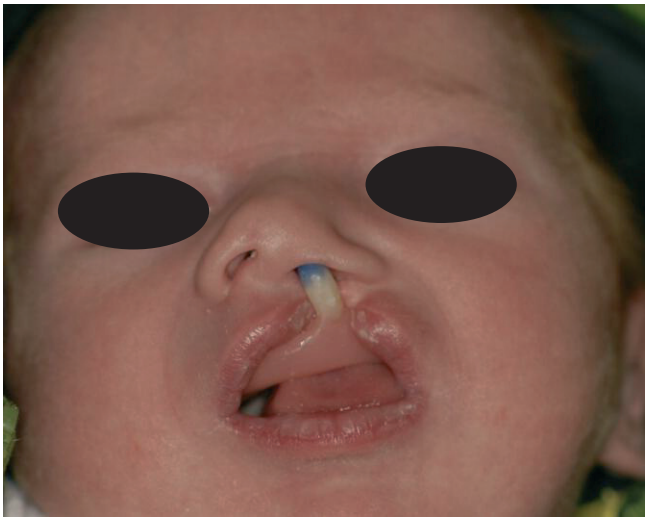


Figure 4: Nasoalveolar molding apparatus in situ.

cartilage starts stiffening in the shape of that moment, so NAM is useful during the first months after birth.[20] The technique of NAM is rapidly evolving.[21-23] Many studies have been published with very promising results, but solid evidence like a randomised controlled trial is not published yet. In **Chapter 3** is aimed to quantify the effect of NAM. Possibly confounders or biases in the published data are searched for.

Speech

Patients with a cleft palate have to encounter issues from a different kind. The palate consists of a hard palate, immobile bone and mucosa, and a soft palate, mobile muscles and mucosa. The soft palate is in the back. The palate is the divider of mouth and nose. The soft palate can be considered as a flexible divider of the oropharynx and nasopharynx, just when it is necessary. In swallowing and the production of particular sounds it is necessary to close the nasopharynx from the oropharynx to prevent leakage of food and sounds through the nose. On the other hand the nose should be connected to the pharynx during nasal breathing and to allow particular sounds through the nose. Like a cleft lip and cleft jaw, the palate can be cleft in different degrees. The midline of the palate is a line of fusion. In embryology the fusion will start in the most anterior point, which makes the palate close like a zipper from the anterior to posterior.[1] Any disturbance in the fusion is able to cause some degree of a cleft palate, dependent on the moment of disturbance in the development. Hence, a late disturbance leads to the most subtle form, a bifid uvula, usually without consequences. The most extended cleft comprises the soft and hard palate, this is called a complete cleft palate. A complete cleft of the palate is an interruption of bone and palatal muscles. With surgical palatal repair both the mucosa and muscles are made continuous with the opposite side, with inevitable scars. Palatal muscles in a cleft palate are underdeveloped and together with retraction and stiffening from the scar, typically the palate will be short and the mobility will be impaired. The result might be a soft palate, the velum, unable to reach the pharyngeal wall and unable to separate the nasal cavity from the pharyngeal cavity. This so called velopharyngeal insufficiency becomes evident in speech. Oral sounds become nasal (hypernasality). Moreover, there is an impossibility to build up

sufficient oral pressure especially in pronouncing plosive sounds, like the letters /p/, /t/, /k/. In more severe cases nasal regurgitation of liquids can occur. The therapy for hypernasality and insufficient oral pressure is usually a surgically creation of a pharyngeal flap. With this procedure the velum is elongated and attached to the pharyngeal posterior wall with a pedicled mucosal flap from the pharyngeal posterior wall (figure 5). For the diagnosis of hypernasality several instruments are available and a possible help in deciding whether a pharyngeal flap is necessary.[24] Some instruments are able to quantify hypernasality. Among those instruments the nasometer is by some considered to be the golden standard,[25, 26] since the benefit of being non-invasive and the ability to measure the nasal proportion of the total sound energy. The nasometer is a combination of headgear, computer and analysing software (figure 6). Nasal and oral sound production are measured during speech by two microphones separated by a plate on the upper lip of the speaker. The outcome is the nasal proportion (%) of the total sound energy. This is subsequently an objective outcome measure. In our outpatient clinic we found it hard to put children from 4 to 6 years of age to the nasometer. They would not always cooperate. The second issue was when we got them to the test, we had trouble to interpret the results, because of a lack of normative values for Dutch children of this age. In **Chapter 4** is described how children from schools and our outpatient clinic from 4 to 6 years of age

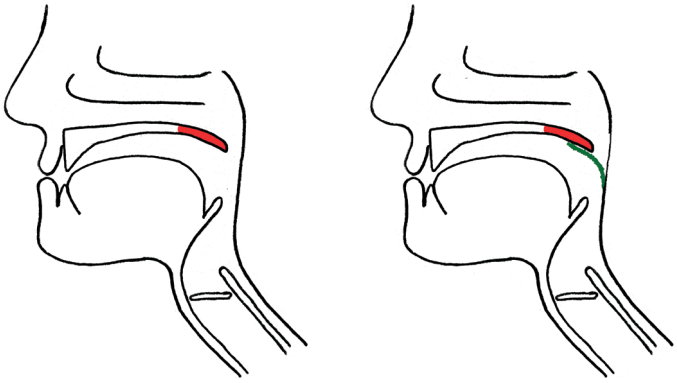


Figure 5: Left; schematic drawing of a short velum (red), unable to reach the posterior pharyngeal wall. Right: schematic drawing of a pharyngeal flap (green), harvested from the pharyngeal wall with a caudal pedicle.

cooperate with the nasometer. The goal was to set a minimum age for the use of the nasometer regarding age. The results from the children who cooperated were set as normative values in **Chapter 5**. With these normative values results of the individual patient can be seen in the proper perspective.

The patient self

As said before the goal of cleft care should be a satisfied patient. He or she should have a life, possibilities and health like their counterparts without a cleft. The whole multidisciplinary team should be aware of this goal. For that reason the practitioners should ask the patient and parents about satisfaction and gather information about the reasons for (dis)satisfaction. Some patients or parents do stress for intervention, others do not care about any further treatment or refuse any treatment. Treatment should be tailored to the patient, because not every patient has the same wishes. It is not always clear what moves patients to the wishes they express. Sometimes the practitioner disagrees with the patient or parents.[27] The disagreement can be both ways. For example, the patient desires a correction of the lip scar, while the surgeon does not see any possibility for improvement. On the other hand the surgeon might observe a deviated nose and propose a correction, because he has in mind that young adults with a facial cleft hope to be like other people[28] and knows that cleft patients are a frequent focus of teasing. But the patient might deny any trouble with function, esthetics or teasing. Hence, insight in the minds of cleft patients would be worthy knowledge.

Chapter 6 describes a search for motivations and backgrounds behind wishes for treatment in adolescent patients with a cleft. Adolescence is the first phase in life a person should be able to express their own wishes and decide about treatment. The method of choice, a qualitative research, is not used very often in the medical literature. Qualitative research is the opposite from quantitative research, which we all are more used to read, practice and appraise. Quantitative research has the benefits of the ability to measure and compare, but they are generic and may be insensitive to particular issues faced by the individual.[29] A qualitative study, following the rules of the grounded theory, should be able to find those particular issues.[29] Chapter 6 has an extended method section in which the grounded theory is explained step by step. The found issues are to be

understood and taken into account by the practitioner when treating the patient. This understanding should help to tailor the treatment. Maybe this tailoring leads to not to test the borders of rhinoplasty in a growing nose.

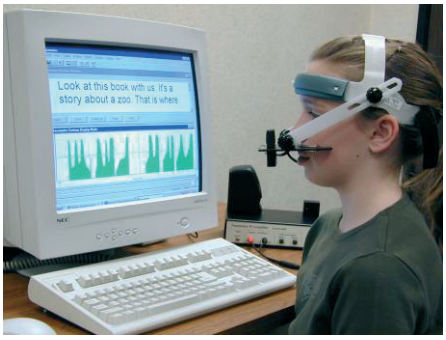


Figure 6: Kay Pentax nasometer II software installed on a computer, hardware on the table and headgear installed on a subject.[30]

Outline of the thesis

This thesis is a capita selecta of the care about cleft patients. The chapters are chosen with the inspiration from our daily work. Like every other team, the Groningen cleft team has discussions about changes for improvement of their treatment protocol, as it should be with elapsing time. In some discussions we could not find clear answers in the literature, at congresses or from other professionals from other teams. This thesis fills some of the dearths in the evidence and rationale of our daily practice.

- *Chapter* 2 is a systematic review of the literature to define the age of the end of facial growth. The practical consequence of this definition is a minimum age of safe rhinoplasty, without disturbing facial growth.
- *Chapter* 3 is a systematic review of the literature to quantify the effect of nasoalveolar molding, a very promising, relatively novice of treatments.
- *Chapter* 4 describes the study and results of cooperation of 4 to 6 years old children with the nasometer, a frequently used instrument to quantify nasalance.
- *Chapter* 5 gives normative data of the nasometer for Dutch children from 4 to 6 years of age.
- *Chapter* 6 shows the need for understanding the wishes of cleft patients and reveals them by means of a qualitative study, using the grounded theory.

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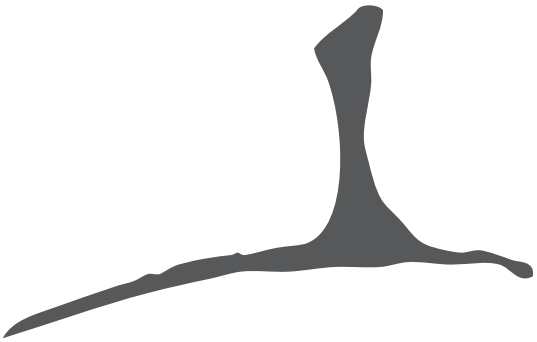
Chapter 2

Nasal growth and maturation age in adolescents



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Arch Otolaryngol Head Neck Surg. 2008 *Dec*;134(12):1288-93

Abstract

Objective: Defining the end of the nasofacial growth spurt, in order to schedule rhinoseptoplasty in cleft patients without disturbing nasofacial growth.

Data sources: Pubmed and Cochrane bibliographic databases. Primary indexing terms: 'facial growth'. Confining search terms: (face OR nose) AND growth AND (cephalometry OR anthropometry). The reference lists of the retrieved articles were searched for missed relevant studies. Articles written in English, German or Dutch. Search results up to December 2007 included.

Study selection: Data for Caucasian children, without genetic disorders or malformations. Their growth pattern should have been followed from at least age 12 until age 18, with intervals between relevant measurements not longer than two years.

Data extraction: No further guidelines used.

Data Synthesis: Growth velocity curves were fit to different relevant measures for nasofacial growth. The end of the nasofacial growth spurt was defined as the age at which these growth velocity curves have their steepest descending slope. This yielded an average age of 13.1 years for girls and 14.7 years for boys. Because no information could be found for the spread in individual nasal growth as a function of age, 2 standard deviations of the age distribution for body height growth velocity were added, giving 98% of caucasian girls being nasally mature at age 15.8 and 98% of caucasian boys at age 16.9.

Conclusion: Rhinoseptoplasty can safely be performed after age 16 in girls and 17 in boys.

Introduction

Patients with a cleft may need many operations between childhood and adolescence, with revising rhinoseptoplasty being one of the last operations to be performed. Because the septal cartilage and nasal bones have an important role in the outgrowth of the midface, reservation in operating on these structures is recommended.[1-3] On the basis of the growth characteristics of the septal cartilage, nasal bones, and midface, growth is expected to cease at the age of 18 years. Therefore, the prevalent opinion of most cleft specialists in the Netherlands is to postpone rhinoseptoplasty until that age. However, the dogma stating that nasal surgery in growing individuals must be avoided is coming under question,[4] and surgery with or without osteotomies is performed in several clinics on patients younger than 18 years.[5-7] Primary corrections and presurgical treatments are evolving rapidly. The fairly new technique of presurgical nasoalveolar molding plates, originally used to facilitate the primary correction of the palate, is often combined with nasal stents to shape the alar cartilage into a more normal position.[8-11] This combination probably has the positive effect of preventing internal and external nose deviations.[9] However, current preadolescent patients with cleft were unable to profit from nasoalveolar molding plates in their early years. In addition to the physical changes, many psychological changes occur during adolescence, and it is common for patients to be preoccupied with and insecure about their appearance. For many young adolescents, facial appearance is a concern within their social environment,[12] especially with a deformity such as a cleft-related nose deviation. A major proportion (54%-68%) of children with cleft are unhappy with their facial appearance,[13] and 59% of children with cleft between 8 and 11 years of age and 37% between 12 and 15 years of age claim to be teased.[14] By far the main focus of teasing is the child's nose and lip.[14] This teasing may lead to decreased self-esteem, social isolation, or worse. Adolescents with cleft indicate that they have a strong desire to have surgeons correct their noses,[15] and they retain that desire into adulthood.[15, 16] To them, improved appearance is even more important than better nasal function.[17] However, if surgeons intend to fulfill this desire, they must take care not to disturb growth by respecting the limitations of rhinoseptoplasty. To that end, surgeons should be aware of the nasofacial growth pattern. Several authors,[18-23] suggest that the end of the

nasofacial growth spurt takes place earlier than 18 years of age, but no conclusive research concerning children with or without cleft has been performed. In our opinion, based on clinical experience at our otorhinolaryngology clinic, 5 measures are relevant in observing nasal growth (Figure **1**): (1) nasal bridge length from nasion to pronasal; (2) nasal protrusion from subnasal to pronasal; (3) nasal height from nasion to subnasal; (4) palatal length from anterior nasal spine (ANS) to posterior nasal spine (PNS); and (5) midfacial protrusion from sella to ANS. The aim of this study is to describe the nasofacial growth pattern of the normal child and adolescent to promote the identification of an adolescent growth spurt and the subsequent slowing of growth. From this, a definition of maturation is derived.

Material and Methods

This article is based on a PubMed and Cochrane search from database inception to December 31, 2007. The following inclusion criteria were used to identify studies for this article: (1) white adolescents without genetic disorders or malformations; (2) growth pattern must be observed between the ages of 12 and 18 years; (3) facial growth evaluated through direct and/or indirect measurements; (4) intervals between measurement ages are not longer than 2 years; (5) the article must provide at least 1 of the 5 relevant measures; and (6) the article must be written in English, German, or Dutch.

Both libraries were searched on the keyword *facial growth*. Because of the large number of search results obtained from PubMed, we adjusted the relative search terms using *growth* AND (*face* OR *nose*) AND (*cephalometry* OR *anthropometry*). The full text was obtained for articles considered relevant based on the title or the abstract. The reference lists of the retrieved articles were searched for relevant studies that could have been missed by the computer search. The search yielded 25 articles and 1 book describing several nasofacial growth items.[18-43] In 4 studies[18, 23, 24, 33] the population was not white, in 10 studies[19, 21, 26, 28, 29, 31, 34, 38, 41, 43] the measurements were not taken from 12- to 18-year-olds or followed up less than every 2 years, and in 8 studies[22, 25, 30, 35, 37, 39, 40, 42] elaborated or raw data could not be retrieved. The authors of these studies were requested by e-mail to clarify their data. This request yielded no additional information.

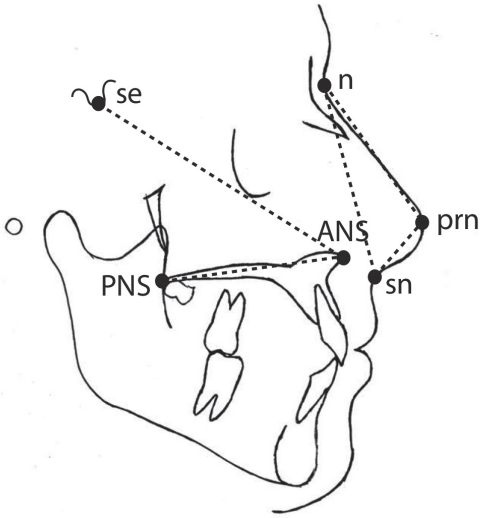

Figure 1. The 5 measures relevant in observing nasal growth: (1) nasal bridge length from nasion (n) to pronasal (prn); (2) nasal protrusion from subnasal (sn) to prn; (3) nasal height from n to sn; (4) palatal length from anterior nasal spine (ANS) to posterior nasal spine (PNS); and (5) midfacial protrusion from sella (se) to ANS

Study selection

Farkas[20] published extensive facial measurements in a reference book. Among many other measurements, results were found for nasal height, nasal protrusion, and nasal bridge length. In total, data were obtained transversally (50 persons per age) for 2326 white adolescents from Calgary, Alberta, Toronto, Ontario, Montreal, and Quebec, Canada, from birth to 25 years of age at intervals of 1 year.

Zankl et al[27] studied the growth of the nasal bridge length, nasal protrusion, and philtrum length from birth until 97 years of age. Their study population was acquired from nurseries for newborn children, day care centers, schools, large companies, the military service, and nursing homes for elderly people. All study participants were of central European descent living in Switzerland. Fifty persons were measured each year of age from birth until 28 years of age.

Ochoa and Nanda[32] compared maxillary growth with mandibular growth by making many measurements using lateral cephalograms, including measuring the distance from ANS to PNS (palatal length). The lateral cephalograms were

derived from the Denver Growth Study.[44] This is a longitudinal study conducted by the Denver Child Research Council between 1927 and 1967. All study participants were white and healthy. Ochoa and Nanda investigated 15 males and 13 females aged 6 to 20 years. Unfortunately, age was determined by hand radiographic analysis instead of chronologic age.

Nanda[36] studied the anteroposterior facial growth shown in lateral cephalograms of female patients conducted annually from the age of 3 years to 18 years, including palatal length (ANS PNS) and midfacial protrusion (ANS sella). The study population was 18 female patients derived from the Denver Growth Study.[44] Age was determined chronologically.

Statistical analysis

The data included were plotted as a function of age. At approximately the age of maximum growth velocity, data were least squares fitted with an S-shaped curve with the following formula:

$y = a1\{1 - \exp[-a2(x - x1)]\} / \{1\_\exp[-a2(x - x1)]\} + a3,$

with y indicating length in millimeters and x indicating age in years; $a1$, $a2$, $a3$, and $x1$ are parameters to be fitted (Figure **2**A).

Growth velocity as a function of age is obtained by differentiation of this formula (Figure 2B). The basis for the formulae used is the observation that growth proceeds at high velocity in early childhood and lower velocity in later childhood, with a growth spurt during adolescence that continues at a low steady pace until old age.[20, 27, 28, 38] The vertical scale in Figure **3** and Figure **4** is not expressed as growth velocity in millimeters per year; for a better comparison between the different measures, it is expressed as the percentage of the length at the age of 18 years per year. For example, if length at the age of 18 years is 50 mm, a velocity of 1 mm/y is thus 2% per year of the length at the age of 18 years. The criterion chosen for maturity is the age at which the velocity curve descends most steeply. At this age, the second derivative of the formula is 0. From that age on, the growth velocity gradually decreases to almost 0.

