

VAN THAI NGUYEN

The first study of the treatment outcomes of
patients with cleft lip and palate in
Central Vietnam



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patients with cleft lip and palate in
Central Vietnam



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LIST OF ORIGINAL PUBLICATIONS

The dissertation is based on the following original publications which are referred to in the text by their Roman numerals (I–VII):

- I. **Van Thai Nguyen**, Hong Loi Nguyen, Toai Nguyen, Triin Jagomägi. Oral health status of patients with repaired cleft lip and palate in Central Vietnam. *Oral Health & Preventive Dentistry*. [Accepted].
- II. **Van Thai Nguyen**, Triin Jagomägi. Maternal experiences of having a child with a cleft. *J Otol Rhinol*. 2018 7:3. doi: 10.4172/2324–8785.1000343
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- IV. **Van Thai Nguyen**, Lagle Lehes, Thi Thuy Hang Truong, Thi Van Anh Hoang, Triin Jagomägi. Normative nasalance scores for Vietnamese-speaking children. *Logoped Phoniatr Vocol*. 2017 Oct 26:1–7. doi: 10.1080/14015439.2017.1389985. [Epub ahead of print]
- V. **Van Thai Nguyen**, Lagle Lehes, Thi Thuy Hang Truong, Thi Van Anh Hoang, Triin Jagomägi. Nasalance scores for Vietnamese-speaking patients with cleft lip and palate [In preparation]
- VI. **Van Thai Nguyen**, Triin Jagomägi. Craniofacial, palatal, and upper airway structures in patients with cleft lip and palate. [In preparation]
- VII. **Van Thai Nguyen**, Martin Persson, Triin Jagomägi. Application of a new patient-reported outcome measure in orofacial clefts: An exploratory study in two countries. [In preparation]

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The contribution of Van Thai Nguyen to the original publications:
Paper I–VII: conception and design of the studies; clinical examination; acquisition, analysis, and interpretation of the data for the studies; writing the articles.

LIST OF ABBREVIATIONS

BCLP	Bilateral cleft lip and palate
CBCT	Cone beam computed tomography
CHASQ	Cleft Hearing, Appearance, and Speech Questionnaire
CSAG	Clinical Standards Advisory Group
CI	Confidence intervals
CL	Cleft lip
CL/P	Cleft lip and/or palate
CL±A	Cleft lip with or without cleft alveolus
CL±P	Cleft lip with or without cleft palate
CLP	Cleft lip and palate
CP	Cleft palate
CP±L	Cleft palate with or without cleft lip
CT	Computed tomography
dmft (DMFT)	Decayed, missing, and filled teeth
ICC	Intraclass correlation coefficient
IPDTC	International Perinatal Database of Typical Oral Clefts
PAS	Pharyngeal airway space
SIG	Special Interest Group
SPSS	Statistical Package for the Social Science
TCDD	Tetrachlorodibenzodioxin
UCLP	Unilateral cleft lip and palate
VAS	Visual analogue scale
VPI	Velopharyngeal insufficiency

1. INTRODUCTION

Cleft lip and/or palate (CL/P) includes cleft lip with or without cleft alveolus (CL±A), cleft lip and palate (CLP), and isolated cleft palate (CP). CL/P affects about 1 per 700 (or 14 per 10,000) live births per year (Mossey and Castillia, 2003). Most cases of CL/P, about 70%, are non-syndromic; i.e. the clefts occur without other anomalies (Stanier and Moore, 2004).

CL/P not only affects appearance, but also feeding, speech, hearing, and psychological development. Patients often have to undergo multiple treatments starting at birth until young adulthood (Stanier and Moore, 2004). These treatments involve specialists from different areas: anaesthesiology, audiology, genetic counselling, nursing, oral and maxillofacial surgery, orthodontics, otolaryngology, paediatrics, paediatric dentistry, plastic surgery, prosthodontics, psychiatry, psychology, social work, and speech-language pathology (American Cleft Palate-Craniofacial Association, 2018). The outcomes of cleft care, therefore, should be evaluated from different perspectives. A standard set of outcome measures for cleft care have been proposed; it contains eight major outcome domains: eating and drinking, dental and oral health, speech/communication, otologic health, breathing, appearance, psychosocial development, and burden of care (Allori et al., 2017a).

The burden of CL/P is more significant in low- and middle-income countries. There are several barriers to CL/P treatment around the world: a lack of trained providers, patient travel costs, a lack of patient awareness, and little financial support for the provision of surgical care (Jenny et al., 2017). Specifically, in Vietnam, although most of the patients have health insurance, a majority of them still rely on charitable cleft care outside of the centralized health care system. For that reason, the treatment for patients with CL/P is usually behind the optimal timetable for treatment compared to developed countries (Yao et al., 2016).

Patients with CL/P in Central Vietnam are operated by different charity organizations, such as Operation Smile, Smile Train, Interplast, Chonbuk University operation team, and Global Care Korea. These charitable cleft operations have been performed for several years. The cleft care focused largely on surgery; other types of cleft treatment such as speech therapy and orthodontic treatment have not been provided. The follow-ups for these patients are usually fragmented. Treatment outcomes of these patients are, therefore, not investigated comprehensively.

The purpose of the present study is to evaluate the treatment outcomes of surgically treated patients with CL/P in Central Vietnam.

2. REVIEW OF LITERATURE

2.1. Aetiology

Causes of non-syndromic CL/P remain unclear. It is generally accepted that the aetiology of CL/P is multifactorial, i.e. genetic factors, environmental risk factors, and the interaction between them. Some growth factors, transcription factors, nutrient metabolism, or immune response have been studied (Mossey et al., 2009). Genes related to syndromic CL/P could possibly increase the risks of having non-syndromic CL/P (Wong FK and Hagg, 2004). There are some lifestyle and environmental risk factors that might play a role in CL/P such as maternal smoking, deficiency of folic acid and zinc, exposure to organic solvents and agricultural chemicals, consumption of anticonvulsant drugs and corticosteroids, or viral infection (Mossey et al., 2009).

2.2. Classification

There have been several classifications of CL/P based on the anatomic and morphologic, or embryologic perspectives (Allori et al., 2017b). Davis and Ritchie (1922) proposed a three-group system of CL/P classification using the alveolar process as a dividing line: 1) prealveolar process cleft; 2) postalveolar process cleft; 3) alveolar process cleft. Fogh-Andersen (1942) suggested using the incisive foramen as a dividing line from an embryological perspective. He proposed a four-group system: 1) cleft lip (CL) extending to the incisive foramen and including clefts of the alveolus; 2) CL and CP; 3) CP identified as being always median and not extending beyond the incisive foramen; 4) rare atypical clefts, e.g. median cleft lip. Kernahan and Stark (1958) supported the use of the incisive foramen and proposed three groups: 1) clefts of structures anterior to the incisive foramen; 2) cleft of structures posterior to the incisive foramen; 3) clefts of structures anterior and posterior to the incisive foramen.

The varieties of clefts can be grouped into three main categories (Berkowitz, 2013). First, clefts may involve the lip and alveolus (i.e. CL±A). A cleft of the lip may be complete or incomplete, and it may be unilateral or bilateral. A complete cleft of the lip extends from the vermilion border to the floor of the nose. A bilateral CL may be symmetrical or asymmetrical (Berkowitz, 2013). Second, clefts that involve the lip and palate (i.e. CLP). CLP may be complete or incomplete, and it may be unilateral or bilateral. Direct communication between the oral and nasal cavities exist on the cleft side of the palate in a complete unilateral CLP. The bilateral CLP may be symmetrical or asymmetrical (Berkowitz, 2013). Third, clefts that involve the palate alone (i.e. CP). This type of cleft does not involve either the lip or the alveolar process. It may involve only the soft palate or both the soft and hard palate but never the hard palate only. A subcategory in the CP is submucous CP. It has a classic diagnostic triad: bifid uvula, a furrow along the midline of the soft palate, and a bony notch in the posterior hard palate (Berkowitz, 2013).

2.3. Prevalence

The overall prevalence of cleft lip with or without cleft palate (CL±P) is 9.92 per 10,000 births, that of CL is 3.28 per 10,000 births, and that of CLP is 6.64 per 10,000 births (IPDTC Working Group, 2011). Prevalence of CL/P varies depending on the type of cleft, ethnicity, and gender.

In term of the type of cleft, CLP generally occurs twice as often as either CL or CP individually. Unilateral clefts are more frequent than bilateral clefts; unilateral clefts occur more frequently on the left than on the right (Perry and Zajac, 2016).

Regarding ethnicity, Asians (Japan, the Philippines) and mixed-race populations (Amerindians, mestizo populations) have the highest rates of CL/P, with intermediate levels in Caucasians, and the lowest level in Africans (Dixon et al., 2011; Mossey and Castillia, 2003). The prevalence of CL/P in the Asian population is 13.0 per 10,000 births (Cooper et al., 2006).

CL±P is more dominant in males, and CP occurs more frequently in females (Mossey et al., 2009; Mossey and Castillia, 2003). The gender ratio (male/female) is 1.81 among cases with CL±P, and 0.93 among cases with CP (Mossey and Castillia, 2003). It is hypothesized that the secondary palate of the female embryo closes at a slower rate than that of the male embryo. Since the female secondary cleft is open for a longer period of time, it might be susceptible to teratogenic disruption during normal palatal closure for a greater period of time (Burdi and Silvey, 1969).

2.4. Cleft-related problems

Patients with CL/P often encounter multiple problems from birth: feeding difficulties, dentofacial and orthodontic abnormalities, abnormal speech, hearing loss and ear infections, breathing problems, differences in appearance, and psychosocial functioning problems (American Cleft Palate-Craniofacial Association, 2018; Nackashi et al., 2002; Stock and Feragen, 2016). Therefore, the patients require a multidisciplinary treatment including plastic and maxillo-facial surgery, otorhinolaryngology, orthodontics, speech and language therapy, and psychological therapy (Stock and Feragen, 2016).

2.4.1. Feeding

Neonates with CL/P have persistent feeding problems that can persist, in some cases, to 14 months of age (Reid et al., 2006). Neonates with CP and CLP have oronasal communication which makes them unable to create negative intraoral pressure to suckle (Peterson-Falzone et al., 2017). The inability to suck can lead to inefficient feeding that in turn results in an excessive air intake, longer feeding times, slow weight gain, and fatigue for both the baby and mother. Nasal regurgitation is also a common problem in CP (Goswami et al., 2016;

Peterson-Falzone et al., 2017; Jindal and Khan, 2013). Neonates with CL±A, on the contrary, usually do not have problems feeding because breast tissue covers the cleft during nursing (Peterson-Falzone et al., 2017).

2.4.2. Dental and oral health

Dental and oral health status is determined by caries status, oral hygiene status, and gingival status (Paul and Brandt, 1998). Systematic reviews and meta-analysis studies have found conflicting results in the prevalence of caries in patients with CL/P. A systematic review found no firm confirmation that patients with CL/P have an increased prevalence of caries due to a low to moderate quality of the studies (Hasslof and Twetman, 2007). Others concluded that patients with CL/P tend to have a higher prevalence of caries in both primary and permanent dentition (Antonarakis et al., 2013; Wong FWL and King, 1998; Pinto et al., 2013). Patients with CL/P have poorer oral hygiene and more gingivitis but not conclusively a higher risk of developing periodontal diseases (Wong FWL and King, 14, 27, 28, 33, 34, 46, 47, 113.998; Paul and Brandt, 1998; Mutthineni et al., 2010).

Patients with CL/P are characterized by class III malocclusion and crossbite. The class III malocclusion is due to maxillary hypoplasia that results from cleft surgery. Crossbite is frequently on the cleft side and in the incisor region (Paradowska-Stolarz and Kawala, 2014).

The cleft is associated with a wide range of dental anomalies, and the dental anomalies occur more frequently on the cleft side. The most common dental anomalies found in patients with CL/P are: multiple missing teeth/hypodontia (usually the maxillary lateral incisors); neonatal teeth; ectopic teeth; impaction; supernumerary teeth; microdontia; maxillary canines and premolars transposition; crown and root malformation; enamel hypoplasia (Haque and Alam, 2015; Kaul et al., 2017).

2.4.3. Speech

While CL should have no effect on speech once the clefts are operated on, CP can affect speech and communication abilities in many ways. CP is the most common cause of velopharyngeal insufficiency (VPI). VPI can impact on articulation, speech resonance, and nasal air emission (Peterson-Falzone et al., 2017).

There are two types of articulation errors: obligatory and compensatory errors. Obligatory errors are errors due to structural abnormalities such as misaligned teeth or oronasal fistula. The underlying structural deformities need to be corrected before speech therapy. Compensatory errors are errors due to maladaptive articulatory placement learned by children. This type of error can be corrected only with speech therapy (Nagarajan et al., 2009).

Resonance disorders include hypernasality (too much nasal resonance), hyponasality (too little nasal resonance), and mixed nasality (resonance characterized by elements of hypernasality and hyponasality) (Peterson-Falzone et al., 2017). The most common disorder of resonance is hypernasality (Sell et al., 2001).

Nasal air emission is the inappropriate release of air pressure through the nasal cavity that affects the high-pressure consonants that require oral airflow under pressure. Nasal emission can be audible or inaudible (Peterson-Falzone et al., 2017).

2.4.4. Otolaryngologic health

The incidence of hearing problems in CL alone is the same as non-cleft individuals because the cleft does not affect the Eustachian tube (Sharma and Nanda, 2009). Infants with CP and CLP, in contrast, universally present with otitis media with effusion. Otitis media with effusion is a condition which presents with middle ear fluid without signs or symptoms of acute infection (Flynn et al., 2009). The main pathogenesis of otitis media in children with clefts is Eustachian tube dysfunction resulting from the tensor veli palatini and the levator veli palatini incompetence (Flynn et al., 2009; Antonelli, 2002).

Otitis media with effusion is clinically rather silent. The most common clinical manifestation of otitis media with effusion is a conductive hearing loss (Antonelli, 2002). The hearing loss can be temporary, persistent, or recurrent, and it can vary in degree. The amount and viscosity of the fluid in the middle ears can influence the degree and configuration of the hearing loss (Gravel and Wallace, 2000).

2.4.5. Airway and breathing

CL/P is frequently associated with nasal deformities such as a deviated septum, vomerine spurs, nostril atresia, alar constriction, and maxillary constriction (Cheung and Oberoi, 2012; Warren et al., 1988). These deformities tend to reduce the size of the nasal airway, increase nasal resistance to airflow, and reduce nasal patency (Fukushiro and Trindade, 2005). The type of cleft also affects the size of the airway. Children with bilateral CLP (BCLP) have the largest airway, followed by unilateral CL, CP, and unilateral CLP (UCLP) (Warren et al., 1988). However, adults with BCLP have a smaller nasal area than ones with UCLP, and ones with CP have an uncompromised nasal area (Fukushiro and Trindade, 2005). Nasal airway size differences due to cleft types might not remain over time. The growth might have a positive effect on the nasal size in patients with CL/P but not normalize it to be the same as non-cleft individuals (Drake et al., 1993).

Patients with CL/P also have a reduced size of the pharyngeal airway because of changes in the craniofacial morphology and cleft surgery (MacLean et al., 2009; Agarwal and Marwah, 2016). Some studies have found that the

pharyngeal airway is restricted in patients with CLP (Shahidi et al., 2016; Agarwal and Marwah, 2016). However, others have found no differences in the pharyngeal airway volume between children with and without CLP (Pimenta et al., 2015; Cheung and Oberoi, 2012).

2.4.6. Appearance

The treatment of CLP should provide good aesthetic and functional results. Aesthetics and facial aesthetics, particularly, play an important role in an individual's general perception of life (Sinko et al., 2005). Patients with CL/P, especially, may feel different from others in their facial appearance despite the fact that multiple surgical and other interventional procedures have been performed until adulthood (Feragen and Stock, 2016). The differences in appearance may have negative psychosocial consequences (Rankin and Borah, 2003).

2.4.7. Psychosocial functioning and mental health

CL/P and its treatment may have an impact on psychological and social functioning—psychosocial functioning (Stock and Feragen, 2016; Hunt et al., 2005). Impacts on psychological functioning include: anxiety, self-esteem, depression, and behavioural problems (Hunt et al., 2007). Impacts on social functioning are related to teasing/bullying, schooling and further education, satisfaction with appearance, satisfaction with speech, marriage, and friendship (Hunt et al., 2007; Hunt et al., 2005).

Children with CP often have depressive symptoms, anxiety, and learning problems; which are related to the degree of speech difficulties. Children with CL have low self-esteem, depressive symptoms, and anxiety related more to facial appearance (Millard and Richman, 2001). Children with CL/P have a high level of internalizing behaviour and a low level of externalizing behaviour (Millard and Richman, 2001; Hunt et al., 2005). Adults with CL/P are more anxious and depressed than controls (Hunt et al., 2005; Ramstad et al., 1995). Dissatisfaction with appearance is a predictor of depression in patients with CL/P (Hunt et al., 2005; Marcusson et al., 2002).

Having been teased, bullied or taunted is the predominant predictor of psychosocial impairment (Hunt et al., 2007). This may lead children to quit school to avoid being teased (Lorot-Marchand et al., 2015). Often, these individuals have no aspiration for further education and are usually unemployed with a low-income aspiration (Hunt et al., 2005; Peter et al., 1975). Some patients are pleased with their facial appearance, but many are not satisfied and desire further treatment (Hunt et al., 2005; Slifer et al., 2003; Marcusson et al., 2002); others are not satisfied with their appearance but appear to be tired of further treatment (Sinko et al., 2005). Few adolescents with CL/P are dissatisfied with their speech (Hunt et al., 2005). Few adults with CL/P marry (Broder et al.,

1994; Hunt et al., 2005). If a marriage does happen, it is usually later in life and frequently childless. Children and young adults with CL/P have fewer friends than their non-cleft peers (Hunt et al., 2005; Bressmann et al., 1999).

Children with CL/P have an increased risk of poor mental health because of low self-esteem, depressed mood, and hearing and speech deficits (Tillman et al., 2018). Danish adults with CL/P have been shown to have an increased risk for psychiatric disorders, all-cause mortality, and suicide (Christensen and Mortensen, 2002; Christensen et al., 2004). Swedish children have been shown to have an increased risk for psychiatric disorders, intellectual disability, language disorder, autism spectrum disorder, attention-deficit/hyperactivity disorder, psychotic disorder, other behavioural and emotional disorders with onset in childhood, and personality disorders. However, Swedish children did not show increases in suicides, anxiety disorders, depression, bipolar disorder, eating disorders, or alcohol or substance use disorder (Tillman et al., 2018).

2.4.8. Parental experiences

The feelings of parents upon the diagnosis of CL/P vary (Nelson P et al., 2012). Research tends to pay more attention to mothers' feelings because of the maternal bond between a mother and a child (Vanpoelvoorde and Shaughnessy, 1991). Fathers are less included in research because theory-driven research has often marginalized fathers and centralized mothers, difficulties in recruiting fathers for research, and an overall lack of attention to the father's potential influence on their child (Phares et al., 2005; Zimmerman et al., 2000; Silverstein, 2002; Costigan and Cox, 2001). In general, parents' common feelings are sadness, shock, anger, grief, and worry (Nelson P et al., 2012). Specifically, mothers reported strong feelings of shock, hurt, disappointment, helpless resentment, hysteria, denial, or suicide (Natsume et al., 1987; Slutsky, 1969). Fathers reported feelings of shock, worry, and sadness (Zeytinoglu et al., 2016).

2.5. Treatment protocols and timings

Treatment protocols and timing of surgery for CL/P varies between cleft centres. However, some treatment modalities are generally accepted (De Ladeira and Alonso, 2012; Nahai et al., 2005; Nackashi et al., 2002).

During the first week after birth, counselling on feeding difficulties is given to the mother. As for babies with CL±A, breastfeeding is viable. Artificial nipples with a large soft base are effective when breastfeeding is not desired. In babies with CP, breastfeeding is more challenging, although it might be possible in the case of a narrow cleft (Devi et al., 2012). Any babies with feeding problems are advised to use specialized feeding equipment (Devi et al., 2012; Jindal and Khan, 2013).

Surgical interventions are carried out from infancy to adolescence; different surgical techniques can be used at each stage (Posnick and Ruiz, 2002). Cleft lip

repair is usually performed at 2–3 months, or 3–6 months of age (Posnick and Ruiz, 2002; Ziak et al., 2010). A general rule for the timing of cleft lip repair is the rule of 10s: 10 weeks of age, 10 pounds (about 4500 grams), and serum haemoglobin of 10 mg/ml (Wilhelmsen and Musgrave, 1966). Cleft palate repair is carried out before 2 years of age, usually from 6 to 12 months of age (Posnick and Ruiz, 2002). The timing of cleft palate repair is to optimize the function of velum and palate before the beginning of speech development and pressure formation of the mouth (Nahai et al., 2005). Bone grafting takes place after the eruption of the permanent maxillary first molars, usually from 7 to 9 years, to achieve reliable and efficient orthodontic anchorage for rapid arch expansion and to allow maximal transverse growth of the maxilla (Posnick and Ruiz, 2002). Orthognathic surgery is carried out when permanent dentition fully erupts, the teeth have been orthodontically aligned, and maxillomandibular growth is complete (14–16 years in females, and 16–18 years in males) (Posnick and Ricalde, 2004; Posnick and Ruiz, 2002).

The initial speech evaluation and speech therapy, if needed, are carried out within 12–14 months of age (Nahai et al., 2005). Secondary cleft palate procedures for the management of VPI could be carried out when VPI is consistent and related to an anatomic problem (Posnick and Ruiz, 2002).

Dental care is also carried out from infancy to adolescence. The supervision of dental care includes the prevention and treatment of oral diseases, an assessment of the developing dentition, and treatment needs related to the cleft such as orthodontic and prosthodontic treatment. General dentists, paediatric dentists, and orthodontists are involved in this process (Farrington, 2002).

2.6. Measuring outcomes in non-syndromic CLP treatment

Auditing clinical outcomes is important to maintain and continually improve patient care. Any outcome measures that are used to audit clinical care must be reliable, reproducible, and valid (Sandy et al., 2012). There are a large number of outcome measures available in cleft care (Jones et al., 2014). However, there are several difficulties in measuring cleft treatment outcomes. First, it requires time, money, and a large sample to conduct randomized controlled trials in the treatment of CL/P. Thus, more studies involve the next level of evidence that is inter-centre comparisons of outcomes (Sandy et al., 2012). The outcome measures from several inter-centre studies are reported in Table 1. Second, no specific recommendations of which outcomes should be assessed, nor how the outcomes should be collected, analysed, and interpreted have been advised (Sitzman et al., 2014). Third, outcome measures are often not perfectly reliable and valid (Jones et al., 2014). Lastly, definite results of the treatment are not visible until later in a patient's lifespan, up to two decades after the primary surgery. The final outcomes usually are unpredictable at the beginning of the treatment due to variations in growth and development as well as the level of cooperation of the patient (Sinko et al., 2005).