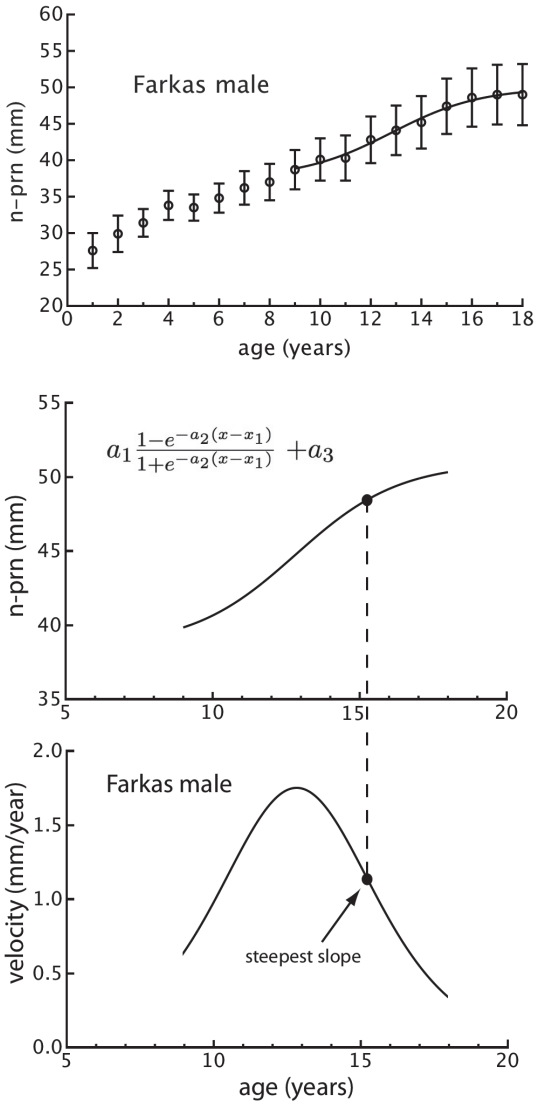

Figure 2. Data plotted as a function of age. At approximately the age of maximum growth velocity, data were least squares fitted with an S-shaped curve with the following formula: $y=a_1\{1-\exp[-a_2(x-x_1)]\}/\{1\_\exp[-a_2(x-x_1)]\}+a_3$, with y indicating length in millimeters and x indicating age in years; a_1, a_2, a_3, and x_1 are parameters to be fitted. Above, example of raw data fitted with an S-shaped curve. Below, example of a fitted curve with a first derivative and a point of steepest slope.

Results

Curves were fitted to 8 growth measures in female patients and to 6 measures in male patients (Figure 2A). The parameters that provided the best fits are given in **Table 1** and **Table 2**. All measures for male and female patients show a period of growth acceleration. In girls (Figure 3), maximum growth velocity ranges from before the age of 8 years until the age of 12 years.[32, 36] In boys (Figure 4), all growth velocity curves (except 1) have their maximum at approximately the age of 13 years. **Table 3** and **Table 4** give the ages for maximum growth deceleration for girls and boys.

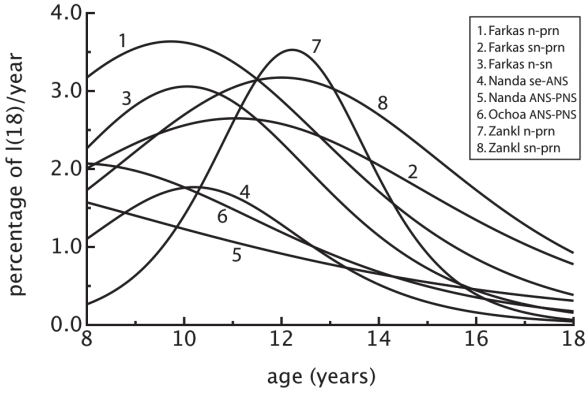

Figure 3. Female growth per year expressed as a percentage of length at the age of 18 years. Numbers next to the curved lines correspond to the order of the authors in Table 1.

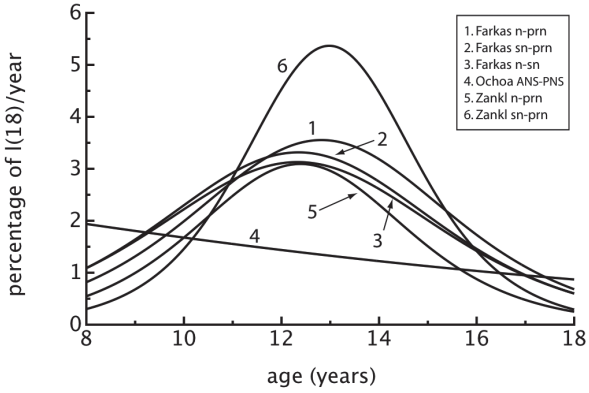

Figure 4. Male growth per year expressed as a percentage of length at the age of 18 years. Numbers next to the curved lines correspond to the order of the authors in Table 2.

Table 1: Parameters that gave the best fits for the S-shaped curve for adolescents girls: $y = a_1\{1-\exp[-a_2(x-x_1)]\} / \{1+\exp[-a_2(x-x_1)]\} + a_3$. Abbreviations: n, nasion; prn, pronasal; sn, subnasal; Se, sella; ANS, anterior nasal spine; PNS, posterior nasal spine.

Source	Measure	a_1	a_2	a_3	x_1
Farkas[20]	n-prn	7.715	0.4324	38.59	9.727
Farkas[20]	sn-prn	2.936	0.4324	17.05	11.06
Farkas[20]	n-sn	55.63	0.5457	44.21	10.06
Nanda et al[36]	Se-ANS	4.508	0.6458	77.93	10.21
Nanda et al[36]	ANS-PNS	10.49	0.2108	42.43	2.676
Ochoa and Nanda[32]	ANS-PNS	5.719	0.3751	46.30	7.839
Zankl et al[27]	n-prn	3.816	0.9327	46.66	12.22
Zankl et al[27]	sn-prn	3.198	0.4093	17.94	12.00

Table 2: Parameters that gave the best fits for the S-shaped curve for adolescents boys: $y = a_1\{1-\exp[-a_2(x-x_1)]\} / \{1+\exp[-a_2(x-x_1)]\} + a_3$. Abbreviations: n, nasion; prn, pronasal; sn, subnasal; Se, sella; ANS, anterior nasal spine; PNS, posterior nasal spine.

Source	Measure	a_1	a_2	a_3	x_1
Farkas[20]	n-prn	6.189	0.5664	43.77	12.82
Farkas[20]	sn-prn	2.500	0.5311	17.76	12.35
Farkas[20]	n-sn	6.477	0.5173	47.72	12.33
Ochoa and Nanda[32]	ANS-PNS	43.59	0.0995	17.63	-9.701
Zankl et al[27]	n-prn	4.643	0.6888	47.25	12.39
Zankl et al[27]	sn-prn	2.720	0.8512	18.92	12.98

Table 3: Age of maximum growth deceleration (the age at which the second derivative of the velocity curve is zero) in adolescent girls. * These numbers are not taken into account (see the "Discussion" section)

Source	Measure	Maturity age, y
Farkas[20]	n-prn	12.78
Farkas[20]	sn-prn	14.08
Farkas[20]	n-sn	12.48
Nanda et al[36]	Se-ANS	12.25
Nanda et al[36]	ANS-PNS	8.92*
Ochoa and Nanda[32]	ANS-PNS	11.36*
Zankl[27]	n-prn	13.30
Zankl[27]	sn-prn	15.22

Table 4: Age of maximum growth deceleration (the age at which the second derivative of the velocity curve is zero) in adolescent boys. * This number is not taken into account (see the "Discussion" section)

Source	Measure	Maturity age, y
Farkas[20]	n-prn	15.15
Farkas[20]	sn-prn	14.83
Farkas[20]	n-sn	14.88
Ochoa and Nanda[32]	ANS-PNS	3.54*
Zankl et al[27]	n-prn	14.30
Zankl et al[27]	sn-prn	14.53

Discussion

Palatal length lacks a growth spurt in adolescence in girls and boys and has a deviating growth pattern compared with the other nasal measures in boys and girls. This can be explained by the fact that the PNS and ANS grow from the sella. Although we did not select a study in which this is measured, it might be concluded that the PNS sella distance has an adolescent growth spurt parallel to the ANS sella distance. Because of the lack of a growth spurt in adolescence, we consider palatal length not to be representative of nasal maturation and have therefore not taken it into account. The age of maturation can be defined in different ways. An obvious definition is the age at which the growth curve flattens to horizontal after the growth spurt during adolescence. This, however, does not occur. Ferarrio et al,[28] Lang et al,[38] West and McNamara,[45] and particularly Zankl et al[27] have shown that the nose continues growing until old age. Farkas[20] defined the age of maturation of the nose statistically by comparing distance measures at a certain age with the corresponding measure at 18 years of age, taking standard errors of the mean of the measurements into account. Personal correspondence by e-mail did not reveal the underlying rationale for this definition. We have defined the age of maturity for a certain nasal measure as the age at which the growth velocity curve for this measure has its steepest descending slope. Maturity ages for the representative measures are given in Tables 3 and 4. The ANS-PNS values shown in Tables 3 and 4 for girls[36] and boys[32] deviate largely from the other values. This finding is unremarkable because palatal length lacks a growth spurt during adolescence. It has a growth pattern that deviates from that of other nasal measures because PNS and ANS grow from the sella,[46] considered to be a stable point of the skull base during growth.[47] If palatal length is not taken into account, the average age of maturity is 13.4 years for girls and 14.7 years for boys. These numbers are in agreement with results from cephalometric studies of facial growth (Burke and Hughes-Lawson,[19] el-Batouti et al,[41] Thilander et al,[43] and Bergersen[42]). The larger spread in the position of the maxima of the growth velocity curves for girls (Figure 3) compared with boys (Figure 4) is remarkable. If the average age of maturity in a large group of girls or boys follows a symmetric distribution, this age will be higher than the given values for half of the group. Unfortunately, no information could be found for the spread in

individual nasal growth as a function of age. However, if we assume that this spread does not differ much from the spread in body height velocity, useful information can be derived from the results of the study by Berkey et al.[48] These authors provide longitudinal height velocity standards for US adolescents. The data points in Figure 5 were derived from their Figure 1. An almost perfect fit to these points could be made with a gaussian curve. The maximum of the curve is at the age of 11.5 years for girls and 13.5 years for boys. The SD (derived from the fit parameters) is 1.2 years for girls and 1.1 years for boys.

Nasal growth velocity is maximal at the mean (SD) age of 11.0 (0.9) years for girls and 12.6 (0.3) years for boys. Therefore, it may be concluded that no substantial difference exists between the age of maximal body height velocity and the age of maximal nasal growth velocity. If (to be on the safe side) 2 SDs for the height velocity distributions are added to the average age of maturity for the nose (as defined in this article), an age of 15.8 years is obtained for girls and 16.9 years for boys. In a systematic review, Flores-Mir et al[49] found that skeletal maturity, determined by hand-wrist radiographic analysis, was well related to overall facial growth velocity. This finding supports the assumption that nasal growth velocity is related to body height velocity. Furthermore, it provides the possibility of determining the stage of individual growth. In conclusion, in 98% of adolescent girls the nose is mature at the age of 15.8 years. For 98% of adolescent boys, this age is 16.9 years. Because the results of nasal interventions performed after maturation age are not likely to be disturbed by nasal growth, rhinoseptoplasty can be performed safely, in most cases, in adolescent girls after the age of 16 years and in adolescent boys after the age of 17 years.

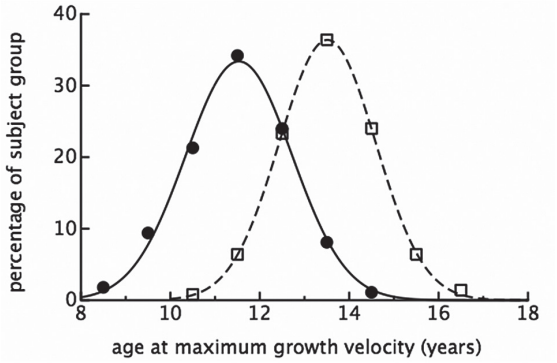

Figure 5. Distribution of the age of maximum height growth velocity for adolescent girls (solid circles) and adolescent boys (open squares). Data were taken for white adolescent boys and adolescent girls from Figure 1 in the article by Berkey et al.[48] The solid and the dashed lines are least-squares fits to the data points with a gaussian curve.

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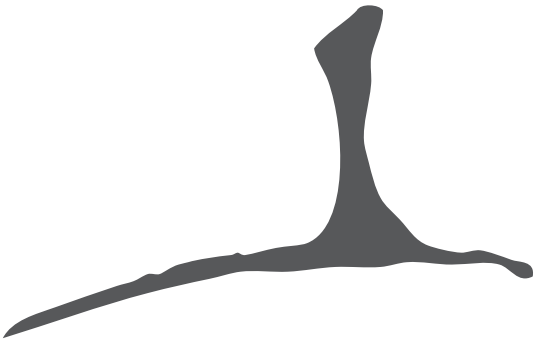
Chapter 3

Limited evidence of the effect of presurgical nasoalveolar molding in unilateral cleft on nasal symmetry. A call for unified research



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Abstract

Background: In the last two decades the appliance of presurgical nasoalveolar molding (NAM) has been increased in the care of patients with a cleft to improve nasal symmetry and facilitate the closure of the lip and secondary rhinoplasty. Many cleft centers do not apply PNAM, because the effect of NAM is disputable. Multiple papers have been published about techniques and effects, but are heterogeneous. This review aims to quantify the effect of nasal symmetry on the long term.

Method: A systematic review of the literature with the intention of a meta-analysis. The search terms "cleft" AND ("molding" OR "moulding") were used in 3 databases. Twelve studies met the following inclusion criteria: (1) participants were humans with non-syndromal unilateral cleft; (2) data concerning the effect of NAM on symmetry of the nose are reported or can be deducted; (3) written in English, German, or Dutch.

Results: The heterogeneity of the study designs, outcome variables, outcome variable expressions, follow-up periods, and inadequate data reporting made it impossible to calculate effect-sizes and to perform a meta-analysis. All included studies had a Low GRADE level. Five studies reported exclusively positive effects on nasal symmetry, 6 studies reported mixed effects, and 1 study reported exclusively no effects.

Conclusion: The results of the studies concerning NAM are inconsistent regarding changes of nasal symmetry, however, there is a trend towards a positive effect. Additionally studies regarding NAM in UCLP are heterogeneous and lack adequate reporting. Recommendations for future research were provided to construct a consensus about the effect of NAM.

Introduction

The surgical correction of the internal and external nose of a patient with a cleft is challenging and sometimes frustrating because of its limitations of surgical possibilities.[1] Secondary rhinoplasty after the adolescent growth spurt is frequently needed to improve esthetics and function of the nose.[2] The difficulty in rhinoplasty after adolescence is the adopted configuration of the cartilage with the tendency of relapse after reshaping the cartilage. For that reason nasoalveolar molding (NAM), originally used to facilitate the primary correction of the palate, is combined with nasal stents to shape the alar cartilage into a more normal position.[3-6] Ideally, a secondary rhinoplasty would not be needed anymore after NAM. The first weeks after birth, the cartilage of the nose is flexible and mouldable as ear cartilage.[7] After birth cartilage starts stiffening in the shape of that moment.[8] Therefore it is preferable to start NAM as soon as possible, as the effect of NAM is dependent on the starting age.[9] The therapy stops at the moment of surgical lip closure, usually around the age of 4 to 5 months. After which the shape of the cartilage will relapse partially in the following year.[10] The technique of NAM is evolving and modified many times, as a result many variations of NAM exist. For example there is NAM with or without taping, with active or passive support or pressure under the nasal dome and the frequency of adjustment is variable. Hence, there is no agreement about the most adequate form of appliance. Actually, the concept of NAM is still under debate.[11] In 2010 only 37% of the United States cleft teams offered NAM to their patients.[11] Opponents of NAM suggest a burden on the family system and an essential compliance failure because of the necessary frequent and time consuming appointments during therapy.[11] Additionally, studies quantifying results of NAM differ regarding design, outcome variables and follow-up time and therefore results are hard to compare.[12] No randomised controlled trial about the effect of NAM is published[12] and no meta-analysis of the literature is available. Therefore this study aims to quantify the effect of NAM in achieving nasal symmetry in patients with unilateral cleft lip, jaw and palate (UCLP) on the long term after surgical treatment by means of a systematic review of the available literature.

Methods

Three data bases PubMed, Embase, and Cochrane were searched (PH) from database inception to June 2011, using the search terms "cleft" AND ("molding" OR "moulding"). The following inclusion criteria were applied for studies in this systematic review:

1) participants were humans with non-syndromal UCLP;
2) data concerning the effect of NAM on symmetry of the nose are reported or can be deducted;
3) written in English, German, or Dutch.