Table 1. Outcome measures of inter-centre studies

Study name (Year)	Cleft type	Age at evaluation (y: years)	Sample size	Number of centres	Outcome measures
A six-centre international study (1992)	UCLP	8–10y	151	6	Craniofacial form and soft tissue profile (Molsted et al., 1992) Dental arch relationships (Mars et al., 1992) Nasolabial appearance (Asher-McDade et al., 1992)
The Clinical Standards Advisory Group (CSAG) Study (2001)	UCLP	5y and 12y	457	50	Dentofacial Outcomes and Patient Satisfaction (Williams et al., 2001) Speech Outcomes (Sell et al., 2001)
The Dutchcleft (2001–2015)	UCLP	Longitudinal study: at birth to 12y	54	3	Effect of infant orthopaedics on: <ul style="list-style-type: none"> – maxillary arch dimension (Prahl et al., 2001; Bongaarts et al., 2006; Noverraz et al., 2015); – collapse of the alveolar segments (Prahl et al., 2003); – occlusion of the deciduous dentition (Bongaarts et al., 2004); – feeding, weight, and length (Prahl et al., 2005); – facial appearance (Prahl et al., 2006; Bongaarts et al., 2008); – mother’s satisfaction in motherhood (Prahl et al., 2008); – facial growth (Bongaarts et al., 2009) Cost-effectiveness of infant orthopaedics treatment regarding speech (Konst et al., 2004)
The Eurocleft study (2005)	UCLP	Longitudinal study: 9, 12, 17y	127	5	Craniofacial form and nasolabial appearance (Brattstrom et al., 2005) Dental arch relationships (Molsted et al., 2005) Relationship among treatment outcome, patient/parent satisfaction, and the burden of care (Semb et al., 2005)
The Americleft (2011)	UCLP	6–12y	172	5	Dental arch relationship (Hathaway et al., 2011) Craniofacial form (Daskalogiannakis et al., 2011) Nasolabial aesthetics (Mercado et al., 2011)

Study name (Year)	Cleft type	Age at evaluation (y: years)	Sample size	Number of centres	Outcome measures
The Cleft Care UK study (CCUK) (2015)	UCLP	5y	268	11	Dentofacial outcomes (Al-Ghatam et al., 2015) Oral health and audiology (Smallridge et al., 2015) Perceptual speech outcomes (Sell et al., 2015) Child psychosocial outcomes and satisfaction with cleft services (Waylen et al., 2015)
A French study (2015–2016)	UCLP, BCLP	5y	80	4	Lip and nose aesthetic results (Dissaux et al., 2015) Facial growth and speech development (Dissaux et al., 2016)
The Scandcleft (2017)	UCLP	5y	448	10	Surgical results (Rautio et al., 2017) Nursing care (Bannister et al., 2017) Speech outcomes (Lohmander et al., 2017; Willadsen et al., 2017) Dental arch relationships (Heliövaara et al., 2017) Occlusion (Karsten et al., 2017) Nasolabial appearance (Molsted et al., 2017) Social and emotional experiences (Fergen et al., 2017a) Parental perceptions of appearance and treatment outcomes (Fergen et al., 2017b)

UCLP: unilateral cleft lip and palate; BCLP: bilateral cleft lip and palate

Sitzman et al. (2014) proposed three main domains for measuring outcomes in cleft care: clinical, psychosocial, and system-based parameters. The clinical domain includes general paediatrics, surgery, dental/orthodontic, speech, and audiology. The psychosocial domain includes psychological well-being and social functioning. The system-based parameters include cost, resource allocation, the process of care, and supplemental/ancillary services. Recently, Allori et al. (2017a) suggested to assess the outcomes in eight major outcome domains: eating and drinking; dental and oral health; speech, otologic health; breathing; appearance; emotional and psychosocial development; and aspects related to process of care or burden of treatment. The authors designed it as a minimum standard set of outcome measures; any extensions are complementary to the standard set.

2.7. An overview of the CL/P situation in Vietnam

2.7.1. Vietnam and its health care system

Vietnam is located in Southeast Asia with an estimated 97 million inhabitants (Worldometers, 2019). The total area is about 331,212 km² including numerous islands. There are 63 cities and provinces which can be grouped into three main regions: Northern, Central, and Southern Vietnam. Vietnam has focused on the development of advanced medical centres in Hanoi (Northern Vietnam), Hue (Central Vietnam), and Ho Chi Minh City (Southern Vietnam) (Pham, 2010). Thua Thien-Hue Province is composed of one provincial city (Hue), two district-level towns, and six districts. In Hue, there are three large hospitals that treat patients with CL/P from the Thua Thien-Hue Province and neighbour cities in Central Vietnam: Hue Central Hospital, Hue University Hospital, and Hue Odonto-Stomatology Hospital.

Although Vietnam's health care system was transformed from a fully public service system to a mixed public-private system in 1989, the public health care system still plays an important role in providing health services (Le et al., 2010). Currently, there is a lack of a healthcare workforce in Vietnam with the number of doctors being quite low (8 doctors/10,000 people) (Takashima et al., 2017).

Vietnam's public health care system consists of four administrative levels: national level, provincial level, district level, and commune level (Le et al., 2010). Accordingly, public medical institutions are classified into four levels: national, provincial, district, and commune level. The primary public medical institution is commune health stations, about 11,000 health stations, which cover nearly all communes in Vietnam and are responsible for primary health care services. However, commune health stations have limited medicine and medical equipment, additionally, there are not many skilled doctors and nurses at these locations. Patients, therefore, might go to higher level medical institutions for examination and treatment (Sakano, 2015). Due to this, two to

three patients sharing a bed is becoming a common problem in many national and provincial hospitals (Takashima et al., 2017).

In 1992, health insurance was introduced (Le et al., 2010). About 86.9% of the Vietnamese population had health insurance in 2018 (Anh Xuan, 2018). The health insurance covers 80–100% of medical expenses depending on individuals. Public medical institutions also run a referral system. The referral system affects the percentage that the health insurance covers, 40–70% of the expenses (EFY Việt Nam, 2014).

2.7.2. Management of CL/P in Vietnam

The prevalence of CL/P in Vietnam is unclear, and it is usually estimated from hospital registries. The estimated prevalence of CL/P in Vietnam is about 14.9 per 10,000 births (Nagato et al., 1998), or 14.1 per 10,000 births (Phan and Hoang, 2007). Agent Orange, which was used as a herbicide during the Vietnam War, contained a synthetic dioxin compound—2,3,7,8-tetrachlorodibenzo-dioxin (TCDD). It allegedly attributed the increased risk of many congenital anomalies including CL/P in Vietnam (Clapp et al., 2014; Nagato et al., 1998). However, there is no national registry for congenital anomalies, CL/P in particular.

In spite of a high proportion of insurance coverage, patients as well as their families still depend on charitable cleft care mainly because of the high cost of care for local services, or their belief in the superiority of foreign doctors (Hoang and Nguyen, 2011; Lam et al., 2010; Yao et al., 2016). Many charity organizations come to Vietnam on a mission that brings smiles back to Vietnamese children, such as Operation Smile, Smile Train, Deutsche Cleft Kinderhilfe, Project Vietnam Foundation, and institutional teams. Specifically, in Hue, Operation Smile, Smile Train, Interplast, Chonbuk University operation team, and Global Care Korea have been collaborating with Hue Central Hospital, Hue University Hospital, and Hue Odonto-Stomatology Hospital to provide free surgery to patients with CL/P for many years.

Surgical treatment provided by charity teams usually lags behind the optimal window of timing compared to developed countries (Yao et al., 2016). Cleft individuals have had their first cleft repair at an average age of 3.2 years according to Yao et al. (2016), or 2.6 to 3.8 years according to Swanson et al. (2017). Also, due to a limited timeframe within each mission, the team can usually perform the operation for one procedure of the surgery protocols, which can create a problem in the continuity of care for short-term medical missions (Hoang and Nguyen, 2011).

There are four barriers to surgical cleft treatment in Vietnam: patient characteristics, family education and socioeconomics, geographic location, and cleft treatment site features. Males are almost two times more likely than females to access surgical treatment before 18 months of age. Paternal education beyond secondary school is associated with timely surgery. Families living within 10

km from the nearest hospital are more likely to attain the surgery. Travel time, cost, and distance to the mission site are not associated with the timing of the treatment. Lastly, hearing about the cleft mission from family, friends, or social media channels are associated with timely treatment (Swanson et al., 2017).

2.7.3. Research on CL/P in Vietnam

A vast majority of research has focused on the comparison of surgical techniques or the evaluation of surgical outcomes (Nguyen TD and Thai, 2004; Nguyen VT, 2013; Nguyen CT and Nguyen, 2007). Epidemiological studies on CL/P have been carried out in certain areas in Vietnam (Nguyen CU, 1999; Lam et al., 2010; Nguyen HL, 2006; Phan and Hoang, 2007). There are some studies about other aspects of CL/P, such as speech, and craniofacial morphology (Nguyen TTC, 2012; Vu et al., 2004; Huynh and Hoang, 2007).

In short, prior research in Vietnam has investigated one single aspect of the cleft treatment outcomes. No research has studied the multiple aspects of the treatment outcomes in patients with CL/P, especially, in Central Vietnam.

3. AIMS OF THE STUDY

The general aim of the study was to investigate the different treatment outcome aspects of patients with CL/P in Central Vietnam.

The specific objectives were:

1. To determine oral health status (caries experience and periodontal status) of patients with CL/P (Paper I);
2. To explore maternal feelings of having a child with CL/P, their belief in the causation of CL/P, and changes in their postpartum life (Paper II);
3. To evaluate the nasolabial aesthetics of patients with CL/P (Paper III);
4. To establish normative nasalance scores for Vietnamese-speaking individuals (Paper IV) and investigate nasalance scores for Vietnamese-speaking patients with repaired CL/P (Paper V);
5. To determine characteristics of craniofacial morphology, maxillary arch dimensions, palatal dimensions, and upper airway structures in patients with CL/P (Paper VI);
6. To explore the satisfaction of patients with CL/P and their parents with the outcomes of cleft treatment (Paper VII).

We hypothesized that surgically treated patients with CL/P in Central Vietnam had an acceptable or a moderate result for each treatment outcome.

4. MATERIALS AND METHODS

4.1. Study population

Clinical records of patients with CL/P operated on by foreign teams at the three aforementioned hospitals in Hue were hand-searched with ethical approval. Two of the hospitals had been documenting patients operated on by foreign teams since 2012. The other hospital allowed us to access a patient list from 2016. Therefore, we collected clinical records of patients with CL/P from 2012 to 2016 in the two hospitals. In the third hospital, we collected clinical records from 2016. The available information on a clinical record was composed of the patient's contact, a simple diagnosis notation, and a brief description of the surgical method used. No dental models, radiographs, nor photos were included in the records. Besides searching through the clinical records, we also announced a recruitment for patients through national and local channels.

We identified 234 patients who might have CL/P through the clinical records. The primary researcher (Nguyen VT) contacted the patients individually to explain the research and set up an appointment for the study. Among the identified patients, 56 patients agreed to participate in the study, 119 patients refused, and 59 patients were not able to be contacted. On the data collection days (21–24 March 2016), 87 patients showed up. We had more patients showed up than the number of patients agreed to participate; that might be because we had the announcement on national and local channels about the recruitment. However, we did not specify where they have learned about the recruitment. To determine eligibility for the study, an initial examination was conducted to confirm the diagnosis of non-syndromic CL/P. From the 87, six patients were excluded because of nasal deformity only without CL/P ($n=4$) or signs of intellectual disability ($n=2$). Therefore, a total of 81 patients were included in the study. Depending on the treatment outcome to be evaluated, specific inclusion and exclusion criteria were applied. Patients who were not eligible for the study still underwent an oral and dental examination, but their data was not analysed. Different control groups were used to compare against the cleft group on certain treatment outcomes. Details of the study samples in each publication are listed in Table 2.

Patients in this study were operated on using the same treatment protocol provided by charity operation teams. The operation teams followed similar surgical techniques to repair the lip and palate in accordance with their timing. The lip was repaired for patients 6 to 12 months old using modified Millard or Tennison technique. The palate was repaired for patients 12 to 24 months old using V-Y pushback technique. The surgical procedures were performed by different surgeons. No orthodontic treatment, bone grafting, nor speech therapy were provided.

Table 2. Summary of the study samples in each publication

Publication No.	Cleft group		Control group	Inclusion criteria	Exclusion criteria
	Sample size	Cleft type			
I	78	CL/P	–	Non-syndromic CL/P	Uncooperative patients (n = 3)
II	76	CL/P	–	Non-syndromic CL/P	Did not come with their parents on the data collection days (n = 5)
III	23	UCLP	33 Estonian patients with UCLP	Patients who had both frontal and profile photos	–
IV	–	–	102 non-cleft Vietnamese children	Non-cleft Vietnamese-speaking children 7 to 9 years old	Resonance disorders, history of cleft palate, cold or nasal blockage, history of speech and/or language acquisition problems, or not able to complete the speech stimuli (n = 4)
V	38	CP±L	–	Non-syndromic CP±L	Unable to complete the speech stimuli, unable to repeat the stimuli, uncooperative, hearing problems, suffering from common cold or nasal congestion (n = 0)
VI	17	UCLP or CP	34 non-cleft Vietnamese individuals	Patients who had both cephalometric radiographs and digital dental models	–
VII	29	CL/P	27 Estonian patients with CL/P	Patients with non-syndromic CL/P ≥ 7 years old	–

CL/P: cleft lip and/or palate; UCLP: unilateral cleft lip and palate; CP±L: cleft palate with or without cleft lip; CP: cleft palate; –: not applicable

4.2. Treatment outcome measures

4.2.1. General information

Questionnaires were used to gather information about the patients (name, gender, age, city of origin), and their parents (occupation, educational attainment). Another questionnaire based on the manual of World Health Organization was used to assess dental visit habit and brushing habit of the patients (World Health Organization, 2013). The questionnaires were filled out either by the patients or their parents.

Socioeconomic status was established using the occupation and educational attainment of the parents. Their occupations were classified into manual and non-manual labour categories. The parents' educational attainment was grouped into three levels: high educational level (tertiary education or higher), middle educational level (secondary education), and low educational level (primary education or less). Parents with high socioeconomic status were identified as those with a non-manual labour and a high educational level. Parents with low socioeconomic status were identified as those with a manual labour and a low educational level. The remaining parents were identified as middle socio-economic status (Zhu et al., 2010).

4.2.2. Oral health status (Paper I)

The oral health assessment comprised of an assessment of dental caries and periodontal status. To assess dental caries, the decayed, missing, and filled teeth (dmft/DMFT) index was used. The dmft index was used for primary teeth, and the DMFT index was used for permanent teeth. We recorded the dmft and DMFT indices separately for primary and permanent teeth in children with mixed dentition. The level of caries is defined as caries-free if dmft/DMFT is 0; very low if dmft/DMFT is < 1.2; low if dmft/DMFT is 1.2 to 2.6; moderate if dmft/DMFT is 2.7 to 4.4; high if dmft/DMFT is 4.5 to 6.5; very high if dmft/DMFT is > 6.5 (World Health Organization, 2013).

To assess periodontal status, two indicators were used: gingival bleeding on probing and periodontal pocket depth. The presence or absence of gingival bleeding was checked at four sites—buccal, lingual, mesial, and distal—for each tooth. The periodontal pocket depth was measured in patients age 15 and older (World Health Organization, 2013).

4.2.3. Maternal experiences (Paper II)

We constructed a questionnaire with open-ended questions to collect information regarding the feelings of the patient's mother towards the cleft diagnosis, their belief or knowledge of causes of CL/P, and changes in their life because of their child with CL/P.

4.2.4. Nasolabial aesthetics evaluation (Paper III)

Frontal and profile photos of each patient were taken using a Canon EOS 6D (Melville, NY). The photos were prepared for the rating process in three steps: 1) photos were levelled according to the interpupillary line; 2) the images were then cropped into a trapezium shape to show only the nasolabial region including the inner canthus, nasal bridge, nostrils, philtrum, and upper lip (Mercado et al., 2011); 3) image files were loaded into Microsoft Office PowerPoint 2013 (Mountain View, CA). The slides were anonymized and coded. The final file was saved as a PDF file and sent to raters.

There were five raters to evaluate the nasolabial aesthetics: one maxillofacial surgeon, one general dentist, one orthodontic resident, and two orthodontists. They evaluated the nasolabial aesthetics using three rating methods: five-point aesthetic index, visual analogue scale (VAS), and reference scores method. The raters familiarized themselves with the rating methods before conducting the evaluation. The raters could check reference photos (if provided) during the rating process. No time limit was enforced for the evaluation process. No calibration test was performed. To assess intra-rater reliability, the raters were asked to re-evaluate 20 randomly selected photos after four weeks.

4.2.4.1. The five-point aesthetic index

The five-point aesthetic index assessed four features of nasolabial aesthetics: nasal form, nasal symmetry, vermilion border, and nasolabial profile (Asher-McDade et al., 1991). The raters were asked to rate each feature on a 5-point scale as follows: 1 = “very good appearance”, 2 = “good appearance”, 3 = “fair appearance”, 4 = “poor appearance”, and 5 = “very poor appearance”. The raters were provided with a complementary description (given by Mercado, 2017) and colour reference photos of each feature to distinguish the scale of severity (Kuijpers-Jagtman et al., 2009; Mercado et al., 2011). The component score of each feature was determined by the average of the five raters’ scores. The total nasolabial score was achieved by averaging the component scores.

Each slide of the PowerPoint file used in this method consisted of one frontal and one profile photo as shown in Figure 1.

4.2.4.2. VAS

The VAS was a 100-mm line representing a spectrum of aesthetics between least aesthetic (0 mm, on the left) and most aesthetic (100 mm, on the right) (Asher-McDade et al., 1991; Fudalej et al., 2017). The raters rated the overall nasolabial aesthetics of a patient by placing a mark across the line at a point reflecting their feeling at the time. The distance of the mark from the left end was measured by a ruler and transformed into continuous variables. No reference photos were provided for this method.

Similar to the five-point aesthetic index, each slide of the PowerPoint file used in this method consisted of one frontal and one profile photo as shown in Figure 1.



Figure 1. A coded slide used for the five-point aesthetic index and VAS method with cropped frontal and profile photos

4.2.4.3. Reference scores method

The reference scores method used a numerical scale from 0 to 200 and a reference photo with a base score arbitrarily set at 100. The raters would increase the score above 100 if the aesthetics of the nasolabial region was considered better than the reference. If the aesthetics were considered worse than the reference, the raters would decrease the score below 100 (Prahl et al., 2006; Fudalej et al., 2017). The raters scored facial and profile views. The total numerical score was averaged from the facial and profile view scores. The reference photos used in this method were photos with the highest agreement among raters based on the five-point aesthetic index. Four photos were selected as reference photos: frontal and profile views of a male patient, and frontal and profile views of a female patient. There were four reference photos of Vietnamese patients and four reference photos of Estonian patients.

About the slide of the PowerPoint file, each patient had two slides. One slide was composed of a patient's frontal photo and a reference frontal photo (Figure 2A). The other slide consisted of a patient's profile photo and a reference profile photo (Figure 2B).

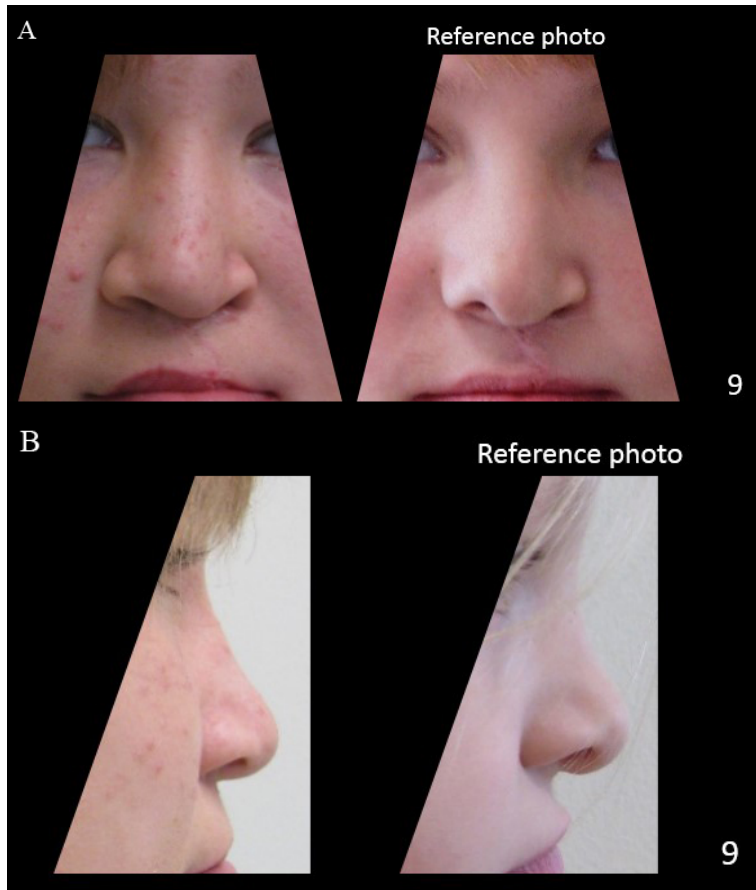


Figure 2. (A) A coded slide used for the reference scores method with a cropped frontal photo of a patient on the left and a reference frontal photo on the right. (B) A coded slide used for the reference scores method with a cropped profile photo of a patient on the left and a reference profile photo on the right.

4.2.5. Nasalance scores (Paper IV, V)

4.2.5.1. Speech material

We developed speech material specifically for the Vietnamese language. The speech material included three stimuli: oral stimuli, oro-nasal stimuli, and nasal stimuli. The oral stimuli, which were devoid of nasal consonants, were comparable to the Zoo passage in English. It had 19 oral words and 18 oral sentences. The oro-nasal stimuli were comparable to the Rainbow passage in English and had eight sentences (33.8% nasal consonants). The nasal stimuli, which were loaded with nasal consonants, had seven sentences (83.0% nasal consonants) (Appendix A).