The full text was obtained for papers considered relevant based on title or abstract (PH, CS). The readily accessibility of full texts papers made an immediate evaluation of the full text possible. For that reason the paper selection was performed on the basis of title, abstract and full text concurrently. The reference lists of relevant studies were searched for studies that were missed in the database search. Data extraction was conducted independently by two authors (PH, CS). Occasional disagreement was resolved by discussion until consensus was reached. The search yielded 134 papers (figure 1). Seventy-three of the excluded papers did not provide data about effects of NAM, but dealt with opinions, surgical solutions, non-measurable outcomes or craniofacial malformations other then cleft, 2 studies reported about nasal symmetry of NAM treated patients, but the achieved degree of symmetry could not be attributed to NAM specifically or another intervention. Other excluded papers were 3 case studies, 11 reviews, 13 'how I do it'/technique descriptions, 8 not in the preferred language, 1 concerning animals, and 11 exclusively concerning bilateral cleft patients. Twelve studies met the inclusion criteria.[3, 5, 9, 10, 13-20]

Methodological quality of the studies was assessed according the Cochrane Collaboration, using the GRADE approach.[21] The following items were assessed: study design; adequate description and comparability of groups; possible selection bias or confounding by indication; intervention properly described and adequate in the context; intervention effect measurement properly described and adequate in the context; follow up time; outcome assessor blind for intervention or control; possible confounders identified and taken into account

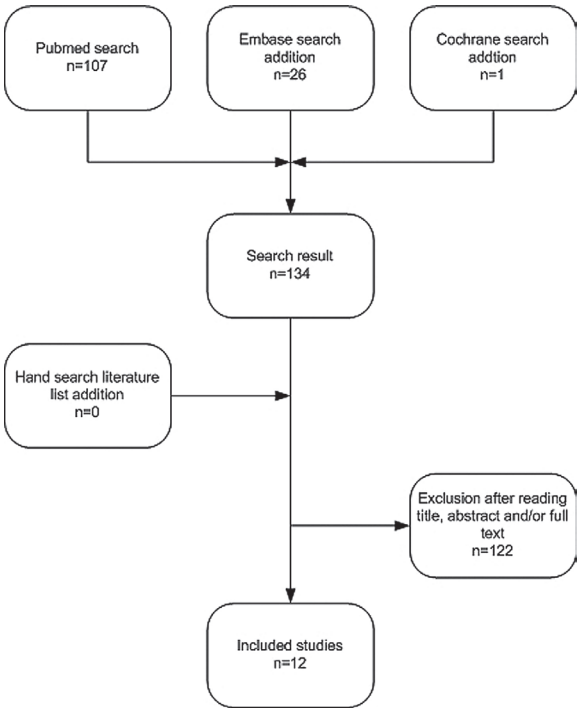

Figure 1: Procedure of study search and selection

for. Studies can be graded as High, Moderate, Low or Very low and be upgraded or downgraded (Table 1). An upgrade followed when the study showed a large effect, confounding factors would underestimate the effect or a dose-response gradient. A downgrade followed when the study showed limitations in the design and implementation suggesting high likelihood of bias, indirectness of evidence,

Table 1: Levels of quality of a body of evidence in the GRADE approach[23]

Underlying methodology	Quality rating
Randomized trials; or double-upgraded observational studies.	High
Downgraded randomized trials; or upgraded observational studies.	Moderate
Double-downgraded randomized trials; or observational studies.	Low
Triple-downgraded randomized trials; or downgraded observational studies; or case series/case reports.	Very low

Table 2: Summary of study characteristics

Author	Design	Patients (n)	Age of starting NAM Mean (days); range	Patient Intervention	Duration of treatment Mean (days); range	Outcome measures #	Control Intervention	Controls (n)	Comparisons	Last measurement (range)
Maull et al., 1999	Cross-sectional patient-control	10	nm	NAM + lip repair	nm	Facial surface registration	Lip repair only; Age 9.1yrs	10	Patient-control	Age 4.6 yrs
Liou et al., 2004	Longitudinal prospective	25	30 (13-53)	NAM + lip repair	78; 38-110	NH; NDH; CH; NW; NaBW	None		Pre- posttreatment	3 yrs after lip repair
Pai et al., 2005	Longitudinal unclear prospective or respective	34	nm	NAM + lip repair	nm (<120)	NH; NW; CA; AW	None		Pre- posttreatment	1 yr after lip repair
Singh et al., 2005	Longitudinal prospective	10	28±2 (nm)	NAM	nm	NaBL; NaH; CH; NW; BAW (2x); NB; $	None		Pre- posttreatment	Before lip repair
Ezzat et al., 2007	Longitudinal prospective	12	26 (16-37)	NAM	110 (71-150)	BAW; CW; CA; NH; NW; ISD; AW	None		Pre- posttreatment	Before lip repair
Barillas et al., 2009	Cross-sectional patient-control	15	nm (<360)	NAM + lip repair	90 (nm)	Alar projection length; dome height; CA; alar groove position; mediolateral nasal dome position; NaBA	Lip repair only	10	Patient-control	Age 9 yrs (7-11)
Kecik and Enacar, 2009	Longitudinal prospective	22	23 (2-42)	NAM	120 (nm)	ClW; arch circ; ant arch w; post arch w; arch l; alv mp; NW; BAW; CA; Narea	None		Pre- posttreatment	Before lip repair
Nakamura et al., 2009	Longitudinal retrospective	15	nm	NAM + lip repair	90	NH/NW; agh ratio; nostril outer line radius	Lip repair only	15	Pre- and post-treatment difference of patient-control	Intervention 2 yrs after lip repair; Control 1 yr after lip repair

Author	Design	Patients (n)	Age of starting NAM Mean (days); range	Patient Intervention	Duration of treatment Mean (days); range	Outcome measures #	Control Intervention	Controls (n)	Comparisons	Last measurement (range)
Mishra et al., 2010	Longitudinal prospective	17	nm (10-360)	NAM + lip repair	70 (60-90)	NH; NW; alar perimeter; CH; AW	Lip repair only	nm	Patient-control	1 yr after lip repair
Chang et al., 2010 @	Longitudinal retrospective	16	nm	NAM + lip repair + postoperative nasal stents	nm	NH; NW; ¼medNH; NaSH; Narea; NH/NW	Lip repair + post-operative nasal stents	23	Patient-control	Age 5 yrs
Clark et al., 2011	Cross-sectional patient-control	20	median 24 (15-36)	NAM + lip repair	median 108 (69-147)	*	Lip repair only	5	Patient-control	5.1 yrs after lip repair (2.1-10.0)
Nazarian Mobin et al., 2011	Longitudinal retrospective	16	39 (nm)	NAM	92 (nm)	AW; ISD; CA; CH; CW; NB; NH; BAW	None		Pre- posttreatment	Before lip repair

nm: not mentioned

@ This study compared 4 variations of treatment, for this study the focus was on NAM + lip repair compared to lip repair only

NH: nostril height; NDH: nasal dome height; CH; columellar height; NW: nostril width; NaBW: nasal base width; CA: columellar angle; AW: alveolar width; NaBL: nasal bridge length; NaH: nasal height; BAW: bialar width; CW: columellar width; sn: subnasal; prn: pronasal; adr: midpoint ala non-cleft side; adl: midpoint ala cleft side; acr: alar curvature non-cleft side; alar curvature cleft side; all: ala cleft side; alr: ala non-cleft side; sballl: subala cleft side; sbalr: subala non-cleft side; stn: soft tissue nasion; SD: intersegmental distance; NaBA: nasal bridge angle; ClW: cleft width; arch circ: arch circumference; ant arch w: anterior arch width; post arch w: posterior arch width; arch l: arch length; alv mp: alveolar midpoint; Narea: nostril area; NH/NW: nostril height nostril width ratio; agh ratio: alar groove heigth ratio; ¼medNH: ¼ medial part of nostil height; NaSH: nasal sill height

* clinical assessment of vermillion, philtrum, white roll, lip scar length; nasal appearance, alar width, alar depression; presence palatal fistula; facial surface registration (landmark position of right ala, left ala, right and left crista philtri, right and left cheilion, prn, sn, laberal superius); maxillary dental midline deviation

$ Angle acr-sn-prn; Angle acl-sn-prn; Angle sn-prn-acl; Angle sn-prn-acr; Angle sn-prn-alr; Angle sn-prn-all; Angle sn-prn-adr; Angle sn-prn-sbalr; Angle sn-prn-sball; Angle prn-stn-sn; Angle sn-prn-stn

unexplained heterogeneity or inconsistency of results or imprecision of results (wide 95% confidence intervals).

Results

Study characteristics (Table 2)

The first study was published in 1999. It took 5 years, until 2004, for the next study to be published, but in the following 8 years 11 studies appeared in the databases. Three study designs were applied; cross-sectional patient-control (3 studies[3, 13, 15]), prospective longitudinal (5 studies[9, 10, 16, 17, 20]), retrospective longitudinal (3 studies[14, 18, 19]), and in 1 longitudinal study[5] we could not identify whether it was performed prospective or retrospective. The mean number of patients in the studies was 18, median 16, ranging from 10 to 34. The starting age of NAM was not reported in 6 studies[3, 5, 9, 13, 14, 18]. In the remaining 6 studies[10, 15-17, 19, 20] the mean age at which NAM was started was 29 days, ranging from 2 to 360 days (median 28 days). The mean treatment period was not reported in 4 studies.[3, 5, 14, 20] In the remaining 8 studies[9, 10, 13, 15-19] the mean treatment period was 95 days, ranging from 38 to 150 days (median; 91 days). In total 64 different outcome variables were used. Actually there were more outcome variables, because some measures, like nostril height, nostril width, columellar length, and bialar width, were differently operationalized between studies. Furthermore, outcome variables are expressed in various ways; absolute values (distances and angles), cleft side to non-cleft side ratios, or differences between cleft and non-cleft side. In 6 studies no control group was studied and only pre-post NAM measurements were compared, at the age of 3 years (1 study[10]), 1 year after the NAM (1 year after NAM[5]), and before lip repair (4 studies[16, 17, 19, 20]). In 6 studies a control group participated, UCLP patients who were treated differently.[3, 9, 13-15, 18] The mean follow-up period of the studies varied from 0 months (4 studies[16, 17, 19, 20]), to 108 months (1 study[13]). The mean follow-up was 28 months (median 18 months).

Study analysis

The heterogeneity of the study designs, outcome variables, outcome variable expressions, follow-up periods, and inadequate data reporting made it impossible to calculate effect-sizes and to perform a meta-analysis. Therefore our analysis is limited to a summary of the study results (Table 3), together with methodological quality, reporting of relapse and side effects, and limitations of the studies.

All 14 studies were of Low quality according to the GRADE approach, because all were observational studies. No studies were upgraded or downgraded, because none of them met the requirements for a down- or upgrade according to the Cochrane Collaboration. No study could meet all the demands necessary to be able to determine the effects of NAM on the nasal symmetry after surgical treatment on the long term. Therefore we choose for a wider range of inclusion of studies and a description of all studies analyzing effects of nasoalveolar molding on nasal symmetry. Implications of this choice are discussed below.

NAM effects

In 4, pre-post design studies,[5, 10, 16, 19] significant improvements over time were found for all outcome variables, which they relate to the use of NAM. In 1 study[3] a significant difference in the nasal symmetry was found in favour of the intervention group (NAM and surgery) compared to the control group (surgery alone). In 1 study[20] no improvements over time were found. In 6 studies[9, 13-15, 17, 18] significant differences as well as non significant differences were found compared to the control group. Over viewing all studies, no particular outcome variable could be pointed out to be affected consistently by NAM.

Relapse and side effects

Relapse was illustrated in 3 studies,[5, 10, 18] of which 1 study[10] provided also statistics about relapse. In this study the columellar length, nostril width and nasal base width had a significant relapse until 1 year postoperatively. Measurements later in the follow-up showed no further relapse.

Only 1 study[9] reported a side effect which was a pressure ulcer. Other studies did not provide information about side effects.

Table 3: Quality and results of included studies

Author	Results of Study		Relapse	Side Effects	GRADE	Possible Confounder	Study Limitations
	Significant difference or improvement	No significant difference or improvement					
Maull et al., 1999	Nasal symmetry		nm	nm	Low	Confounding by indication; Important different mean age of groups	Asymmetry index reproducibility questionable
Liou et al., 2004	NH difference (non-cleft - cleft); NW difference (non-cleft - cleft); NDH difference (non-cleft - cleft); CL difference (non-cleft - cleft); NBW difference (non-cleft - cleft)		Until 1 year after lip repair	nm	Low	Confounding by indication	Measurements from photographs reproducibility questionable; Unclear number of patients per measurement
Pai et al., 2005	NH; NW; CA		Yes	nm	Low	Confounding by indication	Reference line reproducibility questionable; Incomplete and complete cleft analysed together; No mean change or SEM provided
Singh et al., 2005	Angle sn-prn-all; Angle sn-prn-sbalr; Angle sn-prn-sball; Angle prn-stn-sn; Angle sn-prn-stn	Angle acr-sn-prn; Angle acl-sn-prn; Angle sn-prn-acl; Angle sn-prn-acr; Angle sn-prn-alr; Angle sn-prn-adr; NaH; NaBL; CL; NW; BAW; CW; NB	nm	nm	Low		Landmark reproducibility questionable; No mean change or SEM provided
Ezzat et al., 2007	BAW; CW; CA; NH; NW; ISD; AW		nm	nm	Low		Measurements of NH and CA reproducability questionable; Etnic descent might vary; No pre- post data provided
Barillas et al., 2009	Ala projection length; dome height; alar groove position; mediolateral dome position; NBA	CA	nm	nm	Low	Starting age could be late	Measurements reproducibility questionable; Ethnic descent might vary; No mean change or SEM provided

Author	Results of Study		Relapse	Side Effects	GRADE	Possible Confounder	Study Limitations
Kecik and Enacar, 2009	CW; arch circ; arch l; alv mp; NW affected side; BAW; CA; Narea affected side	Ant arch w; post arch w; NW unaffected side; Narea unaffected side	nm	nm	Low	Confounding by indication	No mean change or SEM provided
Nakamura et al., 2009	NH/NW	Agh ratio; nostril outer line radius	Slight relapse	nm	Low	Confounding by indication	No blinding mentioned; No mean change or SEM provided
Mishra et al., 2010	CL	NH; AW; No mention of results of NW; alar perimeter	nm	Pressure ulcer	Low	Confounding by indication; Starting age could be late	No blinding mentioned
Chang et al., 2010	¼medNH; NSH	NH; NW; Narea; NH/NW	nm	nm	Low	Confounding by indication; Learning curve of surgeon might improve results; Selection bias by availability of photos 5 yrs postoperative	
Clark et al., 2011	Vermillion aspect; presence of anterior palatal fistula	Philtrum aspect; lip scar; nasal anatomy; dental arch aspect; nasal measurements; lip measurements; maxillary arch analysis	nm	nm	Low	Confounding by indication	Ethnic descent might vary; No mean change or SEM provided
Nazarian Mobin et al., 2011	NW; CA; NB; BAW	No p-values about the other measures mentioned. Ranges include 0	nm	nm	Low		Landmark reproducibility questionable; Ethnic descent might vary

Confounding and bias

Confounding by indication was possibly present in 8 studies due to a selection of patients for the indication for NAM. The extend of selection bias could not be assessed because of inadequate reporting the selection of patients for NAM. One study[3] compared nasal surface symmetry of the intervention group to a control group of twice the age of the intervention group (4;6 years vs. 9;1 years). Two studies[9, 13] included patients for therapy until 12 weeks after birth, which indicates that patients could have started NAM at a relatively advanced age. One study[14] compared 4 variations of treatment consecutive applied in 11 years. They indicated that all patients had surgery by the same surgeon. An importing contributing factor to a success of the later treatments could be the learning curve of the surgeon in stead of the treatment itself. The same study studied only patients of which photographs were available at the age of 5 years. This selection of patients could introduce a bias, because esthetic outcome might be a reason for patients or parents to return for follow-up.

Eight different phenomenona were identified which could blur the results due to impreciseness of performing the study or presenting the data. In 6 studies[5, 10, 13, 16, 19, 20] the reproducibility of the landmarks, the basis for the measurements, or the measurements was questionable. A small shift of a landmark these studies deal with, could have an important impact on the outcome. These studies did not report information about method errors. In 5 studies[13, 15, 17, 18, 20] the mean change and the standard error of the mean were not reported, so the magnitude of change and the 95% confidence interval can not be placed in perspective. The same lack of data reporting was found in an other study,[16] but here the pre- and posttreatment measurements were missing. Four studies[13, 15, 16, 19] were performed in regions with people from multiple ethnic descents, while no mention was made about these patient characteristics. In 2 studies[9, 18] no mention was made of blinding the observers. One study[3] performed research which is hard to reproduce, because the method of measurement used is not widely accessible. One study[5] reported the results of patients with a complete and incomplete cleft as one group.

Discussion

Over viewing the results of the review there is poor agreement between the 12 studies selected. Some studies reported exclusively positive results, some reported mixed results, and 1 found no effect. All studies were of low GRADE quality with heterogeneity in study designs, research protocols, treatment protocols, follow-up time, outcome variables (64), definitions of variables, and operationalization of variables. Moreover, there was a difference in the methodology, which has consequences for the relevance in relation to our research aim. The patient-controlled studies which could make assumable that NAM was independently responsible for their results, are more informative than pre-post treatment studies without a control group. All these aspects together made comparison of the results of the studies by means of the intended meta-analysis impossible. In addition, this systematic review has not taken into account the techniques of NAM and surgery used in the studies, which would have made comparison of the results even more difficult. Moreover, each study used an unique combination of population and treatment protocol regarding taping, frequency of adjustment, passive or active stent, starting age, treatment duration, timing of surgery, and surgical techniques, which made comparison of every single aspect of treatment impossible. Taking all of the above findings into account it is not clear whether NAM is effective or not in improving nasal symmetry on the long term.

The effect of NAM could be depending on particular aspects of the treatment technique and protocol. On the other hand skills of the dentist, orthodontist and surgeon could also be a decisive factor to achieve improved nasal symmetry. Nasal and facial anatomy and texture, corresponding to ethnic descents, could be an important factor for remodelling a nose in the desired shape. Based on this systematic review it is impossible to identify which factors determine achievement of improved nasal symmetry, because the data from the studies are influenced or blurred by noise from confounders, questionable reproducibility and inadequate reporting in the studies. As the starting age of NAM[9] and the treatment duration are important for the effect of NAM, it is unsatisfactory that about half of the studies did not report about these aspects. Therefore we make some recommendations for future studies (Table 4). Ideally a study would be a randomised controlled trial according to the accepted rules of conducting a

Table 4: Recommendations for future studies

Reporting	Measures	Timing of measurements
Population selection	Nostril heigth	Initial visit
Eligible subjects, participating subjects, drop-out reasons	ratio cleft/non-cleft side	
Treatment description	Nostril width	Immediate before lip repair
Technique and protocol	ratio cleft/non-cleft side	
Starting age	Bialar width	Immediate after lip repair
Mean, sd or median, IQR	absolute value	
Therapy duration	Columellar length	1 year after lip repair
Mean, sd or median, IQR	ratio cleft/non-cleft side	
Basic data	Columellar angle	
Mean, sd or median, IQR	degree	
Measure changes	Nasal angle	
Mean change, SEM or 95% confidence intervals	degree	
Reliability of measurements	Alveolar width	
	absolute value	
	Intersegmental distance	
	absolute value	

trial.[22] However, randomised controlled trials are difficult to conduct, because of the relatively small numbers of homogenous groups uni- or bilateral cleft patients. Multicenter trials are hard to design, because of the varying treatment protocols between cleft centers, like surgical and non-surgical techniques, modifications, and timing which all might influence shape and growth of the nose. The main obstacle would probably be a limited inflow of patients which would make the trial take a long time and the results could be contaminated by other innovations or changes in the cleft treatment during the trial. A second contamination of a time consuming study could be the learning curve of practitioners to influence the effect of a treatment in stead of the treatment itself. We propose, in any chosen study design, that at least an adequate description of the population selection, an adequate description of treatment technique and protocol, starting age of therapy (mean, sd or median, IQR), therapy duration (mean, sd or median, IQR), data of every measurement (mean, sd or median,

IQR), and change of the measures (mean change, standard error of the mean or 95% confidence intervals) are reported. Additionally it would be beneficial for comparison and interpretation of study results if there was consensus in outcome variables. It is preferable to report a limited number of well defined and reproducible measures. We underline the proposed measures of Nagy and Mommearts[23] because of the shown reliability and reproducibility. In our opinion the reported measures should at least be: nostril height, nostril width, bialar width, columellar length, columellar angle, nasal angle, alveolar width and intersegmental distance. Furthermore, we follow the recommendation of Nagy and Mommearts[23] expressing the results of the measurements as absolute values and ratios in stead of differences for the benefit of comparison and reproducibility. The last recommendation is about the timing of measurements, which should be at least at the initial visit, before and after the lip repair, and 1 year after lip repair to be informed about the pretreatment measurements, effect of NAM alone, additional effect of surgery, and relapse. Liou et al.[10] showed that relapse is small 1 year after lip repair, so no later measurements are mandatory. These recommendations would make the construction of a database possible, which has benefits for future data analysis on the effects of NAM.

A relatively small number of studies in the literature deal with NAM, which was the reason a wide search strategy with 2 search terms could be afforded and the search results from the databases could be studied thoroughly. A disadvantage of a research field in development could be multiple descriptions for the same issue, so possibly studies are missed because of other names of NAM. Also, the selection limited to English, German and Dutch papers and restrictions to three databases may have influenced the number of selected studies, because 3 of the excluded studies had an interesting abstract.[24-26] Our aim was defined quite narrow. None of the studies had a design or reported adequately enabling us to answer our research question. However some studies were more valuable for achieving our purpose, despite that they all were of low GRADE quality. Given the study designs this review dealt with, the most valuable information could be retrieved from cross-sectional patient-controlled studies with long term (>1 year) follow-up.[3, 13, 15] These studies reported mixed results, varying from significantly improved nasal asymmetry index measured with nasal surface registration,[3] mainly significantly improved nasal measures indirectly measured from nasal

casts,[13] to no significantly changed nasal measures indirectly measured from 3D anthropometric analysis.[15] Also a retrospective longitudinal study with patient-control comparison on the long term provided valuable information.[14] This study found an improved symmetry, expressed in several measures in the group treated with NAM and surgical lip repair compared to the group treated with lip repair only. However, just 2 out of 6 measures were changed significantly. The choice not to exclude the studies which were more distinct from our research goal was made to provide a complete over view of all relevant studies concerning our aim. The downside could be that studies with more relevance for the research question are not directly obvious. However also in the studies which provided the most valuable information there is no consensus in the results. Finally, the studies were analysed by the first author (PH). When in doubt about any aspect of the study, the second author (PUD) was asked for his analysis. Discussion led to consensus about the aspect of concern. The quality of the studies may have been overestimated, as this procedure may have led to probably more over seeing than overly emphasizing any confounders or data noises. However, the impossibility of a meta-analysis was ascertained by 3 authors (PH, PUD, CS), so the conclusion of this study is unlikely to be influenced by this limitation.

NAM has disadvantages, such as side effects, complexity of appliance, time consuming, expensive,[12] and a burden on the family system.[11] Besides 1 study[9] mentioning a pressure ulcer, none of the analysed studies had made remarks of any disadvantage. As the evidence of a positive effect of NAM is not substantial, practitioners should be conscious about the possible negative consequences of their therapy. In conclusion, NAM seems to be beneficial in achieving nasal symmetry in unilateral cleft patients, however the evidence is not substantial to support it effects. The results of the studies concerning NAM are inconsistent regarding changes of nasal symmetry. Additionally, studies regarding NAM in UCLP are heterogeneous and lack adequate reporting. Recommendations for future research were provided to construct a consensus about the effect of NAM.

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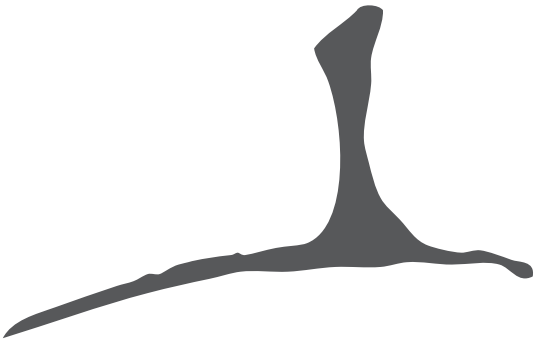
Chapter 4

Nasometry cooperation in children 4-6 years of age



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Abstract

Objective: Hypernasality is a common problem in cleft care. It should be treated before the age of six, because of the impact it can have on speech sound development in young children. An objective method of nasalance evaluation is nasometry. Cooperation of young children, by nature, differs over time and situations. First aim of this study is to indicate a minimum age for cooperation with the nasometer. Second aim is to compare the cooperation of children in the most used research setting (school) with the cooperation of children in the most used setting in daily practise (ENT outpatient clinic).

Method: Children from four to six years of age were recruited from schools. Outpatient clinic children were recruited from the Groningen ENT clinic. Both groups were tested with the nasometer. The cooperation with installation and repetition of speech stimuli were noted.

Results: 118 school children and 41 outpatient clinic children were recruited. Six years old children cooperated significantly better than the five years old. The five years old cooperated better than the four years old. Moreover, school children cooperated significantly better than the outpatient children.

Conclusion: Most children of 6 years of age and older, will show good cooperation with nasometry. In children aged 5, cooperation depends on the situation in which the nasometer is used. In a school setting the cooperation is better than in an outpatient clinic setting. In the 4 years old children the cooperation with the nasometer often is insufficient, probably due to normal, unpredictable cooperative behaviour belonging to this age.

Introduction

Many patients with a cleft palate, after palatal repair, still have velopharyngeal insufficiency (VPI) resulting in hypernasality. Hypernasality means a resonance disorder caused by the impossibility to separate the oral cavity from the nasal cavity. This leads to increased nasal resonance of oral speech sounds and/or nasal air emission. These patients may need a pharyngoplasty. However, the timing of these operations is under discussion as speech and language development have a critical period in early life.[1, 2] Especially in the first years of life, intonation patterns and speech sound production are dependent on several factors, e.g. language and articulatory possibilities.[1, 32] The speech sound characteristics are fixed by neurological stimulation and imprint, by about six years of age. In children with VPI and hypernasality speech is affected, because it reduces intra-oral pressure for fricative and plosive sounds. Moreover children can compensate for the lack of air pressure and may develop compensatory sound productions. As a consequence, when hypernasality is not treated in the first years of life, the compensatory sound productions also becomes fixed in the speech sound system and remain after surgical correction.[4, 5] The critical period for speech and language development is a strong argument in favour of early surgery to avoid a permanent hypernasal speech pattern. Hypernasality can be investigated by the speech pathologist on audible examination. This investigation should be combined with visual inspection of the mobility of the velum by the ENT-surgeon or plastic surgeon[6, 7] and/or a more objective method. Next to invasive and potential harmful investigations like X-ray, multiview videofluoroscopy and nasoendoscopy,[8] nasometry is an objective method. As nasometry is not invasive, this method often is considered to be the golden standard.[9-19] The nasometer is a combination of headgear, computer and analysing software. Nasal and oral sound productions are measured during speech by two microphones separated by a plate on the upper lip of the speaker. Nasometry results in a nasalance score, which represents the nasal proportion of the total sound energy. Hypernasal patients, like in many cleft palate patients, produce an excess of nasal sound (high nasalance score), especially with oral text passages. Hyponasal patients, like patients with nasal obstruction, produce less nasal sound (low nasalance score), especially with nasal text passages.

In studies about nasometry with young children it is sometimes indicated that authors do not have results of all included children. However, it is not mentioned why these results are missing.

In a pilot study in the Groningen ENT clinic (University Medical Center Groningen) it was found that most young children with clefts showed uncooperative behavior with nasometry.[6] This was interpreted as normal as children, by nature, show unpredictable cooperative behavior depending on situations and/or time.[20]

Most studies with the nasometer recruited their children from schools, but the setting in daily practice of the nasometer is the outpatient clinic. First aim of this study is to indicate a minimum age for cooperation to obtain reliable results in evaluating hypernasality with the nasometer. Second aim is to compare the cooperation of children in the most used research setting (school) with the most used setting in daily practise (ENT outpatient clinic).

Material and Method

Subjects

Two groups of children were recruited. The first from pre- and elementary schools in four Dutch locations (Groningen, Yde, Emmen, Staphorst) spread over three northern provinces (Groningen, Drenthe, Overijssel) of The Netherlands. Parents of all children from four to six years of age were asked for informed consent. All children in the regular pre- and elementary schools function, otherwise they would visit special schools. The second group was recruited from the Groningen ENT outpatient clinic. In a period of six weeks parents of all children from four to six years who visited our outpatient clinic for communication disorders, with questions about hearing ability and normal non-verbal functioning, were asked to participate. Subjects were classified by age in three groups: 4;0-4;11, 5;0-5;11 and 6;0-6;11 (the 4, 5 and 6 years age group).

Speech material

Two sets of Dutch sentences were used. The first set was first presented in literature by Van Zundert, see appendix A.[19] The Van Zundert set is built up from five oronasal sentences and six oral sentences. The oronasal sentences are developed on the basis of the percentage nasal consonant corresponding with the Dutch language (11.6%).[21] The oral sentences lack nasal consonants. The sentences must be repeated, as the children can not read yet. The second set was developed on a phonetical balance analysis by Moolenaar-Bijl,[22] and contain three oral sentences, see appendix B. This set is regularly used in the Groningen cleft palate team, because it can easily be repeated by young children.

Instrumentation and data collection

The Kay Pentax Nasometer™ II, model 6400 (Kay Elementrics) was used. Nasometer™ Software was installed on a laptop. Calibration was performed on the beginning of every day in the room of data collection. Data were collected in a separate room in either the school or outpatient clinic by always the same investigator, the second author (HH). Children were verbally instructed. The headgear was installed according to the manual.[23] The above mentioned speech stimuli were spoken by the investigator in a slow, steady pace and were asked to repeat by the child. The child was asked to speak normal, but loud enough for the software to register. When an error occurred the complete sentence was repeated. The speech sample of the child was recorded by the Nasometer™ software.

Analysis and statistics

The degree of cooperation with installation was scored on a two point scale (refusal, accepted). The cooperation with speech stimuli was scored on a three point scale (refusal, with effort or easy), see Table 1. A child was scored 'headgear refused' if it rejected to wear the headgear. It was scored 'speech stimuli refusal' if it refused to repeat any of the speech stimuli after headgear acceptance. The score 'speech stimuli with effort' was given if a child repeated partly or after much stimulation. A child was scored 'speech stimuli easy' if it repeated the speech stimuli without protest. All together a child was scored as uncooperative if the

Table 1: Definition of cooperation scores

Headgear	
Refusal	Total rejection of wearing the headgear
Accepted	Wore the headgear with or without protest

Speech stimuli	
Refusal	While wearing the headgear total refusal to repeat any of the speech stimuli
With effort	Repeated partly or after much stimulation the speech stimuli
Easy	Repeated the speech stimuli without protest

headgear was rejected or the sentences were refused to repeat or were repeated with effort. If the child wore the headgear and cooperated easy with the speech stimuli, good cooperation was scored. IBM SPSS Statistics version 16.0 was used for statistical analysis. The Kruskall-Wallis test was used to compare cooperation of the different age groups and to compare the school group with the outpatient clinic group. $P<0.05$ was considered significant different. The 95% confidence intervals (CI) of the proportions were determined for further comparison.

Results

Patient characteristics (Table 2)

From the four schools 118 children (63 boys, 55 girls) had permission to participate, 42, 36 and 40 subjects from the 4, 5 and 6 years age group respectively. From the outpatient clinic 41 children (32 boys, 9 girls) were included, 16, 13 and 12 children of the 4, 5 and 6 years age group respectively.

Cooperation (Table 3a and 3b and figure 1 and 2)

Out of 118 school children 82 children cooperated well (69%, CI 61-78). From 41 outpatient clinic children 18 cooperated well (44%, CI 29-59). Some children totally refused the headgear or refused to repeat the speech stimuli, that were 11 school children (10%) and 12 outpatient clinic children (30%). Several children

Table 2: Number of children sorted by age and setting

Age	School			Outpatient clinic		
	Boys	Girls	Total	Boys	Girls	Total
4	23	19	42	15	1	16
5	18	18	36	10	3	13
6	22	18	40	7	5	12
Total	63	55	118	32	9	41

cooperated with effort, 25 school children (21%) and 11 outpatient clinic children (27%), and were considered non cooperative.

Cooperation was better in the older children. From the 40 school children in their six years old group 2 were uncooperative (5%, CI 0-12). From 36 five years old school children 11 cooperated not or with effort (31%, 16-46). This is significant more than in the six years old ($p=0.001$). From the 42 four years old school children 23 were uncooperative (55%, CI 40-70). This is significant more than in the five years old ($p=0.033$). From the 12 six years old outpatient clinic children 2 were uncooperative (17%, CI 0-38). Seven of the five years olds were uncooperative (50%, CI 24-76). This is more, but not significant different from the six years olds ($p=0.122$). From the 15 four years old outpatient clinic children 14 were uncooperative (93%, CI 80-100). This is significant more than in the six years olds ($p<0.001$) and the five years olds ($p=0.005$). Significant more four years old school children were cooperative than four years old outpatient clinic children ($p=0.007$). At the ages five and six there were no significant differences between school children and outpatient clinic children, $p=0.582$ and $p=0.188$ respectively.

Table 3a: Cooperation of school and outpatient clinic children

Age	headgear		headgear accepted speech stimuli						
	refusal		Refusal		with effort		easy		
School children									
4	7	17%	2	5%	14	33%	19	45%	42
5	0	0%	0	0%	11	31%	25	69%	36
6	2	5%	0	0%	0	0%	38	95%	40
	9	8%	2	2%	25	21%	82	69%	118
Outpatient clinic children									
4	3	20%	4	27%	7	47%	1	7%	15
5	4	29%	0	0%	3	21%	7	50%	14
6	1	8%	0	0%	1	8%	10	83%	12
	8	20%	4	10%	11	27%	18	44%	41

Table 3b: Cooperativeness and uncooperativeness numbers, proportions (%) and 95% confidence intervals (CI) of the proportion. Uncooperativeness is headgear refusal, speech stimuli refusal and speech stimuli with effort cumulated. Cooperativeness is easy repetition of the speech stimuli after headgear acceptance

Age	Uncooperative			Cooperative		
	n	proportion	95% CI	n	proportion	95%CI
School children						
4	23	55%	40-70	19	45%	30-60
5	11	31%	16-46	25	69%	54-84
6	2	5%	0-12	38	95%	88-100
	36	31%	22-39	82	69%	61-78
Outpatient clinic						
4	14	93%	80-100	1	7%	0-19
5	7	50%	24-76	7	50%	24-76
6	2	17%	0-38	10	83%	62-100
	23	56%	41-71	18	44%	29-59
						p-Values
School children						
4vs5						0,033
5vs6						0,001
4vs6						<0,001
Outpatient clinic						
4vs5						0,005
5vs6						0,122
4vs6						<0,001
School children vs outpatient clinic children						
4vs4						0,007
5vs5						0,058
6vs6						0,188

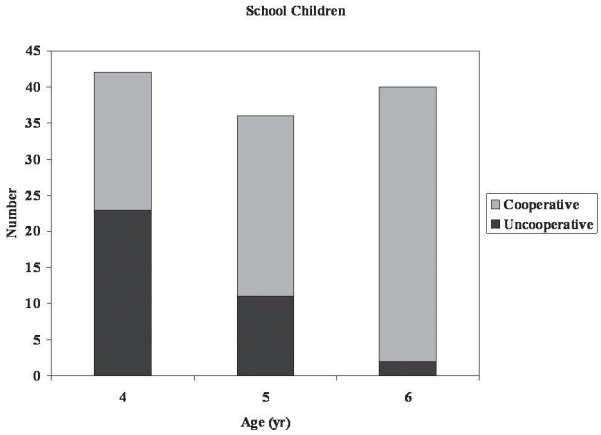

Figure 1: Number of (un)cooperative school children

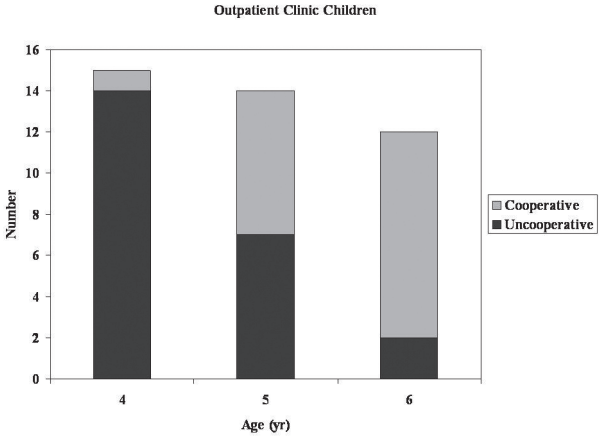

Figure 2: Number of (un)cooperative outpatient clinic children

Discussion

At young age possible hypernasality should be recognised and treated to prevent compensatory sound productions which become fixed in the language system and remain after surgical correction. Nasometry is a method to quantify nasalance[24] and is encouraged to use in the diagnostic process of hypernasality.[8, 10, 17] The technique is considered not invasive and reliable.[10, 15] However, this study indicates that for young children nasometry is not easy to perform. Four years old children cooperated significant worse than five and six years old children. In the school and outpatient setting the majority of the four years old children did not cooperate. The large majority of the six years old children did cooperate in both settings. Half of the five years old did cooperate in the outpatient setting, and 69% of the five years old school children cooperated. For some children the headgear was threatening. In other children the speech instruction was too difficult. The main part of four years old children cooperated insufficient, while at this age treatment of hypernasality is preferred.

Earlier research showed a great test-retest variance of 5 points[15, 16, 25, 26] or even 10 points when the headgear was removed between the tests.[27] None of these studies mention age as a variable, but perhaps the found intra-individual variance was due to the fact that in these studies young children were included. It can be expected that when a child does the speech instruction for the second time, the cooperation is different than the first time.[20]

It is remarkable that cooperation at the school setting was significantly better than at the outpatient clinic. This aspect has been not previously reported. A possible explanation is that at the outpatient clinic, subjects were accompanied by their parents. In contrast, at the school, children were assessed alone. Also, it is possible that children with speech and hearing problems, showed difficulties with the instructions for imitation or modelling. Nonetheless, it seems reasonable that the school setting is a more familiar environment for children.

This study made clear that the school setting and clinical setting has different outcomes in cooperation. Moreover it made clear that for children under the age of 6 reliable nasalance scores cannot always be obtained. Therefore we underline the opinion of Van Lierde,[17] Van Doorn,[16] Seaver,[25] Hardin[28] and the Cleft Palate Committee of IALP[8] based on the amount of reliable speech recordings, that

the nasometer must not be the only diagnostic instrument for determining hypernasality, especially not in young children.

Conclusion

Most children of 6 years of age and older, will show good cooperation with nasometry. In children aged 5, cooperation depends on the situation in which the nasometer is used. In a school setting the cooperation is better than in an outpatient clinic setting. In the 4 years old children the cooperation with the nasometer often is insufficient, probably due to normal, unpredictable cooperative behaviour belonging to this age.