4.2.5.2. Establishing normative nasalance scores (Paper IV)

The speech assessment was conducted in a quiet room. Nasalance scores were obtained using the Nasometer II (model 6450) (PENTAX Medical, Montvale, NJ) and Nasometer™ software (PENTAX Medical, Montvale, NJ). The Nasometer was calibrated daily before assessing participants' speech according to the manufacturer's instruction. The Nasometer headset was positioned on a participant's head. Once the headset was positioned properly, the participants were instructed to repeat the stimuli after the examiner with a short pause in between. Mean nasalance scores and standard deviation of the three stimuli were reported.

To perform the retest analysis, five children were randomly selected. The headset was removed entirely and re-positioned on the child's head. The child was asked to repeat the stimuli as in the test session.

4.2.5.3. Cleft speech assessment (Paper V)

The Nasometer was calibrated similarly to the procedure of establishing normative nasalance scores, such that the headset was positioned on a patient's head, the patient repeated the stimuli after the examiner, and mean nasalance scores and standard deviation were reported. No retest analysis was performed.

The nasalance score of a patient was interpreted based on a cut-off score of 25%. The cut-off score was obtained from normative nasalance scores for the Vietnamese-speaking population (from Paper IV). Thus, nasalance scores higher than 25% signalled an excessive amount of acoustic nasal energy or hypernasality.

4.2.6. Cephalometric analysis (Paper VI)

We evaluated craniofacial morphology and upper airway structures using lateral cephalograms. The lateral cephalograms were taken with Galileos (Dentsply Sirona, Germany) under the following settings: 9.4 seconds, 60–84 kV, and 10–15 mA depending on gender, age, and body types. For a more accurate measurement of the airway, the patient's head was positioned so that the Frankfurt horizontal plane parallel to the floor (Uslu-Akcam, 2017). The teeth were in habitual occlusion and the lips were relaxed. The lateral cephalograms were traced and analysed digitally using Dolphin Imaging software (Dolphin Imaging & Management Solutions, USA) by one examiner (Nguyen VT). The examiner was trained and calibrated before doing the tracing for this study. To assess intra-rater reliability, 20 lateral cephalograms were randomly selected and re-measured after a 4-week interval. Reference landmarks and cephalometric measurements are described in Figure 3 and Table 3.

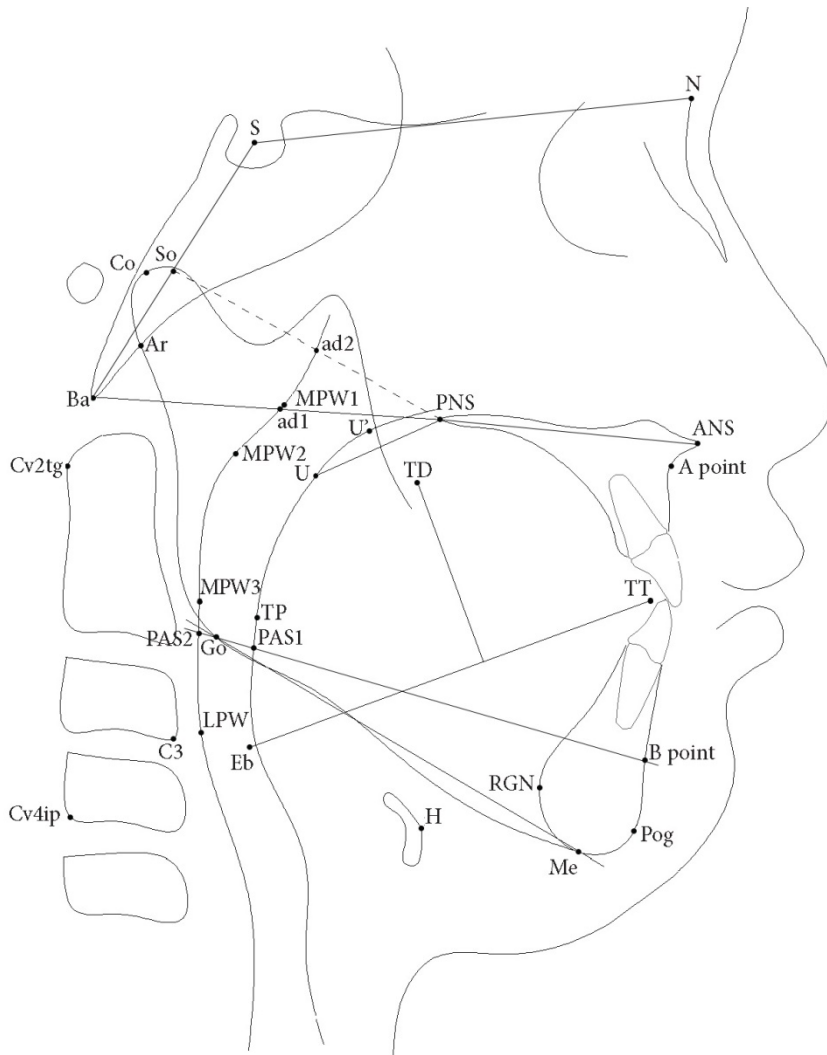


Figure 3. Cephalometric landmarks and planes.

Nasion (N): the intersection of the internasal suture with the nasofrontal suture in the midsagittal plane. **Sella (S):** the centre of the pituitary fossa of the sphenoid bone. **Basion (Ba):** the most inferior posterior point of the occipital bone at the anterior margin of the occipital foramen. **Anterior nasal spine (ANS):** the tip of the anterior nasal spine. **Posterior nasal spine (PNS):** the tip of the posterior nasal spine. **A point:** the deepest point on the curve of the maxilla. **B point:** the most posterior point in the concavity along the anterior border of the symphysis. **Pogonion (Pog):** the most anterior point on the midsagittal symphysis. **Menton (Me):** the most inferior point of the symphysis. **Gonion (Go):** the most convex point where the posterior inferior curve of the ramus meets. **Retrognathion (RGN):** the most posterior point on the mandibular symphysis. **Articulare (Ar):** the posterior border of the neck of the condyle. **Condylion (Co):** the most posterior superior point of the condyle. **Hyoid (H):** the most superior and anterior point on the body of hyoid bone. **Cv2tg:** the tangent point at the superior

and posterior extremity of the odontoid process of the second cervical vertebra. **C3**: the most anterior and inferior point on the corpus of the third cervical vertebra. **Cv4ip**: the most inferior and posterior point on the corpus of the fourth cervical vertebra. **Base of epiglottis (Eb)**: the deepest point of epiglottis. **TT**: tip of tongue. **TD**: tongue dorsum. **TP**: the most posterior point of the tongue. **U**: the most inferior tip of soft palate. **U'**: intersection of the posterior surface of the soft palate and the midline of PNS-U. **So**: the midpoint of the line S-Ba. **ad2**: intersection of the line PNS-So and the posterior pharyngeal wall. **ad1**: intersection of the line PNS-Ba and the posterior pharyngeal wall.

MPW1: intersection of the line from U' parallel to B-Go plane and the posterior pharyngeal wall. **MPW2**: intersection of the line from U parallel to B-Go plane and the posterior pharyngeal wall. **MPW3**: intersection of the line from TP parallel to B-Go plane and the posterior pharyngeal wall. **LPW**: intersection of the line from Eb parallel to B-Go plane and the posterior pharyngeal wall. **PAS1**: intersection of the B-Go line and the anterior pharyngeal wall. **PAS2**: intersection of the B-Go line and the posterior pharyngeal wall.

SN plane (SN): line from S to N. **Mandibular plane (MP)**: line from Go to Me. **Palatal plane (PP)**: line from ANS to PNS. **B-Go plane**: line from B to Go.

Table 3. Cephalometric measurements

Measurements	Description
Craniofacial morphology	
SNA (°)	The angle between line SN and NA
SNB (°)	The angle between line SN and NB
ANB (°)	The angle between line NA and NB
SN-MP (°)	The angle between SN and MP plane
SN-PP (°)	The angle between SN and PP plane
Ar-GoMe (°)	Gonial angle
Ba-SN (°)	Cranial base angle
N-Me (mm)	Anterior face height
N-ANS (mm)	Upper anterior face height
ANS-Me (mm)	Lower anterior face height
S-Go (mm)	Posterior face height
S-Ar (mm)	Posterior cranial base height
Co-Go (mm)	Ramus height
Ba-N (mm)	Total cranial base length
S-N (mm)	Anterior cranial base length
S-Ba (mm)	Posterior cranial base length
ANS-PNS (mm)	Maxillary depth
Co-A (mm)	Maxillary length
Co-Gn (mm)	Total mandibular length
U1-SN (°)	The angle between U1 and SN
U1-PP (°)	Upper incisor inclination to palatal plane
L1-NB (°)	The angle between U1 and NB
L1-MP (°)	Lower incisor inclination to mandibular plane
U1-L1 (°)	Interincisal angle: the angle between the long axis of upper central incisor and lower central incisor

Measurements	Description
Tongue dimensions	
Tongue length (mm)	The distance between Eb and TT
Tongue thickness (mm)	The distance between TD and Eb-TT line
Hyoid bone positions	
H-MP (mm)	The distance between H and MP plane
H-C3 (mm)	The distance between H and C3
C3-RGN (mm)	The distance between C3 and RGN
H-RGN (mm)	The distance between H and RGN
Hyoid angle (°)	The angle between H-Go and H-Me
Pharyngeal airway dimensions	
PNS-ad2 (mm)	Superior nasopharyngeal airway space (the distance between PNS and ad2)
PNS-ad1 (mm)	Inferior nasopharyngeal airway space (the distance between PNS and ad1)
U'-MPW1 (mm)	Superior oropharyngeal airway space (the distance between U' and MPW1)
U-MPW2 (mm)	Middle oropharyngeal airway space (the distance between U and MPW2)
TP-MPW3 (mm)	Inferior oropharyngeal airway space (the distance between TP and MPW3)
PAS min	Retroglossal airway dimension (the distance between PAS1 and PAS2)
Eb-LPW (mm)	Hypopharyngeal airway space (the distance between Eb and LPW)
PNS-Eb (mm)	Vertical airway length
Head posture	
SN-CVT (°)	The angle between SN and Cv2tg-Cv4ip line
Soft palate dimensions	
Soft palate length (mm)	The distance between PNS and U
Soft palate thickness (mm)	The maximum thickness of soft palate measured on the line perpendicular to PNS-U line

4.2.7. Dental model analysis (Paper VI)

We obtained digital dental models from the participants using the intraoral scanner TRIOS[®] 3 Colour Pod (3Shape, Denmark). The model analysis consisted of measuring maxillary arch dimensions (maxillary arch widths, maxillary arch lengths) and palatal dimensions. The model analysis was performed using OrthoAnalyzer[™] 2015 (3Shape, Denmark). To assess intra-rater reliability, 20 digital models were randomly selected and re-measured after a 4-week interval. Reference points are described in Figure 4 and 5.

The maxillary arch widths included intercanine width, interpremolar width, and intermolar width. The intercanine width was the distance between the left and right canines. The interpremolar width was the distance between the left

and right second premolars or second primary molars. The intermolar width was the distance between the left and right first molars.

The maxillary arch lengths included canine arch length and molar arch length. The canine arch length was the distance from the midpoint of central incisors to the line connecting the canines. The molar arch length was the distance from the midpoint of central incisors to the line connecting the first molars.

The palatal dimensions included palatal widths, palatal lengths, palatal depths, and palatal angles. The palatal width was the distance between the highest points on the gingival margins of the palatal surfaces of the left and right teeth (Kilpelainen et al., 1996). The palatal length was the distance between the frontal edge of the incisive papilla and the midpoint on the palatal width (Kilpelainen et al., 1996). The palatal depth was the distance between the midpoint on the palatal width and the palatal vault (Kilpelainen et al., 1996). The palatal angle was the angle between the lines connecting the highest points on the gingival margins and the point of the palatal vault on the midpalatal raphe (Kilpelainen et al., 1996).