Appendix A: Set of sentences by Van Zundert

Oronasal passage:

Miep is op school.
(*Miep is at school*)
Nu gaat zij kleuren.
(*Now she will paint*)
Zij tekent de juf.
(*She paints the teacher*)
Dat wordt heel mooi.
(*This becomes very nice*)
Juf geeft Miep stickers.
(*Teacher gives Miep stickers*)

Oral passage:

Jos heeft feest.
(*Jos has a party*)
Hij is jarig.
(*It is his birthday*)
Hij krijgt veel cadeautjes.
(*He gets a lot of presents*)
Ook is er taart.
(*There is also cake*)
De taart heeft vijf kaarsjes.
(*The cake has five candles*)
Jos blaast ze uit.
(*Jos blows them*)

Appendix B: Set of sentences by Moolenaar-Bijl

Kees zit op de fiets.
(*Kees sits on the bicycle*)
Ida kijkt op de klok.
(*Ida watches the clock*)
De poes zit op de stoep.
(*The cat sits on the sidewalk*)

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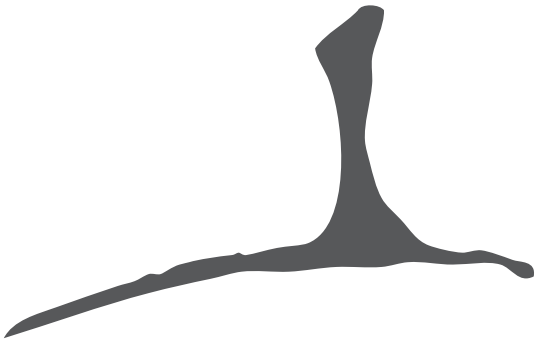
Chapter 5

Nasometry normative data for young Dutch children



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Abstract

Objective: Hypernasality is a common problem in cleft care. It should be treated before the age of six, because of the impact it can have on speech sound development in young children. An objective method of nasalance evaluation is nasometry. To decide whether a nasometer test result is normal or abnormal, normative data and cut off points are needed. Normative data for children are not available for every language and age. For Dutch children two sets Dutch speech stimuli, the van Zundert sentences or the Moolenaar-Bijl, sentences, are often used in the diagnostic process for hypernasality. Primary goal of this study is to determine normative data and cut off points for two sets of Dutch speech stimuli for Dutch children from four to six years of age. Secondary is to compare those two sets of oral sentences.

Method: Children without clefts were recruited from schools. According to their teachers their speech was normal. They were tested with the nasometer with the two sets of speech stimuli. The set from Van Zundert has oral and oronasal sentences , the Moolenaar-Bijl set only has oral sentences

Results: 118 children were recruited. Out of these children, 55 produced recording samples which were suitable for analysis. There were no significant differences between age groups or gender. The two different sets speech stimuli used were significant different, but the confidence intervals overlapped.

Conclusions: Normal nasalance scores of the tested sentences are between 3-19% for oral sentences and between 17-37% for oronasal sentences. The Moolenaar-Bijl speech sentences are preferred to evaluate hypernasality in young Dutch children, because of the shortness and intelligibility. Normative nasalance scores are applicable to the whole group of children from four to six years of age.

Introduction

Many patients with a cleft palate, after palatal repair, still have velopharyngeal insufficiency (VPI) resulting in hypernasality. Hypernasality means a resonance disorder caused by the impossibility to separate the oral cavity from the nasal cavity. This leads to nasalisation of oral speech sounds and/or nasal air emission. These patients may need a pharyngoplasty. However, the timing of these operations is under discussion as speech and language development have a critical period in early life.[1, 2] Especially in the first years of life, intonation patterns and speech sound production develop language specific.[2, 3] The speech sound characteristics are fixed by neurological stimulation and imprint, by about six years of age. In children with VPI, the nasal air emission affects speech because it reduces intra-oral pressure for oral sound. Moreover children can compensate for the lack of air pressure and may develop compensatory sound productions. As a consequence, when hypernasality is not treated in the first years of life, the compensatory sound productions also becomes fixed in the speech system and remain after surgical correction.[4, 5]

Hypernasality can be investigated by the speech pathologist on audible examination.[4, 5] Besides this there are more objective methods. Some of these are invasive and potential harmful investigations like X-ray, multiview videofluoroscopy and nasoendoscopy.[8] Nasometry is another objective method. As nasometry is not invasive, this method often is considered the golden standard.[9-19] The nasometer is a combination of headgear, computer and analysing software. Nasal and oral sound productions are measured during speech by two microphones separated by a plate on the upper lip of the speaker. Standardized text passages are used and analysed. This results in a score, which represents nasal proportion of the total sound energy. Hypernasal patients, like in many cleft palate patients, produce an excess of nasal sound (high nasalance score), especially with oral text passages. Hyponasal patients, like patients with nasal obstruction, produce less nasal sound (low nasalance score), especially with nasal text passages.

Some studies have measured normative data for nasalance scores in children, see Table 1.[10, 12, 14-16, 18-20] These studies show close but varying results due to varying age and language. The variance also could be partly explained by a

Table 1: Mean nasalance scores (%) and standard deviations for studies with children

Author	Year of publication	Language	Age (yrs)	Number	Nasalance				Instrumentation
					Oral	SD	Oronasal	SD	
Brunnegard	2009	Swedish	4-11	220	12.7	5,6	29.5	6.1	Kay Nasometer II 6400
Hirschberg	2006	Hungarian	4-9	30	11	-	31.7	-	Kay Nasometer II 6400
Sweeney	2004	English (IRE)	5-7	70	14-16	5,6	26	5	Kay Nasometer I 6200
Van Lierde	2003	Dutch (BE)	7-13	33	11.3	4,7	31.9	4.8	Kay Nasometer I 6200
Van Doorn	1998	English (AUS)	4-13	245	13.1	5,9	-		Kay Nasometer I 6200
Van Zundert	1999	Dutch (NL)	4-6	50	13.2	4,5	26.0	4.4	Kay Nasometer I 6200
Prathanee	2003	Thai	7-12	188	14.3	5.8	35.6	5.9	Nasometer, type not reported

different vowel composition in the tested passages in the different languages. For the reasons above there is a plea for normative data for different languages.[17]

In most reported studies the very young children are not represented. The Groningen cleft palate team treats hypernasality before the age of six[7] and nasometry is used in addition tot audible examination. Therefore normative data from children from four to six years of age are needed. Van Zundert formulated Dutch oronasal and oral text passages to evaluate nasalance and determined normative nasalance scores with these passages for Dutch children from four to six years of age.[19] Moolenaar-Bijl formulated three oral sentences for the nasalance evaluation,[21] but normative nasalance scores for these three sentences were never determined.

The primary goal of this research is to determine normative data for Dutch children from four to six years of age. The secondary goal is to measure comparability between the two sets of oral sentences.

Material and Method

Subjects

Children without clefts were recruited from pre- and elementary schools in four Dutch locations (Groningen, Yde, Emmen, Staphorst) spread over three northern provinces (Groningen, Drenthe, Overijssel) of The Netherlands. Parents of all children from four to six years of age (first, second and third class) were asked for informed consent. According to the teachers all children had normal speech Subjects were excluded when there was a history of speech therapy or non native Dutch speaking parents. Subjects were classified by age in three groups: 4;0 – 4;11, 5,0-5;11 and 6;0-6;11 years of age (the 4, 5 and 6 years age group).

Speech material

Two sets of Dutch passages were used. The first set was first presented in literature by Van Zundert, see appendix A.[19] Young children can not read yet, and therefore must imitate the sentences. The sentences are not too complex for young children to understand and repeat fluently. The Van Zundert set is built up

from five oronasal sentences and six oral sentences. The oronasal sentences are developed on the basis of the percentage nasal consonant corresponding with the Dutch language (11.6%).[22] The oral sentences lack nasal consonants. The second set was developed on a phonetical balance analysis by Moolenaar-Bijl,[21] and contain three oral sentences, see appendix B. This set is regularly used in the Groningen cleft palate team, because it can easily be repeated by young children.

Instrumentation and data collection

The Kay Pentax Nasometer™ II, model 6400 (Kay Elemetrics) was used. Nasometer™ Software was installed on a laptop. Calibration was performed on the beginning of every day in the room of data collection. Data were collected in a separate room by always the same investigator, the second author (HH). Children were verbally instructed. The headgear was installed according to the manual.[23] All the above mentioned speech stimuli were spoken by the investigator in a slow, steady pace and were asked to repeat by the child. The child was asked to speak normal, but loud enough for the software to register. When an error occurred the complete sentence was repeated. The speech sample of the child was recorded by the Nasometer™ software.

Analysis and statistics

IBM SPSS Statistics version 16.0 was used for statistical analysis. The mean and standard error of the nasalance scores were calculated for each separate sentence. The scores of the sentences of the same passage were combined to form the mean score of the corresponding passage. Disturbing sounds like coughing or sighing were cut out, in order to analyse only the speech sample. To evaluate normal distribution of the nasalance scores the Kolmogorov-Smirnov test was performed. Values between -1 and 1 are considered to represent normal distribution. The student-t test was used to compare the nasalance scores of the different age groups. The paired sample t-test and 95% confidence intervals were used for comparison of the oral Van Zundert passage and the oral Moolenaar-Bijl sentences. P-values <0.05 were considered significant.

Results

Record collection

A total of 118 children (63 boys, 55 girls) were allowed to participate. 42 children of the 4 years age group,, 36 from 5 years age group and 40 from the 6 years age group. Out these 118, 46 children were excluded: 10 because of a history of speech therapy, 3 because of non-native Dutch speaking parents and 33 because of bad cooperation. Furthermore, 17 recordings appeared not suitable for analysis because of too many flaws in the output for reliable analysis. These flaws resulted in a scattered output line, which has more defects than blue line. The lack of a blue line is analysed by the software as a nasalance of 0%, which can not be the case during a whole spoken sentence. We detected these flaws during analysing, so we had not the opportunity to repeat the procedure with this subject. A total

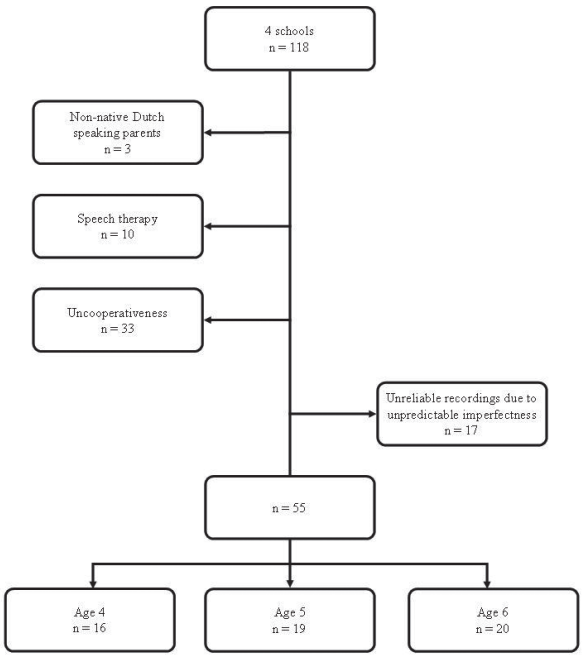

Figure 1: Flowchart of inclusion and exclusion of children

of 55 recordings remained for analysis, 16 of 4 years old children, 19 of 5 years old children and 20 of 6 years old children, see figure 1.

Nasalance scores

The mean nasalance score and standard deviation for all ages for the oral Van Zundert passage were 11% ±4. For the different age groups the scores were 10% ±4 for the four years old, 11% ±4 for the 5 years old and 10% ±4 for the six years old. The three oral sentences from Moolenaar-Bijl resulted overall in 13% ±5, for the 4 years old 12% ±4, 5 years old 14% ±4 and 6 years old 13% ±5, see table 2 and figure 2. For the oronasal Van Zundert passage the mean nasalance score and standard deviation for all ages were 27% ±5, and for the ages 4, 5 and 6 years, 26% ±5, 28% ±5 and 27% ±5 respectively. There are no significant differences in nasalance between the age groups or gender. The nasalance scores for the three Moolenaar-Bijl sentences (0.944), oronasal passage (0.604) and oral passage (0.264) were normally distributed. The means of the oral Moolenaar-Bijl sentences and oral Van Zundert passage differed significantly ($p<0.001$). However, the 95% confidence intervals of the mean nasalance scores overlapped (Moolenaar-Bijl 11.7-14.3 and oral Van Zundert 9.9-12.1).

Table 2: Mean nasalance score per age

Age	Van Zundert oronasal		Van Zundert oral		Moolenaar-Bijl oral	
	Mean	SD	Mean	SD	Mean	SD
4	26	5	10	4	12	4
5	28	5	11	4	14	4
6	27	5	10	4	13	5
Overall	27	5	11	4	13	5

Discussion

When using the nasometer in clinical practise, cut off points in the normative data are necessary to distinguish abnormal nasalance from normal. The cut off points are formed by placing two standard deviations beyond the mean to include 95% of the normal population. This statistical procedure is justified by the normal distribution according to the Kolmogorov-Smirnov test. Applying this procedure on our data shows that nasalance scores between 3-9% for the oral passage 17-37% for the oronasal passage indicate normal nasalance. Children with higher nasalance scores than the cut off scores can be considered hypernasal. Our cut off points are in agreement with Van Zundert, who found cut off scores 4-22% and 17-35%.[19] The mean nasalance scores in our study for Dutch children are quite similar to earlier studies published about Swedish, Hungarian, Irish English, Australian English, Dutch and Flemish children, see Table 1. Despite differences in age, gender and language all scores of these studies vary from 11 to 16% for the oral passages and 26 to 36% for the oronasal passages. The means have approximately the same standard deviation, 4-5.9 (oral) and 4.8-6.1 (oronasal). This indicates that the investigated languages are not an important variable. Also the norms given by the McKay nasometer itself (McKay-Kummer SNAP Test-R , 2005) show cut off scores for 10-16% (+/- 4) for oral sentences.

The three age groups did not differ in nasalance scores in the used oral nasal and the two sets of oral sentences, see figure 2. This means that the found

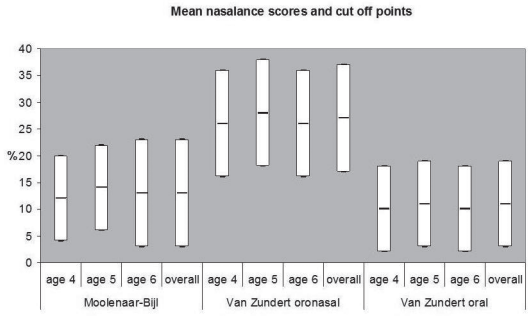

Figure 2: Nasalance scores per passage. Middle dash indicates the mean. The ends of the columns are two standard deviations of the mean, indicating the cut off points.

normative data are not age specific for the Dutch children 4 – 6 years of age and can be used for the whole group.

Test-retest variability, several times determined, is within 5 points.[10, 15, 16, 24, 25] Given the intra-individual variation Brunnegard recommends passage repetition for three times to determine one persons nasalance score,[10] especially when the score will be used for clinical decision making or pre- and postoperative monitoring. Our results show this seems not suitable for young children. Already in one attempt 33 children out of 118 (28%) did not cooperate enough for reliable speech recordings. Repetition of tests to gather three reliable speech recordings will probably succeed in a higher proportion of uncooperative children, because of attention deficit and changing performance belonging to this young ages.[26] Therefore we underline the opinion of Van Lierde,[17] Van Doorn,[16] Seaver,[24] Hardin[27] and the Cleft Palate Committee of IALP[8] based on the amount of reliable speech recordings, that the nasometer must not be the only diagnostic instrument for determining hypernasality.

There is a significant difference of nasalance scores between the oral Van Zundert passage and the three oral Moolenaar-Bijl sentences. This probably has to do with a different composition of vowels in the two sets of sentences. However the means of the nasalance scores are very near, 11% and 13%. The 95% confidence intervals of the mean of the nasalance scores overlap, as do a large proportion of the cut off point intervals. Therefore the significant difference does not mean a clinical relevant difference. The Moolenaar-Bijl set has the strength of the shortness and intelligibility. That is why we advocate the use of the three oral sentences as a suitable tool for screening for hypernasality in young children during consultation. Of course, more oral sentences and oronasal sentences, like in the Van Zundert set, represent a given language in a more normal way, but especially for young children given tasks should be short. Cooperation in young children is extremely dependant on situation and length of tasks.[26] In future research we will try to determine a minimum age for reliable results in evaluation of hypernasality with the nasometer.

In this research we found not only uncooperative behaviour in a great proportion of the children (28%), but also a reduced proportion of reliable speech recordings. We couldn't explain this in a proper way, as the nasometer has been never reported about as unpredictable. Perhaps, like stated by the MacKay's

clinical implications, the found spikes must be considered as an effect of nasal rustle. The nasometer picks up resonance (including hypernasality) and nasal air emission. Probably it was also overlooked that the children could have had a cold or did some odd things during the procedure.

Conclusion

In Dutch children aged four to six, the hypernasality cut off scores, when using the nasometer, are 19% for the used oral passage and 37% for the used oronasal passage for children. Although nasometry can be a valuable objective tool in diagnosing hypernasality in the speech production of young children, it must be kept in mind that a great proportion of the children can show non-cooperative behaviour. Therefore also other diagnostic methods should be used to examine hypernasality.

The normative data derived form the oral van Zundert sentences and the three oral Moolenaar-Bijl sentences are almost the same. Due to its better use we prefer the Moolenaar-Bijl sentences for the evaluation of hypernasality for young Dutch children.

The normative nasalances scores are applicable to the total group of children aged four to six.

Appendix A. 2 passages by Van Zundert

Oronasal passage:

Miep is op school.
(Miep is at school)
Nu gaat zij kleuren.
(Now she will paint)
Zij tekent de juf.
(She paints the teacher)
Dat wordt heel mooi.
(This becomes very nice)
Juf geeft Miep stickers.
(Teacher gives Miep stickers)

Oral passage:

Jos heeft feest.
(Jos has a party)
Hij is jarig.
(It is his birthday)
Hij krijgt veel kadootjes.
(He gets a lot of presents)
Ook is er taart.
(There is also cake)
De taart heeft vijf kaarsjes.
(The cake has five candles)
Jos blaast ze uit.
(Jos blows them out)

Appendix B. Moolenaar-Bijl passage

Kees zit op de fiets.
(Kees sits on the bicycle)
Ida kijkt op de klok.
(Ida watches the clock)
De poes zit op de stoep.
(The cat sits on the sidewalk)

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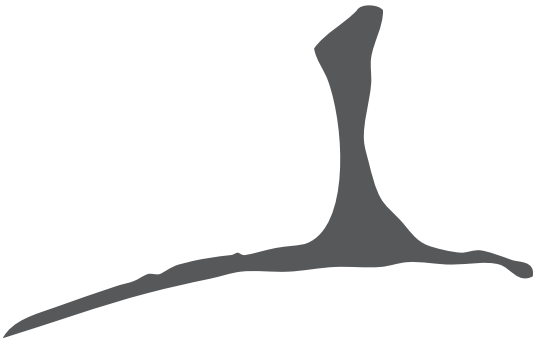
Chapter 6

Motivation behind wishes for treatment in adolescent cleft patients: a qualitative study



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Submitted for publication

Abstract

Introduction: Cleft patients can be diverse and surprising for clinicians in terms of their wish for further treatment. Some adolescent patients do not feel or do not express the urge for further facial corrections for a major nose deviation, whereas other patients do stress the urge for a correction for a minor lip scar. The aim of this study is to reveal the motivations that adolescent cleft patients have when seeking or rejecting treatment.

Method: The grounded theory was applied by means of semi-structured interviews. Thirteen patients with cleft palate, cleft lip, unilateral cleft lip and palate, or bilateral cleft lip and palate, participated.

Results: A flowchart was formulated to illustrate how topics (treatment history; "everybody has something"; presumption of disabilities on the part of others; parental attitude; perceived teasing or gestures) might influence satisfaction through "categories of acceptance" and finally influence considerations as to whether to seek treatment.

Conclusion: The decision to seek treatment seems to be influenced directly by the treatment history, "satisfaction so far" and expectations of further satisfaction, risk of complications, and side effects of the treatment. Personal acceptance and perceived environmental acceptance seem to determine satisfaction. In general, adolescent patients consider themselves unable to decide about further corrections. Therefore, patient follow-up should not stop at age 18 years.

Introduction

In the past few decades more attention has been paid to the psychosocial effects of cleft and cleft care. A major proportion (54%-68%) of children with cleft are unhappy with their facial appearance[1] and teasing by peers is common.[2-4] Dissatisfaction with facial esthetics is related to lower self-esteem,[5, 6] and patients with a cleft are prone to behavioral problems.[7] Dissatisfaction with issues as a consequence of cleft is widely expressed in the literature, as is the wish for further treatment to improve facial appearance.[8] Young adults with a cleft hope to be like other people and not to deviate from the norm, whatever that norm might be.[9] Not only is the patient affected by the cleft, it also impacts on the whole family.[10] Despite all these findings it is also reported that children and adults with a cleft are generally fairly satisfied with their body image and do not show major psychosocial problems.[8]

For many young adolescents, facial appearance is a concern within their social environment,[11] and a common focus of teasing.[12] In adolescence the last phase of cleft treatment is reached, which is that of facial esthetics. Clinically, patients are quite diverse in expressing their urge for improving facial esthetics. Some adolescent patients with a major nose deviation do not feel or do not express the urge for further nasal correction, whereas others with a minor lip scar stress their urge for a correction. For a clinician both scenarios may come as a surprise, and quite often the clinician and patient have different opinions regarding the extent of the facial deformities.[13, 14] In the literature, motivations, explanations, and backgrounds for a wish for treatment receive only sparse mention. Hypotheses and remarks by surgically orientated researchers are mainly aimed at facial appearance in and of itself,[15] while social pressure or emotional instability might also be contributory factors when asking for treatment. Adolescents should be able to make their own decisions for further treatment.[16] So it would be interesting to find what motivates them in their decisions.

Many studies have used questionnaires to quantify satisfaction with function and esthetics, functioning of the affected areas, and the social impact of cleft and cleft treatment.[17-23] These studies link dissatisfaction with function and esthetics in terms of the wish for treatment. Standardized questionnaires have

several benefits such as the ability to measure and compare, but they are generic and may be insensitive to particular issues faced by the individual.[24] Therefore, qualitative studies are needed to capture the subjective impact of living with a disfigurement as a result of a cleft.

The aim of this study was to gain more understanding about the motivation of adolescent cleft patients when making their choices to ask for or reject treatment. Because of the possible wide range of outcomes and the absence of appropriate standardized questionnaires, a qualitative study was our method of choice.

Method

This qualitative study was performed according to the grounded theory first published in 1967 by Glaser and Strauss.[25] In a grounded-theory study, concepts (hypotheses, ideas) are generated from empirical data rather than from the existing literature. The researcher strives to explain the main concern(s) of participants in a specific situation and find out how participants resolve or process this or these main concern(s).[26] The theory is based on the assumption that "all is data." What is of interest will become evident in the process of research and must be verified later with the same participant using questions formulated in a different way about the same topic (triangulation).[9, 25] In addition, the topic must be verified in other participants.[9, 25] The result which emerges is presented either as a hypothesis, as a model, or as an abstract conceptual theory, which is then verified or explored in subsequent sessions of data gathering, preferably along with deviant cases, in order to refine the theory. The theory is built up around a core category and related categories.[26]

Study group

From April 2009 until January 2011, a selection of cleft patients who had the cognitive abilities necessary to be interviewed was sent an invitation for an interview. Initially patients were selected at random from the regularly scheduled consultation roster at our outpatient clinic.The rosters were examined, after which the records of the children between 12 and 20 years were searched for notes of

level of education by the first author, as the cleft team also does a psychosocial evaluation. Notes of very low level of education or verbal expression abilities led to exclusion. On average 2 or 3 children per roster were sent an invitation. Some candidates or parents ignored the invitation letter. These were asked at the desk by the cleft team secretary for ad hoc participation if the interviewer was available. Overall about one third of the candidates agreed to participate. After eight interviews, enough information was gathered to formulate a primary conceptual theory. To refine and complete the theory, deviant cases were then invited. The selection of deviant cases was based on information in the medical files of the patients. First, patients were invited who had those types of cleft which were not well represented so in the first 8 participants as to gather more information about the whole spectrum of types of cleft. After these patients, the files of the next group of possible candidates were searched for discussion between the patient or parents and the practitioner about facial esthetics or surgical corrections. In addition, a history of teasing or psychosocial problems led to an invitation. All participants, and parents in the case of minors, gave their consent. The participants were patients with an isolated cleft palate (CP); isolated cleft lip (CL); unilateral cleft lip, jaw and palate (UCLP); and bilateral cleft lip, jaw

Table 1: Demographics of the participants

Participant	Gender	Age, y	Cleft type
1	F	14	Cleft Palate
2	M	17	Bilateral Cleft Lip, Jaw, and Palate
3	M	13	Unilateral Cleft Lip, Jaw, and Palate
4	F	17	Unilateral Cleft Lip, Jaw, and Palate
5	M	19	Unilateral Cleft Lip, Jaw, and Palate
6	M	15	Bilateral Cleft Lip, Jaw, and Palate
7	M	17	Cleft Palate
8	M	16	Unilateral Cleft Lip, Jaw, and Palate
9	M	14	Incomplete Cleft Lip
10	M	12	Cleft Palate
11	F	18	Bilateral Cleft Lip, Jaw, and Palate
12	M	16	Cleft Palate
13	F	17	Unilateral Cleft Lip, Jaw, and Palate

and palate (BCLP). All patients were of Caucasian descent and had been raised in the north of the Netherlands. The ages ranged from 12 to 19 years of age (Table 1).

Interviews

The interviewer (PH, senior resident otolaryngology, PhD student, special interest in facial esthetics, no prior experience in performing qualitative research) was unknown to the participants and vice versa. The interviews were conducted on the same day, and prior to visiting the consultation room and seeing the cleft team members. Interviews were face to face and audio-recorded after a verbal introduction by the interviewer and an explanation of the intentions and procedures of the interview and study. The interviews were semi-structured, with prescribed open-ended questions regarding the topics. This procedure always resulted in deeper questions subsequently being asked. On several occasions, the questions prescribed for guiding the interviews were modified and adapted to the interim information that had been gathered in the previous interviews. In the first interviews, it became clear that some items, previously thought to be relevant, appeared to be of no relevance to the participants. These items were left out in later interviews. Other items came up frequently in response to the applied questions. These items were then standardly asked in subsequent interviews. The interviews began with questions about age, education, and professional ambitions in order to put the participant at ease and to familiarize the participant with the interviewer. Further items in the interviews were nasal breathing, nasal esthetics, labial esthetics, dental function and esthetics, otologic functioning, speech, and the social-life impact of cleft such as its daily consequences, influence on relationships, and psychosocial involvement. During the interviews, a new item was broached with a question about the degree of satisfaction about that item and why. A subsequent question concerned the wish for an intervention/treatment of any kind that the patient could think of, and why he or she wished for that intervention/treatment. The final version of the interview is translated from Dutch and provided in Appendix A. Once a motivation for an answer was given, this answer was verified later in the interview by means of other questions formulated ad hoc in order to evaluate the consistency of the answers

(triangulation). A mismatch between satisfaction and wish for further treatment was a reason to ask for clarification. Parents were discouraged but allowed to be present; however, they were not allowed to answer any questions from the interviewer or the participant unless specifically requested by the interviewer when it came to concrete information about that portion of the history which the participant was unable to remember. Three participants were interviewed without a parent being present. Most interviews lasted 22-25 minutes. Analysis was performed after two to four interviews in order to have a chance to adapt the questions for subsequent interviews to the interim information and the preliminary model. This procedure continued until data saturation was reached and no additional new information was revealed. The Medical Ethical Committee of the University Medical Center Groningen approved this study.

Analysis

The recordings were transcribed verbatim into text. The first step involved unitizing the information, meaning that the interviews were examined line by line to identify codes of information regarding the same issues, for example, esthetics of nose or lip, teasing, parental influence, or hearing problems. The codes were the result of unitization of information with the same content. The topics were formulated in words used by the respondents themselves. The topics were issues of concern. The essential task of coding and formulating topics concerned bringing together the units of information that were related to the same category.[27, 28] The categories were an assemblage of topics with similarities. Codes, topics, and categories were adjusted or saturated with information from later interviews. A model was formulated, which was then related to all topics and categories identified in the interviews. The eleventh interview did not reveal any new information in terms of the topics or categories, so saturation was considered to be reached. The addition of two more participants confirmed saturation. For some items, dental esthetics for example, saturation was reached earlier. The second author (PD, professor, clinical epidemiologist) studied the model as proposed by the first author and initially textually analyzed four interviews to verify coding, topics, and categories. In the case of disagreement, consensus was reached easily in an open discussion and led to adjustment of

topics, categories, and the model. The discussion entailed whether the statements made by the participants were properly reflected by the model and whether the model covered the content of the statements. As a result of these discussions, more interviews needed to be analyzed by the second author. After the second author had analyzed nine interviews, no disagreements remained.

Results

Thirteen patients volunteered to participate. Among these participants 3 had a CP, 2 a CL, 3 a BCLP, and 5 a UCLP (Table 1). The participants were only able to reflect on treatments and thoughts from recent years for the simple reason that they could not remember what had happened before they were approximately eight years of age. In general, the participants were satisfied with their treatments and the results of their treatments so far. In the end, the deviant cases did not deviate that much. The patient with an incomplete cleft lip (#9) had hardly any problems and could not philosophize about the trouble others might have. The same observation applied to the patient with a cleft palate (#10). The psychosocial and behavioral problems appeared to originate from family break-up (#11), limited cognitive capabilities (#12), or frequent moving and settlement issues (#13). These patients had essentially no other opinions about treatment, so it was considered that data saturation had been reached. The model formulated consisted of five topics which were a composition of the ideas of the participants about factors influencing satisfaction, as expressed in their own words. The topics have influence on either acceptance by the participant him or herself or to perceived acceptance by the environment. Both categories of acceptance together influenced a participant's satisfaction and consideration of treatment, with eventually two possible outcomes (Figure 1). The topics were treatment history, "everybody has something," presumption of disabilities on the part of others, parental attitude, and perceived teasing or gestures. The satisfaction and treatment history were important for the outcome of considering treatment, either seeking treatment or "it is good (enough) as it is." All topics, categories, and levels of satisfaction could be negative or positive. In the following sections, quotations will be written in italics and put in quotation marks.

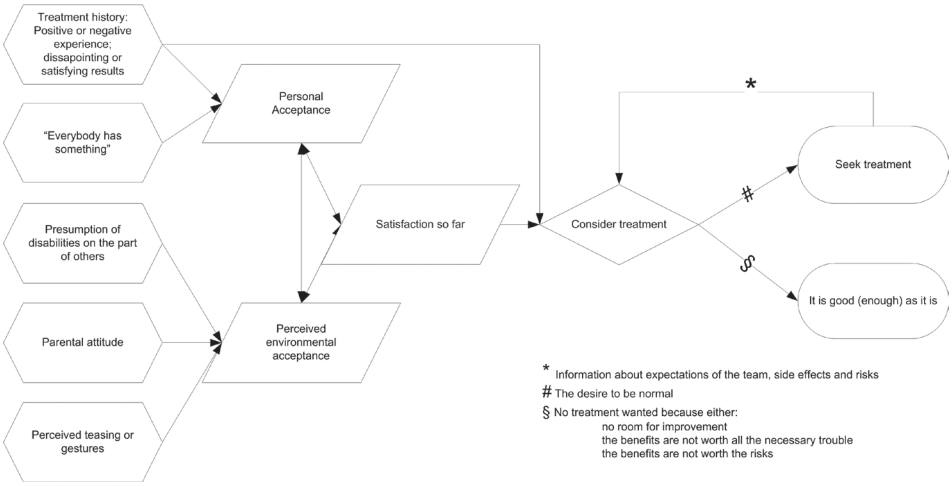

Figure 1: Flowchart illustrating how topics (left column) seem to influence through the categories of acceptance (second left column) and satisfaction, and finally when weighing the decision of whether or not to seek treatment.

Treatment history

Except for the CP and CL patients, all participants were living through or had had a long period of orthodontic treatment often combined with orthodontic and maxillary surgery. In the recollection of the participants this part of their treatment had been the most burdensome. Although they found it worth the burden, they were looking forward to the end of it or were happy to have it completed. With this burden in mind, those participants who were satisfied could therefore just be reluctant to ask for future surgery ("*too much trouble for (too) small an issue.*") Generally speaking, fear of surgery or surgical care was the result of negative experiences in the past and influenced the choice of seeking future treatment.

Girl, age 16, UCLP:
Girl: "*I am fairly satisfied about my nasal breathing … it could be improved.*"
PH: "*What kind of treatment for your nasal breathing would you choose if you could choose?*"
Girl: "*Breathing exercises.*"
PH: "*Why?*"
Girl: "*Because then I don't have to have surgery any more.*"

One particular participant was disappointed about the treatment result from maxillary surgery. For her this was a reason to lose faith in the proposed nasal surgery. This example clearly illustrates the influence of treatment history on personal acceptance as well as on considering treatment.

"Everybody has something"

Most participants felt they looked different from other people. Because they looked different, they received extra attention, not the least because of their frequent hospital visits for consultation, orthodontics, and surgery. This attention frequently led to interested questions and remarks from others, which were then answered by the participants. There were two ways participants could deal with this issue. When they were fed up with answering or with the extra attention, some experienced a growing feeling of being abnormal. On the other hand, when participants could put their cleft into perspective, they stated that this attention was not of any great importance. They realized imperfections of various kinds were present in everybody, including non-cleft people, (*"nobody is perfect"*), or they saw the disfigurement related to their own cleft relative to the (larger) disfigurement of others with a cleft, *"less lucky patients."*

Boy, age 12, CL: *"I think my lip looks fine. I saw some lips that were totally different. Compared to them, my lip is OK."*
Boy, age 15, BCLP: *"What does a cleft mean for me? I had to visit the dentist often and had lots of operations. My speech might be less* (intelligible, PH) *compared to others; that's about it. … It's just the way it is. Everybody has something. …Of course I would prefer not to have a cleft, but it's just the way it is."*

One participant was even proud of the fact that he had to explain why he needed to visit the hospital. He considered this as a compliment to the invisibility of his CL scar. Another participant considered his scars from the UCLP to be status-enhancing and was for that reason proud of his cleft.

Personal acceptance of facial esthetics seemed to be influenced, as compared to the disfigurement of other patients with clefts, by the own perceived

disfigurement and shame, or their own facial appearance on photos before all their treatments.

Boy, age 13, UCLP: "*What do I think of my lip? I think it looks fine. …When I look back at how it was, it looked much worse, but now it looks neat.*"
Girl, age 17, ULCP: "*Having a cleft is who I am. I would be a totally different person without it* (a cleft, PH). …*Maybe I would be less insecure ((starts crying))* …*We moved a few times and it's hard to build up everything all over again* (social life, PH) …*Sometimes I see people looking at me; even that hurts.*"

Presumption of disabilities on the part of others

Participants acknowledged other peoples' thoughts about their appearance and function. The opinion of the cleft team was mentioned as only a minor factor in their satisfaction with any topic. They were aware that some people might link their appearance to presumed functional disabilities, even though they did not experience any disability themselves. Most participants let their own thoughts about disabilities dominate over thoughts in their environment surrounding a presumed disability. However, some participants were convinced that other people presumed they had disabilities, which might influence their career opportunities. Sometimes it was just an unexplainable belief on the part of the participants.

Boy, age 15, BLCP: "*I am a little dissatisfied about my nose. …I would prefer surgery before I go to be tested for military service* (in 3 weeks from the interview, PH). …*I don't think my nose will have any influence on doing the military job, but I'm not sure about the military testing.*

Parental attitude

The parents influenced the participants through their support. According to the participants parental attitude varied from "*They want what I want,*" "*It's as good as it can be,*" and letting the participant feel free about what to do, to "*It can always be improved,*" which might give the participant the feeling that things needed to be improved.

Perceived teasing, remarks, or provocative gestures

Some participants were subjected to (perceived) teasing, remarks, or provocative gestures, and sometimes started a fight over it. Three boys had had frequent fights, but had quit doing so. These boys brought up the moment they accepted that every person had some kind of imperfection; they were then able to ignore the teasing, and then the teasing stopped.

Man, age 19, UCLP: "*It's how you deal with teasing. If you react, it will never stop. It's caused lots of trouble. …It stopped* (fighting, PH) *after I turned 15 or 16. It made me three times wiser* (than I would have been without cleft, PH)."

Satisfaction so far

Personal acceptance and perceived environmental acceptance seem to be the two contributing categories for determining satisfaction. Both categories of acceptance can increase or decrease satisfaction, depending on the weight given to them by the participant, and indirectly depending on the given weight and content of the topics mentioned above. "Satisfaction so far" seemed to be a decisive category when considering treatment.

Considering treatment with two possible outcomes: It is good (enough) as it is or seek treatment

In the end participants decided whether they found further treatment not worth the trouble and expressed that how they were was good (enough) or, if they wanted improvement in esthetics or function, they would seek treatment. Satisfaction and the recollection of their treatment history, both the positive and negative aspects, were weighed against each other. This implies that all participants recognized their cleft, but not all considered the cleft as a problem big enough to seek treatment. Information about side effects, risks of complications, effort, and expectations was obtained when a participant considered treatment. This extra information made the participants reconsider treatment and renounce further requests, or the opposite, stimulated them to seek further treatment.

Boy, age 15, UCLP: "*I can always get my nose pointier, but I won't. It's good enough now. . . . I'm satisfied with the way I look now. What if it* (surgery, PH) *goes wrong or it* (the results, PH) *is not exactly as I expected? It's just fine.*"

Dissatisfied participants were focused on the expected (approximation of) normal appearance and the accompanying better life, and downplayed the risks of complications and the unpleasant period of hospitalization and discomfort.

Overarching aspects

Only a minority was dissatisfied with several aspects of their cleft. The major concern of all participants was the wish to be "normal," expressed in terms of several aspects. The general answer to the question, "If you wished for improvement for your nose/lip/teeth, etc., what would it be?" was "*It should look more normal,*" or "*More like everybody else,*" or "*Nothing, my scar is hardly visible.*" It was remarkable that hardly any concrete change in anatomy or function was mentioned as a wish. Sometimes personal characteristics were mentioned as the underlying drive for a wish for treatment.

Girl, age 17, BCLP: "*When my nose is corrected and becomes less obvious, I will be stared at less often and will become less insecure.*"

All participants denied any influence from partners and close friends when it came to their wish for treatment. The participants claimed that their friends would not be their friends if they did not accept them as the persons they were.

Decision-making

Apparently the participants were insecure about making major decisions. When asked about the timing of potential surgery – "Would you prefer surgery to improve your esthetics before age 15, between 15 and 18, or later?" – several participants answered that they would postpone surgery to adulthood. The main reasons were that they had gone through enough in the recent past and that they considered that they would be more capable of making the right decision when

they were grown up. Some wanted to wait because they did not want to miss any more school time.