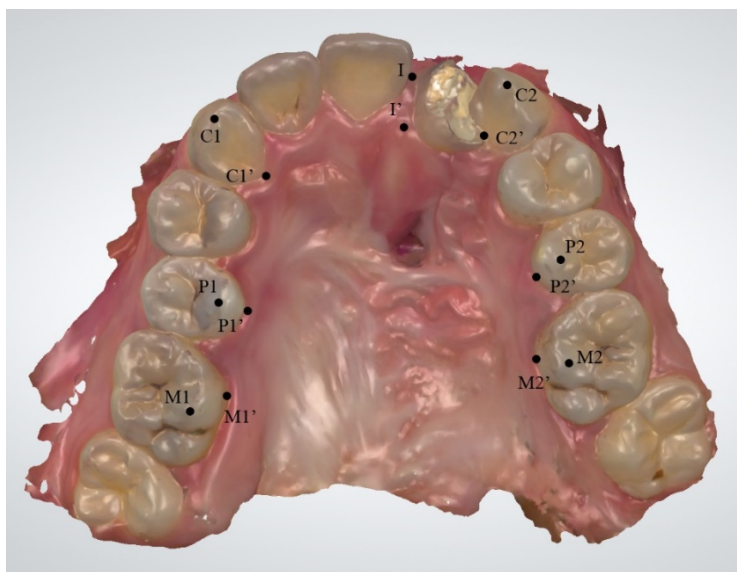


Figure 4. Reference points for the model analysis.

I: the midpoint of the central incisors (or the diastema). **I':** The frontal edge of the incisive papilla. **C1 and C2:** cusp tips of the canines. **C1' and C2':** the highest points on the gingival margins of the palatal surfaces of the canines. **P1 and P2:** the mesiolingual cusp tips of the deciduous second molars or the lingual cusp tips of the permanent second premolars. **P1' and P2':** the highest points on the gingival margins of the palatal surfaces of the premolars. **M1 and M2:** the mesiolingual cusp tips of the permanent first molars. **M1' and M2':** the highest points on the gingival margins of the palatal surfaces of the molars.

The centre of the facet was used in case the tip was worn away. If the tooth was not present, an estimated point of the mesiolingual or lingual cusp tip was chosen. In case the first permanent molars did not erupt, the intermolar width was not measured.

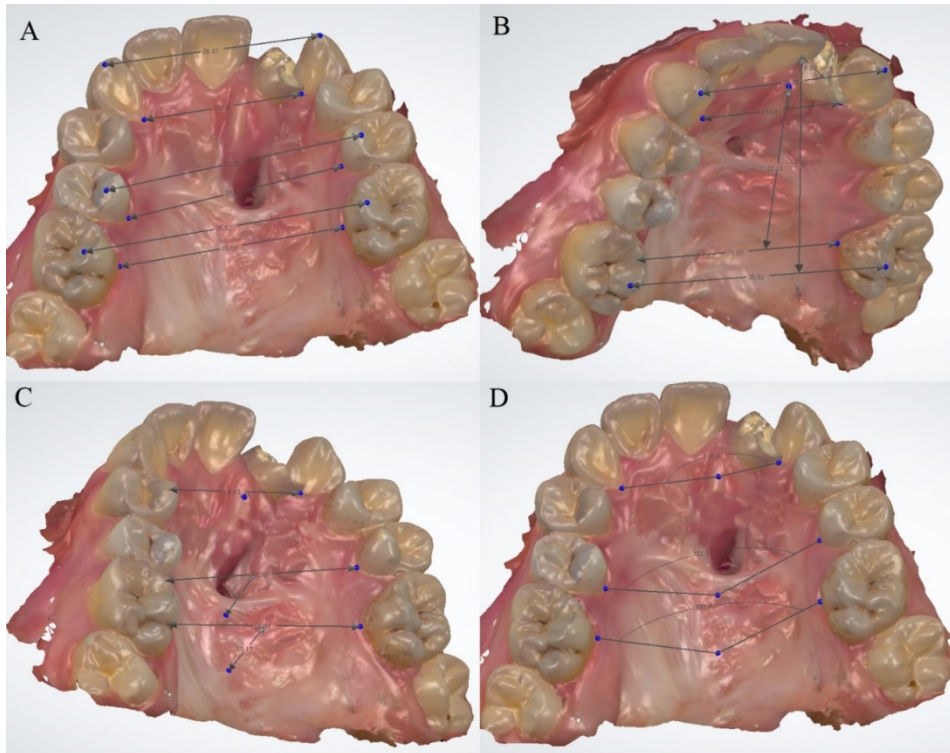


Figure 5. Maxillary arch dimensions and palatal dimensions: **(A)** maxillary arch widths and palatal widths, **(B)** maxillary arch lengths and palatal lengths, **(C)** palatal depths, and **(D)** palatal angles.

4.2.8. Patient satisfaction (Paper VII)

4.2.8.1. The Cleft Hearing, Appearance, and Speech Questionnaire (CHASQ)

We utilized CHASQ, which is a simple and easy-to-use, yet comprehensive, questionnaire that assesses satisfaction of a subject on 15 items: face, whole appearance, side view/profile, good-looking, nose, lips, chin, teeth, cheeks, hair, ears, eyes, speech, hearing, and noticeability (Appendix B). The 15 items can be grouped into two factors using an exploratory factor analysis with promax rotation. Factor 1 includes features that are associated with having been born

with a cleft. Factor 2 includes features that are less associated with having been born with a cleft (Cleft Psychology Special Interest Group (SIG), 2014).

The subjects can rate their satisfaction on an 11-point scale ranging from 0 (“very unhappy”, “not at all good-looking”, or “very noticeable”) to 10 (“very happy”, “very good-looking”, or “not at all noticeable”). The score 6–10 is the norm; 1–5 is less satisfied than the norm; and 0 is much less satisfied than the norm (Cleft Psychology Special Interest Group (SIG), 2014).

The CHASQ was translated into the Vietnamese and Estonian languages following a validation process. The process consisted of three stages: forward translation, backward translation, and patient testing (Mapi Research Institute, 2005). After testing, the final versions were released (Appendix C and D).

4.2.8.2. Satisfaction assessment

We assessed the satisfaction of both patients and their parents with the outcomes of the cleft treatment. The parents and patients completed the CHASQ independently. They could have assistance from an interviewer when completing the questionnaire if they did not understand certain questions. The procedure was the same for the Vietnamese and Estonian samples.

4.3. Statistical analysis

The data was analysed using Statistical Package for the Social Science (SPSS) version 22.0 (SPSS Inc, Chicago, IL). The chi-square test was used to compare categorical variables. Independent t-test and one-way ANOVA were used to compare continuous variables. The difference was statistically significant when the *p*-value was smaller than 0.05.

In paper III, intraclass correlation coefficient (ICC) based on a mean-rating ($k = 5$), absolute agreement, and two-way random-effects was used to calculate inter-rater reliability. ICC based on a mean rating ($k = 5$), absolute agreement, and two-way mixed-effects was used to calculate intra-rater reliability. For each ICC score, 95% confidence intervals (95% CI) were calculated (Koo and Li, 2016). Cronbach’s alpha (α) was used to calculate the reliability of the five-point aesthetic index and reference scores method.

In paper IV, test-retest reliability was examined by calculating differences in the mean scores between the test and retest sessions for each stimulus. The differences were categorized as being <1 , ≥ 1 and <2 , etc. The number of subject in each category was determined, then cumulative frequencies were converted into cumulative percentages (Van Doorn and Purcell, 1998; Whitehill, 2001).

In paper VI, the intra-examiner errors of cast measurement were measured with a paired t-test (systematic error). The method errors of cephalometric measurement were calculated using Dahlberg’s formula (Cançado and Lauris, 2014; Dahlberg, 1940).

In paper VII, A Mann-Whitney U test was used to compare the differences in the ratings between Vietnamese and Estonian patients. A Wilcoxon signed-rank test was conducted to compare the differences in the satisfaction between patients and their parents. A Spearman correlation coefficient was used to test the level of agreement between patients and their parents.

4.4. Ethical considerations

All studies were approved by the Ethics Committee of Hue University of Medicine and Pharmacy (24th December 2015). The studies related to Estonian samples were additionally approved by the Ethics Committee of the University of Tartu (reference number 278/T-1). Informed consent was obtained from the patients, controls, and parents. In case the participants were younger than 18 years, informed consent was obtained from their parents. In the consent form, participants also allowed to use their photos in printed publications. Informed consent was obtained before participants were included in the study. The ones who did not meet the inclusion criteria or did not want to participate were excluded from the study.

Data using in the present studies such as questionnaires, speech assessment, models, photos, and radiographs were anonymized and coded. Only the primary researcher can link these codes back to the subjects.

5. RESULTS

5.1. General information

The ratio between female and male was 1:1. The ratio between CL±A, CLP, and CP was 1:3:1. There was a 1:1 female to male ratio for CL±A and CLP, 2:1 female to male ratio for CP, 4:1 left to right-sided unilateral CLP, and 2:1 left to right-sided unilateral CL±A. The age of patients ranged from 1 to 54 years old with a median age of 6.0 years old.

Most patients came from Thua Thien-Hue Province (80.8%): Hue (29.5%), district-level towns (16.7%), and districts (34.6%); the other patients came from neighbour cities in central Vietnam (19.2%). The socioeconomic status of parents was mostly middle socioeconomic status (63.6% of the father, 65.4% of the mother).

Distribution of patients and demographic characteristics of the samples in our publications are described in Table 4.

Table 4. Distribution of patients and demographic characteristics

Publication No.	Cleft group				Control group				
	Sample size	Cleft types	Median age (years)	Gender (F/M)	Sample size	Ethnicity	Cleft types	Median age (years)	Gender (F/M)
I	78	15 CL±A, 46 CLP, 17 CP	6.0	40/38	–	–	–	–	–
II	76 (parents)	–	–	–	–	–	–	–	–
III	23	UCLP	6.0	13/10	33	Estonian	UCLP	10.0	9/24
IV	–	–	–	–	102	Vietnamese	Non-cleft	7.0	57/45
V	38	28 CLP, 10 CP	8.0	21/17	–	–	–	–	–
VI	17	11 CLP, 6 CP	9.0	11/6	34	Vietnamese	Non-cleft	9.5	13/21
VII	29	7 CL±A, 15 CLP, 7 CP	15.0	19/10	27	Estonian	4 CL±A, 17 CLP, 6 CP	12.3	11/16

F: female; M: male; CL±A: cleft lip with or without cleft alveolus; CLP: cleft lip and palate; UCLP: unilateral cleft lip and palate; CP: cleft palate
–: not applicable

5.2. Oral health status (Paper I)

More than half of the patients (51.3%) visited dentists at least once a year due to the following reasons: treatment/follow-up treatment (47.5%); pain or trouble with teeth, gums, or mouth (42.5%). A majority of patients brushed their teeth at least once a day (87.2%) using a toothbrush (89.7%) with toothpaste (84.6%). Some patients reported other methods to clean their teeth including: scrubbing their teeth using gauze with or without saline, scrubbing the teeth with lime, brushing with salt, or rinsing with saline or mouthwash.