Boy, age 14, CL: *"Surgery can wait until I'm 16, 17, or 18, I think. . . .Getting older . . .just being more mature; I can't exactly say why."*

Discussion

The motivation behind seeking treatment is the result of weighing several factors on imaginary scales. In this process, at least for our participants, "satisfaction so far," treatment history and side effects of treatment, and expectations are taken into account. Every participant placed some weight in both scales. Even the most satisfied participants acknowledged some burden because of their cleft, but overall these participants were not suffering. The input from the cleft team as perceived and reported by the participants was relatively small. Most of the time the wish for possible treatment was already formed before information from the cleft team was obtained. Information they had received up until then was mainly from their parents, since the cleft team mainly informs parents rather than patients.[9] Parental attitude seemed to be important in this matter, because their attitude seemed to determine to what extent, which, and how information was given to the participants. In general it is unknown whether parents transfer the information completely, partially, or in a distorted way.[22] Moreover, the child and parents act as a dyad. Interviewing dyads, as well as seeing them as one practitioner, presents its own problems, as in this case where the dyad presents neither solely the parent's nor solely the child's version of thinking.[29] In our study, participants and parents seem to agree on most aspects as claimed by the participants when asked specifically for. This agreement was on concerning concrete terms and terms where a judgment was required, When interviewing parents and patients separately, on the other hand, little agreement has been reported between parents and children regarding satisfaction with facial appearance[8] or psychosocial issues requiring judgment.[30] Most parents wanted to be present during the interview or the participants wanted them to be present. This could have influenced the expressed opinions of the participants, despite the fact that parents did not answer questions. Sometimes, however, they gave nonverbal reactions and in that way may have influenced the outcomes of the interviews.

The major concern of the participants was the wish to be "normal," expressed in terms of several aspects. The general answer to the question "If you wished for improvement for your nose/lip/teeth, etc., what would it be?" was "It

should look more normal" or *"More like everybody else."* This type of answer was heard remarkably more often than any wish for a concrete change in anatomy or function. Sometimes a deeper emotional problem such as feelings of depression or being insecure was the motivation for the wish for an approximation of the participant's norm. This finding is congruent with findings in adult cleft patients.[9] However, many adult patients do ask for treatment,[13] while most of our adolescent participants did not ask for treatment. In our model, partners and friends are not mentioned as influencing factors, because the participants clearly claimed friends and relationships had no influence, none at all. On the other hand, it is hard to imagine that adolescents would not be susceptible to peer influence,[31, 32] although our participants stated that this was so. Anyhow, when asked about this in the consultancy room, the cleft patient might deny, as our participants did, the influence of friends. Hence, we did not take peer influence into account in our model.

Our participants, except for the case of the isolated CL and CP patients, had just completed or were about to finish an intensive period of maxillary and orthodontic treatment. They claimed to have a need for a pause in treatment, since the maxillary and orthodontic treatment was experienced as very burdensome.

Our participants were not talkative, which might be expected of adolescents. As a matter of fact they were extremely brief in their answers, for example, "*yes*," "*no*," "*just because*," or "*I don't know*," and did not on their own initiate any move to explain the motivation behind their answers. But when asked, they tried to explain the motivations behind their answers. Qualitative research with semi-structured interviews turned out to be the right choice of research method, despite these limitations. Questionnaires with closed or open-ended questions were unlikely to reveal underlying motivations and thoughts based on the experiences from the interviews. Moreover, during the study our focus shifted from topics concerning function and esthetics, initially thought to be the main concern, to topics concerning social impact and acceptance related to esthetics. The downside of interviewing participants who were nonchalant or pretending to be nonchalant was the phenomenon that sometimes several questions from the interviewer were needed in order to reveal their underlying thoughts. Sometimes the interviewer was unable to uncover their underlying

thoughts despite repeated and reformulated questions. Participants of this age might be ashamed to answer certain topics, especially children with an orofacial cleft.[33] Maybe they do not have the capacity for introspection as yet and are not able to formulate answers, as is often normal for adolescents.[34] Some participants did not have any problem, so asking them about problems resulted, naturally, in extremely short answers.

This study has several limitations. In general, one limitation of interviewing can be that the interviewer may tend to guide the participant towards the wished answers. The second author did not notice this having been occurred when reading over the interviews. A second limitation could have been the interviewer going on to the next topic too early before relevant answers were obtained. In retrospect this might have happened a few times, because of a dearth of answers. Nevertheless, to a large extent most of the background and the thoughts underlying the answers came to the surface, and data saturation was reached. The brevity of the answers was a main contributor to the rather brief length of the interviews. The interviewer's inexperience with qualitative research could also be contributing to this brevity. Our patient selection might have introduced a bias, however just a few candidates were considered not eligible for an interview. The portion of patients which volunteered to participate could be of more importance. It is imaginable that merely satisfied patients and parents cooperated and that we interviewed only patients who wished to keep things the way they are. Motivations for surgery might have been obscured in this way. The patient selection of deviant cases was made on the basis of the records. This procedure relies on precise documentation of the clinicians. It could be that we missed deviant cases because of a lack of documentation. However, it can be assumed that clear dissatisfaction or psychosocial trouble are noticed by the cleft team and noted in the patient records.

The emphasis in cleft care on facial esthetics during adolescence is comprehensible, but this study suggests that it is not always appropriately timed. Based on our experience it is questionable whether adolescents are able or willing to make major decisions about facial esthetics, although they should be able to.[16, 35] The burdensome treatment recently experienced also plays a role; as a result, our

participants tended towards "its good (enough)." Cleft patient follow-up is regular up until the age of 18 years, but many participants seemed unready for any final decisions. For this reason, follow-up should not stop at the age of 18 years. It would seem reasonable to see cleft patients once again in their twenties or at least to keep the door open for consultation occasionally in order to discuss any change in wishes.

This study used a selected category of patients from one cleft team in one region of the Netherlands. It could be interesting to know whether these findings could be verified, complemented, or contested in other regions of the country or the continent in order to discover any center effects or regional cultural effects. In addition, it would be interesting to know whether these findings change with age; young adults in their twenties could be a subject of study in this regard. Furthermore, the results might have been different if the parents would not have been allowed to be present. The same study without parents would be of interest. The strength of a qualitative study lies in describing a range of possible thoughts and backgrounds, but it cannot properly describe the quantity of the findings. This proposed model might be a guide for a questionnaire as an instrument to perform a quantitative study and learn more about, for example, the extent of parental pressure or the degree of burden from previous treatment.

Conclusion

The decision to seek treatment seems to be influenced directly by the treatment history, by "satisfaction so far" and expectations, by risk of complications, and by side effects from the treatment. Personal acceptance and perceived environmental acceptance could determine satisfaction. These categories of acceptance could be influenced by several topics. The main concern of the participants seems to be the wish to become normal, despite the fact that they are not concrete in their definition of normal. Interviewing adolescents to find a foundation for their wishes or concerns is challenging due to their short answers and lack of initiative in terms of elaborating their answers to questions.

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Appendix A:
Final version of the interview guide translated from Dutch.

- Q1: First I would like to know who you are:
  - What is your age?
  - What kind of education do you follow?
  - What would you like to become after your education? Why?

- Q2: How satisfied are you about your nasal breathing?
  - Why is that?
  - Do you usually breath through your mouth or nose?
    - How do you feel about that?
  - What do you think others think about your nasal breathing?
    - Do you receive remarks? From who?
    - Can you imagine why they make remarks?
    - How do you feel about those remarks?
  - Are there things you would like to do more often, but you do not because of your nasal breathing? Why is that?
  - What do you think about the treatments you had for your nasal breathing?
    - Do you wish the treatment would have been different? Why is that?
  - Have you thought about other kinds of treatments?
    - Why is that?
    - What do you expect from those treatments?
  - Do you think your parents have thought about other or more treatments for your nasal breathing?
    - How do you think about that?

- Q3: How satisfied are you about the looks of your nose?
  - Why is that?
  - What do you think others think about the looks of your nose?
    - Do you receive remarks? From who?
    - Can you imagine why they make remarks?
    - How do you feel about those remarks?
  - Are there things you would like to do more often, but you do not because of the looks of your nose? Why is that?
  - What do you think about the treatments you had for the looks of your nose?
    - Do you wish the treatment would have been different? Why is that?
  - Have you thought about other kinds of treatments?
    - Why is that?
    - What do you expect from those treatments?

- Do you think your parents have thought about other or more treatments for the looks of your nose?
  - How do you think about that?
- What if an operation could make your nose better? Have you thought about that?
  - What would you like to have changed? Why is that?
  - *(12 – 15 years of age)* Would you like to have that operation now or would you like to wait until you are 17 years old? Why is that?
  - *(16-18 years of age)* Would you like to have had that surgery before you were 15 years of age, or is now early enough? Why is that?
  - Do you think your parents would like you to be operated upon for your nose? Why is that?

- Q4: How satisfied are you about your speech?
  - Why is that?
  - What do you think others think about your speech?
    - Do you receive remarks? From who?
    - Can you imagine why they make remarks?
    - How do you feel about those remarks?
  - Are there things you would like to do more often, but you do not because of your speech? Why is that?
  - What do you think about the treatments you had for your speech?
    - Have you had speech therapy? Do you know for how long? What think about that?
    - Do you wish the treatment would have been different? Why is that?
  - Have you thought about other kinds of treatments?
    - Why is that?
    - What do you expect from those treatments?
  - Do you think your parents have thought about other or more treatments for your speech?
    - What kind of treatments?
    - How do you think about that?

- Q5: How satisfied are you about your lip?
  - Why is that?
  - What do you think others think about your lip?
    - Do you receive remarks? From who?
    - Can you imagine why they make remarks?
    - How do you feel about those remarks?
  - Are there things you would like to do more often, but you do not because of your lip? Why is that?
  - What do you think about the treatments you had for your lip?
    - Do you wish the treatment would have been different? Why is that?

- Have you thought about other kinds of treatments?
  - Why is that?
  - What do you expect from those treatments?
- Do you think your parents have thought about other or more treatments for your lip?
  - What kind of treatments?
  - How do you think about that?

- Q6: How satisfied are you about your set of teeth?
  - Why is that?
  - What do you think others think about your set of teeth?
    - Do you receive remarks? From who?
    - Can you imagine why they make remarks?
    - How do you feel about those remarks?
  - Are there things you would like to do more often, but you do not because of your set of teeth? Why is that?
  - What do you think about the treatments you had for your set of teeth?
    - Do you wish the treatment would have been different? Why is that?
  - Have you thought about other kinds of treatments?
    - Why is that?
    - What do you expect from those treatments?
  - Do you think your parents have thought about other or more treatments for your set of teeth?
    - What kind of treatments?
    - How do you think about that?

- Q7: Have you had troubles with your ears?
  - Can you explain what you have had with your ears?
  - How do you think about that?

- Q8: Almost the last questions; What does it mean for you to have a cleft?
  - Why is that?
  - Do you think your cleft makes a difference for having friends? Why is that?
  - Do you think your cleft makes a difference for choosing a profession? Why is that?
  - Do you think your cleft makes a difference to others? Why is that?
  - Do you think your cleft makes a difference for choosing your education? Why is that?
  - Do you think your cleft makes a difference for having /getting a boy-, or girlfriend? Why is that?
  - Do you think it matters to your parents you have a cleft? Why is that?
  - Do you think they have thought about that differently when you were just born?
  - I have heard or read about research results that other patients with a cleft do not like to have a cleft. And usually they say that they disliked it the most when they were about your age. Can you help me to understand why they say that? How would you explain that?

- Have you been mad or sad or happy because you have a cleft? Why is that?
- Have there been people who have been doing stupid about your cleft?
  - How did you react?
  - What happened further?
  - Can you imagine why they did stupid? How do you feel about that?
- Do you think you are like other people or are you different from them ? Why is that?
- Have you changed your thoughts about your cleft in the last years? Why is that and what has been that change?

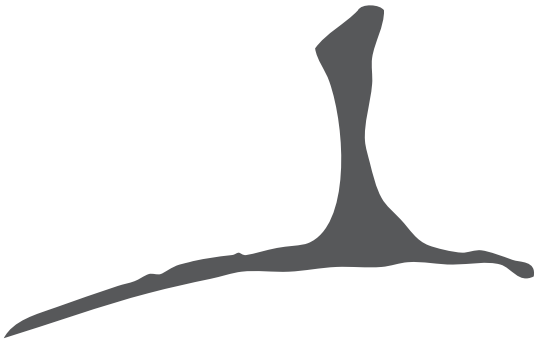
- Q9: We just have discussed many items concerning your cleft. Which item is the most important item for you? If you can not remember, we spoke about nasal breathing, the looks of your nose, your speech, your lip, your set of teeth, your ears and what your cleft means for you. You may also mention another item/ topic if that's the most important for you.
  - Why do you choose that one?

- Q10: Which part of all your treatments did you dislike most? Why is that?

- Q11: Which advice would give the cleft team? Why is that?

Chapter 7

Summary and Conclusions



This thesis described how we investigated several aspects of the care for a patient with a cleft. The investigated aspects became subject of research because of (new) developments in the literature or discussion in our cleft team which was not answered with available or existing evidence or information from other teams. The aim of the studies was to affirm or to improve our existing protocol with the information and evidence being found and to supply evidence in the literature for improved cleft care.

Some adolescent patients request for a surgical correction of their nose for improved function and esthetics. The deviation and functional handicap are sometimes evident and striking. Nevertheless, the request is not granted automatically, because of the possible affection of the growth of the face by surgery nasal surgery. Scars and others lesions might disturb facial growth,[1, 2] and growth can disturb the results of surgery. As a rule rhinoplasty is postponed until the face has ceased growing. However, it is not clear when a face stops growing. For this reason a systematic review was performed which was described in **Chapter 2**. The literature was searched for studies which described measured facial growth of white adolescents aged 12 to 18 years at least biannually. Four studies[3-6] met our inclusion criteria. The data from these studies were analysed and uniformed to have the opportunity to compare. With the uniformed data the velocity of growth could be plotted as a function of age. To define the end of growth, the fact that the nose never stops growing had to be encountered.[5, 7-9] Therefore a definition for facial maturation was set as the age with the steepest descending slope in the growth velocity curve. This definition was applied to the growth velocity curves. Following the definition and the curves it was stated that 98% of the girls are mature regarding facial growth at the age of 16 years. For boys it was stated that 98% are mature regarding facial growth at the age of 17 years. These statements suggest that rhinoseptoplasty is safe after these ages for almost the whole population of white adolescents without craniofacial malformations. The patients in the studied population of this systematic literature review were without cleft. This is important when our findings would be applied to patients with a cleft, because patients with a cleft are likely to have a different growth pattern.[10, 11] Furthermore half of the girls are facially mature at the age of 13.4 years and half of the boys at the age of 14.7 years. According to our definition

many individuals are full-grown earlier than 16 or 17 years of age and could have earlier rhinoseptoplasty.

Rhinoseptoplasty to improve esthetics and function of the nose is a challenge and sometimes frustrating for patients with a cleft and their practitioners. In the case of unilateral cleft lip and palate (UCLP) the maxillary jaw and ala are usually retracted on the cleft side resulting in an asymmetric nose. In the case of bilateral cleft lip and palate (BCLP) both sides of the maxilla are retracted resulting in a flattened, short nose. Surgical correction of the nose in both types of cleft should be postponed until facial growth has ceased (Chapter 2). However, the difficulty in rhinoplasty during or after adolescence is the adopted configuration of the cartilage with the tendency of relapse after reshaping the cartilage. Nasoalveolar molding (NAM) is the molding of the nasal cartilage in a more normal position and shape during the first months of life. The aim is a symmetric normal nose. Ideally a rhinoplasty later in life would not be necessary. NAM has had a quick and promising rise which is still going on. The founders and followers who publish the results of NAM are enthusiastic about the results.[12-16] On the other hand many cleft teams do not implement NAM in their protocol.[17] Up to the present no randomised controlled trial about the effect of NAM is published[16] and no meta-analysis of the literature is available. **Chapter 3** described our systematic review of the literature with the intention of a meta-analysis. The aim was to quantify the effect of NAM on the symmetry of the nose in patients with a UCLP. The evidence of the effect of NAM seemed still not solid. Despite an extensive search of the literature no study could be found with a GRADE level[18] above Low (range High, Moderate, Low, Very Low). Fourteen studies met our inclusion criteria. No meta-analysis could be performed because of inadequate reporting of data and heterogeneity of the study designs and outcome variables. Heterogeneity prevents the pooling of results to compare or to calculate effect sizes. Furthermore, the results of analysed studies were inconsistent about improvement of their measures and deducted nasal symmetry. However, every analysed study was unique in research protocol and treatment protocol, so besides a meta-analysis it was even difficult to formulate conclusions from descriptive comparison. In conclusion, NAM could be beneficial in achieving nasal symmetry in unilateral cleft patients, however the evidence is limited. Recommendations for conduction

of future research were provided to construct a consensus for evaluating the effect of NAM. Time has come for a randomised controlled trial to deny or verify the positive opinion of NAM in the literature.

Patients with a cleft palate are prone to velopharyngeal insufficiency (VPI), with hypernasality as a consequence. Speech has a critical learning period until the age of 6 years.[19] The conditions for proper speech should be adequate and therefore VPI should be treated before this age. The most applied treatment for VPI is a pharyngeal flap. Besides audible examination, multiple instruments are important for the quantification of hypernasality and the indication of pharyngeal flap surgery, like multiview videofluoroscopy, nasoendoscopy and nasometry.[20] For some the nasometer is considered the golden standard.[21, 22] The nasometer is a combination of headgear, computer and analysing software. Nasal and oral sound production are measured during speech by two microphones separated by a plate on the upper lip of the speaker. The outcome is the nasal proportion (%) of the total sound energy. In our practise we frequently experienced reluctant children when we tried to obtain objective nasality values with the nasometer. No reports concerning cooperation of young children could be found in the literature. Moreover, in studies about nasometry with young children it is sometimes indicated that authors do not have results of all included children. However, it is not mentioned why these results are missing. Therefore we studied the cooperation of 118 children recruited from schools and 41 children from our outpatient clinic. All children were aged 4, 5 or 6 years. We aimed to set a minimal age at which reliable results could be obtained with the nasometer. In our study, the younger the child was, the more unwilling the child was to cooperate with the examination with the nasometer (**Chapter 4**). Furthermore children recruited from school cooperated better than outpatient clinic children did, while the latter are the children of our clinical concern. In the 4 years old children the cooperation was mostly insufficient. Most 6 years old children showed good cooperation. In children aged 5 years, cooperation depended on the setting. About 50% of the 5 years old outpatient clinic children cooperated. This age was set as the minimum age worth to try the nasometer in clinical practise. This implicates that many of the possible candidates for pharyngeal flap are not to be tested, because many of them are younger than 5 years of age.