Caries prevalence in patients with CL/P in Central Vietnam was 87.2%. Dental caries experience levels were classified as very high based on the dmft/DMFT index. The dmft of children with CL/P ≤ 5 years old was 7.4 ± 6.6 . The dmft and DMFT of children with CL/P ages 6–12 were 9.0 ± 5.1 and 1.6 ± 1.8 respectively. The DMFT of patients with CL/P ≥ 13 years old was 6.7 ± 5.0 . No significant differences were found in the caries experience between the age groups, cleft types, side of the cleft, or gender ($p > 0.05$) except the DMFT between 6–12 years and ≥ 13 years old groups ($p < 0.05$) (Table 5). There was an association between caries experience and socioeconomic status of the parents ($p < 0.05$). There were no statistically significant differences in caries experience related to living areas ($p > 0.05$).

Table 5. Caries prevalence and dmft/DMFT index of the study population

		Caries prevalence	dmft	DMFT
Age group	≤ 5 years	79.4%	7.4 ± 6.6	-
	6–12 years	100%	9.0 ± 5.1	1.6 ± 1.8
	≥ 13 years	86.4%	-	6.7 ± 5.0
Cleft type	CL±A	86.7%	6.1 ± 4.8	4.9 ± 5.7
	CLP	89.1%	8.0 ± 5.6	4.1 ± 4.5
	CP	82.4%	9.2 ± 7.4	3.6 ± 3.6
Side of cleft	Unilateral	85.4%	8.2 ± 5.7	3.5 ± 3.1
	Bilateral	95.0%	6.4 ± 4.8	5.3 ± 6.3
Gender	Female	90.0%	8.9 ± 6.7	4.5 ± 4.1
	Male	84.2%	7.3 ± 5.3	3.6 ± 5.1

dmft/DMFT: decayed, missing, and filled teeth; CL±A: cleft lip with or without cleft alveolus; CLP: cleft lip and palate; CP: cleft palate

–: not applicable

About 60% of patients with CL/P experienced bleeding on probing, and 5.3% (patients > 15 years old, $n = 19$) had periodontal pockets with depths of 3.5–5 mm. The mean averages for the number of teeth without bleeding, and with bleeding were 18.5 ± 5.2 , and 2.7 ± 3.7 , respectively. There was a significant difference in the presence or absence of bleeding on probing between age

groups ($p < 0.05$) (Table 6). There was no association between periodontal diseases and socioeconomic status of the parents ($p > 0.05$). There were no statistically significant differences in periodontal diseases related to living areas ($p > 0.05$).

Table 6. Gingival bleeding status of the study population

		No bleeding on probing	Bleeding on probing	p-value
Age group	≤ 5 years	20 (58.8%)	14 (41.2%)	0.004*
	6–12 years	10 (45.5%)	12 (54.5%)	
	≥ 13 years	3 (13.6%)	19 (86.4%)	
Cleft type	CL±A	5 (33.3%)	10 (66.7%)	0.712
	CLP	20 (43.5%)	26 (56.5%)	
	CP	8 (47.1%)	9 (52.9%)	
Side of cleft	Unilateral	18 (43.9%)	23 (56.1%)	0.357
	Bilateral	7 (35.0%)	13 (65.0%)	
Gender	Female	14 (35.0%)	26 (65.0%)	0.180
	Male	19 (50.0%)	19 (50.0%)	

CL±A: cleft lip with or without cleft alveolus; CLP: cleft lip and palate; CP: cleft palate;

* $p < 0.05$

5.3. Maternal experiences (Paper II)

The mothers expressed their feelings of having a child with CL/P as a single feeling or a combined feeling. The single feelings were afraid, anxious, tired, varying degrees of sadness (sad or very sad). The combined feelings were: anxious and nervous; anxious and sad; misery and desperate; sad and afraid; sad and afraid to give birth; sad and cried; sad and depressed; sad and discouraged; sad and heartbroken; sad and shock; surprise and anxious. The most common feeling was sad (60.5% as a single feeling, or 84.2% as a combined feeling). The feelings of the mothers were not associated with the cleft type, prenatal, or postnatal diagnosis ($p > 0.05$).

Almost half of the mothers could not think of what caused CL/P in their child (47.4%). Others listed several causes of CL/P according to their opinions: diseases or abnormal conditions (27.6%), medications (11.8%), chemicals (3.9%), or hereditary factors (9.3%). They believed CL/P could have been caused during pregnancy from: a common cold, fever, hyperthyroidism, meningitis, sleeplessness, stress, or old age during pregnancy. They mentioned the medications could be excessive vitamin A or anti-cold medicine; the chemicals could be dioxin or pesticide. Educational level or socioeconomic status did not affect the belief of the mothers ($p > 0.05$).

Most of the mothers had support from their husband and/or family members (92.1%). About 40% of the mother reported that having a child with CL/P did not cause major changes in their life. Other mothers listed some challenges such

as financial issues, feeding problems, mental depression, or general difficulties. A majority of the mothers did not hide their child from the public (78.9%). The cleft type was not associated with the support from families nor changes in the mother's postpartum life ($p > 0.05$).

5.4. Nasolabial aesthetics (Paper III)

The reliability of the five-point aesthetic index was good ($\alpha = 0.80$), and the reliability of the reference scores method was acceptable ($\alpha = 0.69$). The inter-rater reliability test showed a moderate (ICC = 0.630, reference scores method) to a good agreement (ICC = 0.864, five-point aesthetic index) of the five raters. The intra-rater reliability agreement ranged from moderate to excellent reliability.

Among the four features assessed in the five-point aesthetic index, the nasal symmetry was rated lowest (2.7 ± 0.9) in the Vietnamese sample, whereas nasolabial profile was rated lowest (2.7 ± 1.0) in the Estonian sample. No significant differences in nasolabial aesthetics between the two samples were observed ($p > 0.05$) except for nasal symmetry (Table 7). Overall, the nasolabial aesthetics of operated patients with CL/P in both samples showed a fair appearance regardless of the rating method.

Table 7. Nasolabial aesthetics (mean score \pm standard deviation) in the Vietnamese and Estonian samples evaluated by three methods

		Vietnamese sample (n = 23)	Estonian sample (n = 33)	p-value
The five- point aesthetic index	Nasal form	2.8 ± 1.2	3.2 ± 0.9	0.241
	Nasal symmetry	2.7 ± 0.9	3.1 ± 0.8	0.039*
	Vermilion border	3.1 ± 0.8	3.0 ± 0.7	0.678
	Nasolabial profile	3.1 ± 0.9	2.7 ± 1.0	0.076
	Nasolabial scores	2.9 ± 0.8	3.0 ± 0.7	0.729
VAS method	VAS score	54.6 ± 14.0	53.7 ± 15.2	0.824
Reference scores method	Facial	103.7 ± 16.9	102.2 ± 17.7	0.752
	Profile	102.3 ± 12.1	110.1 ± 19.5	0.072
	Total	103.0 ± 12.4	106.2 ± 16.7	0.423

VAS: visual analogue scale

* $p < 0.05$

5.5. Nasalance scores (Paper IV, V)

The test-retest reliability of obtaining normative nasalance scores was acceptable. The test-retest difference in mean nasalance scores was within seven points in over 85% of the children for the oral stimuli; within seven points in about 70% of the children for the oro-nasal stimuli; within ten points in over 75% of the children for the nasal stimuli.

The mean nasalance scores for non-cleft Vietnamese-speaking children were 13.1% for oral stimuli, 30.7% for oro-nasal stimuli, and 56.9% for nasal stimuli. No significant differences between genders were found ($p > 0.05$).

The mean nasalance scores for Vietnamese-speaking patients with CP±L were 30.2% for oral stimuli, 42.8% for oro-nasal stimuli, and 58.7% for nasal stimuli. More than half of the patients (52.6%) had hypernasality. Adult patients had significantly higher nasalance scores in three of the speech stimuli compared to the child patients ($p < 0.05$) (Table 8).

Table 8. Nasalance scores (mean score ± standard deviation) for operated Vietnamese-speaking children and adults with CP±L

	Oral words	Oral sentences	Oral stimuli	Oro-nasal stimuli	Nasal stimuli
Children (n = 27)	24.6 ± 14.9	29.0 ± 17.4	26.8 ± 16.1	39.9 ± 12.6	56.8 ± 8.2
Adults (n = 11)	35.0 ± 14.6	41.7 ± 15.1*	38.3 ± 14.8*	49.9 ± 12.1*	63.5 ± 7.4*
Total (n = 38)	27.6 ± 15.4	32.7 ± 17.6	30.2 ± 16.4	42.8 ± 13.2	58.7 ± 8.5

CP±L: cleft palate with or without cleft lip;

* $p < 0.05$

5.6. Craniofacial morphology and upper airway structures (Paper VI)

The method errors for the linear and angular measurements were not statistically significant and did not exceed 1 mm and 1°, respectively ($p < 0.05$).

The craniofacial morphology of children with CL/P included: a more acute cranial base angle (Ba-SN), shorter cranial base length (Ba-N), shorter and more retruded maxilla (Co-A, ANS-PNS, SNA), more class III skeletal (ANB), shorter anterior face height (N-Me, N-ANS, ANS-Me), and shorter mandibular length (Co-Gn). The upper airway structures of children with CL/P had a more anteriorly positioned hyoid bone, smaller inferior oropharyngeal airway space and retroglottal airway dimensions, and a shorter soft palate (Table 9).

The craniofacial morphology of adults with CL/P also showed a class III skeletal, a hyperdivergent skeletal pattern, shorter anterior cranial base length, and shorter maxilla length. The upper airway structures of adults with CL/P had a more posteriorly positioned hyoid bone, and a shorter soft palate (Table 9).

5.7. Maxillary arch dimensions and palatal dimensions (Paper VI)

The paired samples correlations ranged from 0.66 to 0.98. There were no statistically significant systematic errors ($p < 0.05$).

Children with CL/P had significantly smaller dimensions of the maxillary arch in three-dimensional planes. They had significantly narrower arch widths and palatal widths at the canine and premolar level, shorter arch lengths and palatal lengths, and a shallower palate. However, the arch width and palatal width at the molar level were not significantly different ($p > 0.05$) (Table 10).

Adults with CL/P had a significantly narrower arch and palatal widths (at the canine, premolar, and molar level), and shorter arch and palatal lengths. The palatal depths and angles were not significantly different between the cleft and non-cleft group ($p > 0.05$) (Table 10).