Other objective instruments should be considered if an objective measure of hypernasality is warranted, despite their invasive (nasoendoscopy) or potential harmful character (multiview videofluoroscopy). The other option is to rely solely on visual examination of the velum mobility and audible examination.
The outcome of any instrument in the indication of a treatment is preferably distinctive. Therefore it is wishful that the outcome of the nasometer would be 'go' or 'no-go'. Normative data for the nasometer for young Dutch children are lacking. A nasality value obtained with the nasometer is not to be interpreted without normative data. For this reason the nasality values of healthy children aged 4 to 6 years were collected. The children were recruited from elementary schools. They were the cooperative children from the study described in chapter 4. The children were asked to repeat standardized oral and oronasal text passages. In **chapter 5** the obtained values were categorised per age and set as normative data for Dutch children aged 4 to 6 years. Nasality was not related to age. To capture 95% of the normal scores in the normative data, 2 standard deviations were subtracted from or added to the mean. This resulted in a wide range of normal values. The normal ranges of oral and oronasal passages overlap. The ranges of normal nasality values are 3-19% for the oral passage and 17-37% for the oronasal passage. The wide range of normal values has the disadvantage of being not distinctive. For example, a patient with a cleft could show a high-normal value when testing him, but it is not known whether this is the true value of the patient or if it would be lower when the patient would not have had a cleft. The latter would mean that the obtained value is abnormal despite that the value is in the normal range. This means that the nasometer definitely does not distinguish between 'go' or 'no-go'. For this reason the results from the nasometer should be combined with other examinations in the indication of VPI treatment of individuals. The nasometer does seem suitable for the evaluation of hypernasality treatment on group level, because mean intra-individual changes between the preoperative and postoperative situation can be measured.

A patient with a cleft has to endure lots of treatments, but also might have additional desires which are not according to the treatment protocol. Some desires are dubious, because they could have adverse effects or not solve the problem the patient faces. The practitioner and patient with or without parents

might disagree about the appropriate treatment for a particular issue like facial esthetics or functional disabilities. The disagreement can be both ways. For example, the patient desires a correction of a scar of the lip, while the surgeon does not see any possibility for improvement. Or the surgeon observes a deviated nose and proposes a correction, but the patient denies any trouble with function, esthetics or teasing. Hence, it might be interesting to know how patients with a cleft are moved to the motivation for treatment or to the reluctant attitude to treatment. **Chapter 6** describes our qualitative study following the rules of the grounded theory[23] about the motivations behind a possible wish for treatment. We interviewed 13 adolescent patients with various types of cleft. We asked them how satisfied they were with several aspects of their treatment, and subsequently why. Other questions were about whether they considered seeking treatment, and subsequently why or why not. It was found that both the acceptance by the patient self as the acceptance of the environment as perceived by the patient were the main contributors to the satisfaction with the situation. Together with the experiences and results from the earlier treatments, the satisfaction seemed to determine the outcome of the consideration whether to seek treatment or not. The basic motivation to seek treatment turned out to be a desire to be as normal as possible. The main reasons for not asking for treatment were the opinions that there was no room for improvement, the benefits would not be worth the necessary trouble and the benefits would not be worth the risks. Furthermore many participants liked to postpone their thoughts of further treatment until they would be grown up and become capable of making the right decision. The latter suggests that many patients are not ready for final decisions. All together it was concluded that adolescent patients with a cleft had much to endure and might need a pause of treatment. In addition it was concluded that they might consider themselves not capable of making major decisions. Hence, follow-up should not stop at the age of 18 years. It is recommendable to see cleft patients at least once in their twenties to discuss possible changes in wishes for treatment.

Future research and perspectives

The formulation of answers to some questions from daily practise will not be complete without further research and will lead to subsequent questions. The found ages of facial maturation in chapter 2 are, as said above, applicable to a population without facial malformations, while patients with a cleft could have another facial growth pattern. Difficulty in analysing facial growth of cleft patients is caused by other growth disturbing factors like multiple surgical interventions of the lip, palate and jaw. An impression of a not influenced growth pattern could be obtained from unoperated adolescent cleft patients in for example developing countries. For an individual advice we should be able to predict or ascertain facial maturation of the individual patient we face in our clinic. So it would be interesting and helpful if future research would aim at the ages of maturation of different body parts in relation to each other. Different parts of a human body have different growth patterns as the growth spurt of feet is earlier than the torso. If facial maturation is preceded by for example leg maturation, we could predict the facial maturation by studying easy measurable leg length.

In chapter 3 the lack of evidence of the effect of NAM on nasal symmetry is concluded. Besides that there is an inadequacy of reporting of results. Despite all the disadvantages it seems time to perform a randomised controlled trial.

The nasometer was subject of research because of our experienced trouble in the execution of determining the degree of VPI in young children. The limitations of the nasometer are described in chapter 4 and 5 and indicate a desire for other instruments to measure VPI. It can be proposed that the evaluation of the end result of treating VPI should be subjective, that is a normal speech in the perspective of the patient and peers. Future studies might aim at the additional value of objective instruments compared to subjective instruments.

Qualitative research has many benefits as described in chapter 6. On the other hand qualitative research has disadvantages like the possibility of being subject to a distorted perception or interpretation of the interviews. Before solid conclusions can be drawn from chapter 6, the results should be proven to be reproducible by future research, preferably qualitative and quantitative. An important factor of possible influence in our study could be the presence of the parents during the interviews. A subsequent qualitative study with the same population, but without

parents would be very interesting for the reproducibility and the influence of the parents on the expressed opinions of the participants.

Above all is the observation of heterogeneity of the treatment protocols from different cleft teams. These differences might be caused by a lack of convincing evidence. However, heterogeneity of treatment protocols prevents the possibility of comparable research results and subsequently solid evidence. Chapter 3 can be seen as an example of the lack of consensus of performing and reporting research concerning cleft. There is a need for unified research and database building in order to achieve comparable research and protocols based on evidence in stead of experience.

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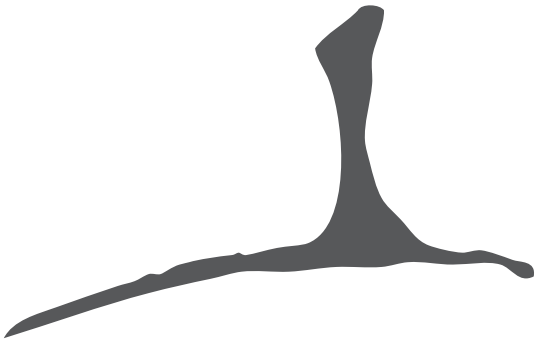
Chapter 8

Nederlandse samenvatting



Bij een medisch specialist, die patiënten met een schisis behandelt, komen regelmatig vraagstukken, dilemma's en nieuwe ontwikkelingen aan de orde waarvan het nog niet duidelijk is hoe daar mee omgegaan moet worden. Dit proefschrift beschrijft enkele veel voorkomende vragen uit de praktijk en hoe deze door middel van eigen onderzoek uitgewerkt zijn.

Een veel voorkomende vraag van patiënten met een schisis is correctie van een afwijkende vorm van de neus om cosmetische en functionele reden. De vraag kan al vroeg in de puberteit komen, hoewel op dat moment nog niet overgegaan kan worden tot chirurgische behandeling (rhinoplastiek) vanwege de groei van het aangezicht. De groei kan het resultaat van een chirurgie verstoren en chirurgie kan door de verdere groei van het middelste horizontale deel van het gezicht verstoren. Daarom zou een rhinoplastiek uitgesteld moeten worden tot het moment dat de groei van het aangezicht gestopt is. Het is echter niet helemaal duidelijk wanneer dat het geval is. Daarom is een systematische literatuurstudie uitgevoerd om deze vraag te beantwoorden (**Hoofdstuk 2**). Vier studies voldeden uiteindelijk aan onze inclusiecriteria van metingen van het aangezicht van gezonde personen van 12 tot 18 jaar. De metingen zijn geanalyseerd en geüniformeerd. Er diende rekening gehouden te worden met het feit dat het gezicht nooit stopt met groeien tot in de verre ouderdom, dus er moest een definitie van een volwassen gezicht worden opgesteld. Volgens de door ons gestelde definitie en analyse is het skelet van het aangezicht van 98% van de jongens volwassen op 17 jarige leeftijd. Voor meisjes geldt dat 98% op 16 jarige een uitgegroeid skelet van het gezicht heeft. Bij de vertaling naar de praktijk moet rekening gehouden worden met de gebruikte populatie van gezonde personen. Patiënten met een schisis zouden een ander groeipatroon kunnen hebben. Daarnaast moet worden opgemerkt dat de gestelde definitie 98% van de populatie dekt. Individueel kan een uitgegroeid skelet van het gezicht eerder bereikt zijn, te weten dat jongens dat gemiddeld bereikt hebben op 14,7 jarige leeftijd en meiden op 13,4 jarige leeftijd.

Een rhinoplastiek (neusoperatie) bij een patiënt met schisis kan uitdagend zijn en de resultaten soms teleurstellend vanwege de vorm en slechte kwaliteit van het kraakbeen in de neus. In de eerste weken van het leven is kraakbeen nog vervormbaar door hormonale invloed van de moeder rond de bevalling. Een

nieuwe veelbelovende ontwikkeling is nasoalveolaire molding (NAM). NAM maakt gebruik van de vervormbaarheid van het kraakbeen direct na de geboorte. Deze zogenoemde prechirurgische orthodontie brengt de neus van de baby in een meer symmetrische vorm met als doel een blijvende symmetrische neus te bereiken om een rhinoplastiek te voorkomen. De pioniers van NAM en volgers die hierover publiceren zijn in het algemeen lovend over het resultaat, maar toch wordt lang niet in iedere praktijk deze techniek toegepast. Tot op heden is geen meta-analyse of trial verricht over NAM. **Hoofdstuk 3** beschrijft een systematische literatuurstudie met de intentie van een meta-analyse om het effect van NAM op de symmetrie van de neus te toetsen. Er werden 14 studies geïncludeerd volgens onze inclusiecriteria. Al deze studies waren van 'Low' of 'Very low' kwaliteit volgens de GRADE kwalificatie. Een meta-analyse kon niet worden uitgevoerd door inadequate rapportage van de data en de grote heterogeniteit van studieopzetten en uitkomstvariabelen. De heterogeniteit voorkomt de mogelijkheid van datapooling en -uniformering, zodat niet onderling vergeleken of 'effect size' berekend kan worden. De resultaten van de studies waren eveneens verschillend over het effect van de interventies. Verder was iedere studie uniek in studieopzet en behandelprotocol. Daarom was het onmogelijk om een meta-analyse te verrichten en zelfs moeilijk om op een beschrijvende wijze conclusies te trekken over het effect van NAM. Concluderend was er te weinig bewijs om over het effect van NAM op de symmetrie van de neus te kunnen oordelen. Er werden suggesties voor toekomstig onderzoek gedaan om wel tot bewijskrachtige resultaten te kunnen komen.

Patiënten met een schisis van het gehemelte hebben een grote kans op velopharyngeale insufficiëntie (VPI) met hypernasaliteit (teveel geluid via de neus bij spreken) als gevolg. Idealiter wordt de mate van hypernasaliteit uitgedrukt in een getal om de ernst te kunnen bepalen. Er zijn verschillende methoden om hypernasaliteit te beoordelen, waarvan de nasometer er een is met de mogelijkheid tot kwantificering in getal. De nasometer berekent het percentage geluid dat via de neus naar buiten komt bij spreken. Het teveel aan geluid via de neus zou gecorrigeerd moeten worden. Idealiter worden spraakproblemen voor het 7^{e} levensjaar behandeld om te voorkomen dat afwijkende spraakpatronen neurologisch ingeprent raken. De nasometer moet dus bij jonge kinderen

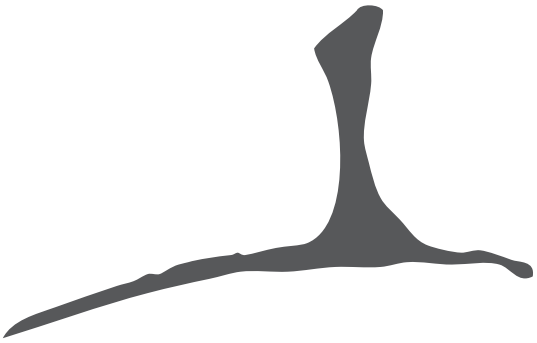
gebruikt worden om de mate van hypernasaliteit vast te stellen. In de praktijk blijken veel jonge kinderen niet mee te werken met de nasometer, ondanks het niet-invasieve karakter. Om een minimumleeftijd voor het gebruik van de nasometer te kunnen stellen zijn 118 gezonde schoolkinderen en 41 kinderen die de polikliniek KNO van het UMCG bezochten van 4 tot en met 6 jaar oud getest met de nasometer op coöperatie. (**Hoofdstuk 4**). Het bleek dat jongere kinderen minder goed meewerkten dan ouderen en de kinderen op scholen werkten beter mee dan de kinderen op de polikliniek. De 4 jarige kinderen waren merendeels niet coöperatief. De meeste 6 jarige kinderen werkten goed mee. Bij de 5 jarige kinderen verschilde dat, namelijk de schoolkinderen deden beter mee dan de kinderen op de polikliniek. Van de laatsten werkten 50% mee. Daarom is 5 jaar gesteld als de minimum leeftijd om de nasometer te gebruiken op de polikliniek, vanwege de kans op succes. Andere methoden om hypernasaliteit te beoordelen zullen moeten worden overwogen als een objectief oordeel gewenst is.

Testen met een instrument als de nasometer kunnen behulpzaam zijn in de indicatiestelling voor een behandeling. Idealiter vertelt de uitslag van de test of de behandeling uitgevoerd zou moeten worden of niet. In het geval van hypernasaliteit waren normwaarden voor Nederlandse jonge kinderen niet bestaand. Zonder normwaarden is een verkregen waarde van de test niet te interpreteren. Daarom zijn de nasaliteitswaarden verzameld van 4 tot en met 6 jarige gezonde kinderen, gecategoriseerd per leeftijd en gesteld als normwaarden (**Hoofdstuk 5**). De kinderen zijn gerekruteerd op basisscholen en waren de gezonde coöperatieve kinderen uit hoofdstuk 4. Zij werden gevraagd om oronasale en nasale teksten na te zeggen, die werden opgenomen en verwerkt door de nasometer. Om normaalwaarden te kunnen stellen waarin 95% van de populatie wordt vertegenwoordigd, werden 2 standaard deviaties van de gemiddelde waarde afgetrokken en bij op geteld. De gestelde normaalwaarden van de oronasale teksten en nasale teksten overlapten elkaar. Deze lagen namelijk tussen de 3 en 19% in het geval van de nasale teksten en van de oronasale teksten tussen de 17 en 37%. Met deze grote spreiding van normaalwaarden met overlapping kunnen geen beslissingen genomen worden, omdat hiermee normaal en abnormaal niet duidelijk onderscheden kunnen worden. Om deze reden is gesteld dat in de indicatiestelling van een pharynxplastiek het resultaat

van de nasometer niet beslissend kan zijn en daarom gecombineerd zal moeten worden met andere onderzoeksmethoden. De nasometer kan wel gebruikt worden om op groepsniveau het effect van behandelingen van hypernasaliteit te meten.

Patiënten met een schisis worden protocollair voor het laatst multidisciplinair gezien door het schisis team rond hun 18e jaar. In deze fase is er veel aandacht voor esthetiek en functie van de neus, aangezien de overige behandelingen normaalgesproken zijn afgerond. Niet altijd hebben de professional en de patiënt dezelfde ideeën over een eventuele volgende behandeling. Dit verschil was de reden om meer te weten van de achtergronden van de meningen van adolescenten wat betreft behandeling van hun schisis. **Hoofdstuk 6** beschrijft een kwalitatieve studie over de motivaties van adolescente patiënten met een schisis om tot een uitgesproken mening over hun behandeling te komen. Dertien patiënten met verschillende vormen van schisis zijn geïnterviewd. Ze werden gevraagd hun mening te geven over bepaalde aspecten die te maken hebben met hun schisis, zoals neusademhaling, uiterlijk van de neus, spraak, lipuiterlijk, gebit, oorproblemen en sociale impact, en vervolgens waarom ze er zo over dachten. Na analyse bleek dat zelfacceptatie en acceptatie van de omgeving, zoals de patiënt dat waarneemt, bepalen of de patiënt op dat moment tevreden is. Samen met de ondervonden last en winst van de behandelvoorgeschiedenis zorgde de tevredenheid klaarblijkelijk ervoor of een patiënt een behandeling zocht of niet. De meest basale motivatie was een verlangen om zo normaal mogelijk te zijn. Veel geïnterviewde patiënten waren echter terughoudend ten opzichte van een behandeling omdat ze de risico's, moeite of te verwachte hinder van de operatie niet vonden opwegen tegen het te verwachten resultaat. Daarnaast vonden een aantal geïnterviewden zichzelf nog niet in staat om een beslissing te nemen en stelden dat liever uit tot na hun 18e jaar. Mede hierdoor is het aan te raden om patiënten met een schisis een controle midden in hun twintiger jaren aan te bieden.

Dankwoord



Dit proefschrift was nooit mogelijk geweest zonder de hulp van veel mensen. Op deze plek wil ik iedereen die aan dit proefschrift bijgedragen heeft hartelijk danken en een aantal mensen in het bijzonder.

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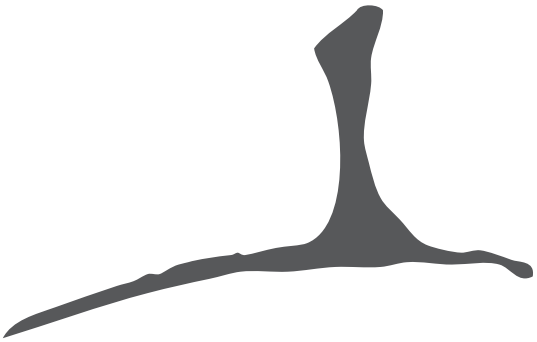
Hannarixt, Bregt en Meike, jullie steun is onmisbaar in alles wat ik doe. Ik wil heel graag met jullie samen oud worden.

Curriculum Vitae



Perry van der Heijden is geboren op 24 september 1980 te Rhenen. Vanaf het eerste levensjaar is hij opgegroeid in Voorthuizen. Van 1992 tot 1998 heeft hij op het Johannes Fontanus College te Barneveld het VWO gevolgd. In 1998 werd begonnen aan de studie Geneeskunde aan de Universiteit van Utrecht, dat tussentijds werd bezegeld met het behalen van het doctoraal examen in 2002 en succesvol werd afgerond in 2005 met het arts-examen. Na de studie Geneeskunde heeft hij bijna 1 jaar als arts-assistent-niet-in-opleiding gewerkt in het Centraal Militair Hospitaal te Utrecht, alvorens hij in 2006 startte met de opleiding tot Keel-, Neus- en Oorarts in het Universitair Medisch Centrum te Groningen. Gedurende de opleiding is een perifere stage van 1 jaar gevolgd in de Isala Klinieken te Zwolle. Per 1 november 2011 is de opleiding afgerond. Samen met zijn vriendin Hannarixt en hun kinderen Bregt (2008) en Meike (2011) is hij naar Harderwijk verhuisd om per 1 februari 2012 te gaan werken als Keel-, Neus- en Oorarts in de maatschap KNO in het Ziekenhuis St Jansdal te Harderwijk. In aansluiting op het onderwerp van dit proefschrift heeft hij speciale interesse en werkzaamheden in de aangezichts- en bijholtechirurgie.