Table 9. Craniofacial morphology and upper airway structures of children and adults with CL/P

	Cleft children (n = 12)	Non-cleft children (n = 24)	p-value	Cleft adults (n = 5)	Non-cleft adults (n = 10)	p-value
SNA (°)	78.2 ± 3.7	81.6 ± 4.6	.028	78.3 ± 4.3	82.9 ± 3.1	ns
SNB (°)	77.2 ± 3.2	77.9 ± 3.6	ns	77.9 ± 1.2	79.2 ± 3.6	ns
ANB (°)	1.0 ± 2.9	3.6 ± 2.4	.016	0.4 ± 3.6	3.7 ± 1.6	.027
SN-MP (°)	39.3 ± 4.7	39.9 ± 5.0	ns	39.3 ± 4.6	32.8 ± 4.6	.031
SN-PP (°)	1.2 ± 3.8	0.9 ± 3.3	ns	-1.9 ± 5.4	0.5 ± 4.5	ns
Ar-GoMe (°)	135.5 ± 5.2	133.2 ± 6.2	ns	128.8 ± 6.2	124.6 ± 5.5	ns
Ba-SN (°)	128.6 ± 6.4	133.2 ± 5.0	.044	129.3 ± 6.0	132.0 ± 4.8	ns
N-Me (mm)	107.1 ± 6.3	113.0 ± 6.5	.016	123.2 ± 8.8	124.5 ± 9.7	ns
N-ANS (mm)	43.6 ± 3.3	46.0 ± 2.6	.038	46.7 ± 5.4	49.6 ± 5.7	ns
ANS-Me (mm)	54.5 ± 3.7	58.3 ± 4.7	.015	65.9 ± 4.5	65.0 ± 5.4	ns
S-Go (mm)	59.8 ± 5.4	62.8 ± 5.2	ns	68.9 ± 6.6	76.2 ± 5.0	ns
S-Ar (mm)	27.9 ± 2.9	28.7 ± 3.2	ns	31.5 ± 3.4	32.9 ± 3.3	ns
Co-Go (mm)	44.3 ± 4.1	46.6 ± 3.6	ns	50.8 ± 6.1	57.4 ± 4.1	ns
Ba-N (mm)	88.3 ± 4.0	92.2 ± 4.6	.014	92.4 ± 6.1	99.4 ± 4.9	ns
S-N (mm)	59.3 ± 3.6	59.6 ± 2.6	ns	61.4 ± 1.9	65.5 ± 4.0	.017
S-Ba (mm)	38.2 ± 3.7	40.7 ± 3.8	ns	40.3 ± 5.8	42.8 ± 1.8	ns
ANS-PNS (mm)	34.7 ± 2.9	40.3 ± 2.8	< 0.001	39.4 ± 5.2	46.0 ± 4.4	0.021
Co-A (mm)	68.5 ± 2.9	73.8 ± 4.6	< 0.001	72.8 ± 3.9	80.5 ± 4.7	.008
Co-Gn (mm)	95.9 ± 5.9	101.5 ± 4.7	0.004	109.5 ± 9.7	113.0 ± 7.0	ns
U1-SN (°)	99.8 ± 8.8	108.0 ± 5.8	.010	101.8 ± 5.4	104.2 ± 11.7	ns
U1-PP (°)	108.0 ± 8.4	115.9 ± 4.4	.009	106.9 ± 4.7	111.8 ± 11.7	ns
L1-NB (°)	19.9 ± 7.5	30.0 ± 3.8	.001	24.3 ± 12.4	30.1 ± 5.7	ns
L1-MP (°)	6.6 ± 9.3	-2.1 ± 5.7	.009	2.9 ± 12.1	-8.1 ± 9.3	ns
U1-L1 (°)	137.5 ± 11.3	119.9 ± 5.3	< 0.001	131.8 ± 15.3	124.9 ± 13.7	ns
Tongue length (mm)	53.5 ± 5.6	56.7 ± 3.7	ns	63.5 ± 3.7	67.2 ± 5.2	ns
Tongue thickness (mm)	25.7 ± 2.0	26.9 ± 2.6	ns	30.6 ± 1.9	30.2 ± 2.8	ns
H-MP (mm)	10.3 ± 4.8	12.6 ± 5.4	ns	16.0 ± 5.9	13.4 ± 4.6	ns

	Cleft children (n = 12)	Non-cleft children (n = 24)	p-value	Cleft adults (n = 5)	Non-cleft adults (n = 10)	p-value
H-C3 (mm)	28.5 ± 6.5	29.9 ± 3.2	ns	32.0 ± 2.0	35.2 ± 3.8	.047
C3-RGN (mm)	54.0 ± 6.5	59.2 ± 4.6	.025	65.0 ± 6.6	65.8 ± 5.0	ns
H-RGN (mm)	26.6 ± 5.6	30.8 ± 4.4	.036	35.2 ± 6.0	34.0 ± 4.6	ns
Hyoid angle (°)	138.7 ± 18.1	133.1 ± 17.6	ns	126.8 ± 20.4	134.8 ± 15.3	ns
PNS-ad2 (mm)	16.4 ± 4.5	15.7 ± 2.7	ns	21.2 ± 4.4	25.6 ± 3.0	ns
PNS-ad1 (mm)	20.2 ± 3.7	22.2 ± 4.0	ns	23.5 ± 6.0	27.1 ± 3.0	ns
U'-MPW1 (mm)	10.7 ± 2.8	11.5 ± 2.1	ns	14.8 ± 2.9	13.3 ± 4.1	ns
U-MPW2 (mm)	8.9 ± 2.2	10.5 ± 2.3	ns	12.8 ± 1.7	9.5 ± 4.8	ns
TP-MPW3 (mm)	11.3 ± 3.0	13.6 ± 3.0	.041	13.2 ± 1.9	12.0 ± 4.7	ns
PAS min (mm)	9.6 ± 2.9	13.0 ± 2.8	.003	11.3 ± 1.2	11.3 ± 4.3	ns
Eb-LPW (mm)	11.6 ± 4.3	14.2 ± 3.2	ns	17.0 ± 1.0	14.6 ± 3.9	ns
PNS-Eb (mm)	47.5 ± 3.8	49.8 ± 4.6	ns	61.3 ± 5.1	60.5 ± 6.7	ns
SN-CVT (°)	102.4 ± 7.9	105.8 ± 8.4	ns	108.0 ± 8.1	107.9 ± 7.3	ns
Soft palate length (mm)	23.7 ± 3.7	27.5 ± 4.9	.014	24.0 ± 2.5	31.6 ± 5.8	.004
Soft palate thickness (mm)	6.8 ± 1.7	7.6 ± 1.2	ns	6.7 ± 2.5	9.2 ± 1.6	ns

CL/P: cleft lip and/or palate;

ns: not significant

Table 10. Maxillary arch dimensions and palatal dimensions of children and adults with CL/P

	Cleft children (n = 12)	Non-cleft children (n = 24)	p-value	Cleft adults (n = 5)	Non-cleft adults (n = 10)	p-value
ICW (mm)	28.1 ± 3.6	32.5 ± 2.6	< 0.001	23.3 ± 5.9	32.1 ± 1.8	.026
IPW (mm)	32.0 ± 4.4	37.3 ± 3.6	0.001	31.2 ± 3.9	38.1 ± 1.6	.013
IMW (mm)	40.0 ± 3.1	41.3 ± 3.1	ns	36.4 ± 3.6	40.8 ± 2.1	.011
CAL (mm)	5.7 ± 2.2	8.6 ± 1.2	0.001	5.4 ± 2.7	7.9 ± 1.2	.027
MAL (mm)	23.3 ± 3.0	32.2 ± 1.9	< 0.001	23.9 ± 2.7	28.6 ± 1.5	0.001
Palatal width C (mm)	22.8 ± 2.6	27.3 ± 2.2	< 0.001	19.1 ± 3.7	24.9 ± 1.6	0.021
Palatal width P (mm)	25.5 ± 9.1	32.3 ± 2.6	0.027	27.6 ± 3.6	35.3 ± 1.2	< 0.001
Palatal width M (mm)	32.5 ± 3.5	34.3 ± 2.3	ns	31.0 ± 2.7	36.7 ± 1.8	< 0.001
Palatal length C (mm)	4.8 ± 2.5	6.5 ± 0.8	0.41	5.7 ± 2.0	7.5 ± 1.0	ns
Palatal length M (mm)	23.3 ± 1.8	28.2 ± 1.6	< 0.001	21.7 ± 1.8	25.8 ± 1.4	< 0.001
Palatal depth C (mm)	2.2 ± 1.3	3.4 ± 1.1	0.007	2.5 ± 1.3	3.9 ± 0.7	0.018
Palatal depth P (mm)	5.4 ± 2.8	11.6 ± 1.6	< 0.001	10.9 ± 2.4	11.2 ± 1.7	ns
Palatal depth M (mm)	7.0 ± 2.8	11.2 ± 1.7	< 0.001	10.5 ± 3.6	10.8 ± 1.9	ns
Palatal angle C (°)	156.8 ± 14.6	151.4 ± 8.7	ns	148.4 ± 22.0	145.5 ± 6.0	ns
Palatal angle P (°)	122.0 ± 40.9	108.4 ± 9.2	ns	103.6 ± 12.4	115.1 ± 8.7	ns
Palatal angle M (°)	134.4 ± 14.3	113.8 ± 9.8	< 0.001	112.5 ± 18.2	119.4 ± 10.0	ns

CL/P: cleft lip and/or palate;

ICW: intercanine width; IPW: interpremolar width; IMW: intermolar width; CAL: canine arch length; MAL: molar arch length; C: at the canine level; P: at the premolar level; M: at the molar level
ns: not significant

5.8. Patient satisfaction (Paper VII)

Patients rated their satisfaction above the norm on a majority of CHASQ items. The satisfaction towards teeth and lips was rated below the norm by Vietnamese patients. Whereas, Estonian patients did not express their satisfaction below the norm for any items. Comparing between Vietnamese and Estonian samples, Vietnamese patients scored their satisfaction significantly lower than Estonian patients on every item ($p < 0.05$) except for speech ($p > 0.05$) (Figure 6).

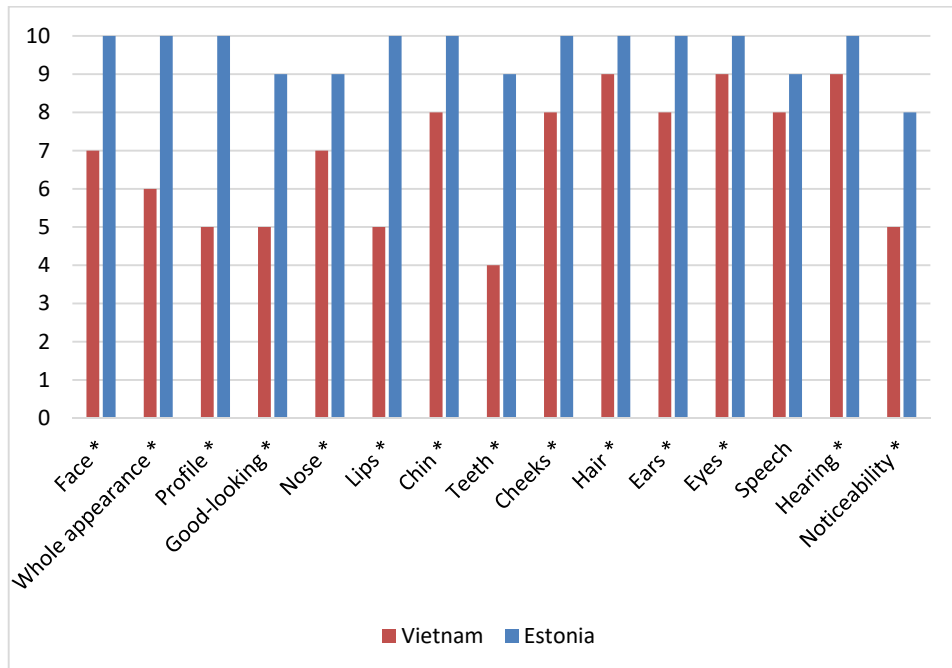


Figure 6. Median scores of each item of the CHASQ scored by Vietnamese and Estonia patients. The Mann-Whitney U test was used to compare the scores between Vietnamese and Estonian samples (* $p < 0.05$)

Parents scored their satisfaction above the norm for all CHASQ items. Vietnamese parents tended to rate their satisfaction higher than their children ($p < 0.05$) (Figure 7A), whereas Estonian parents rated their satisfaction lower than their children ($p < 0.05$) (Figure 7B).

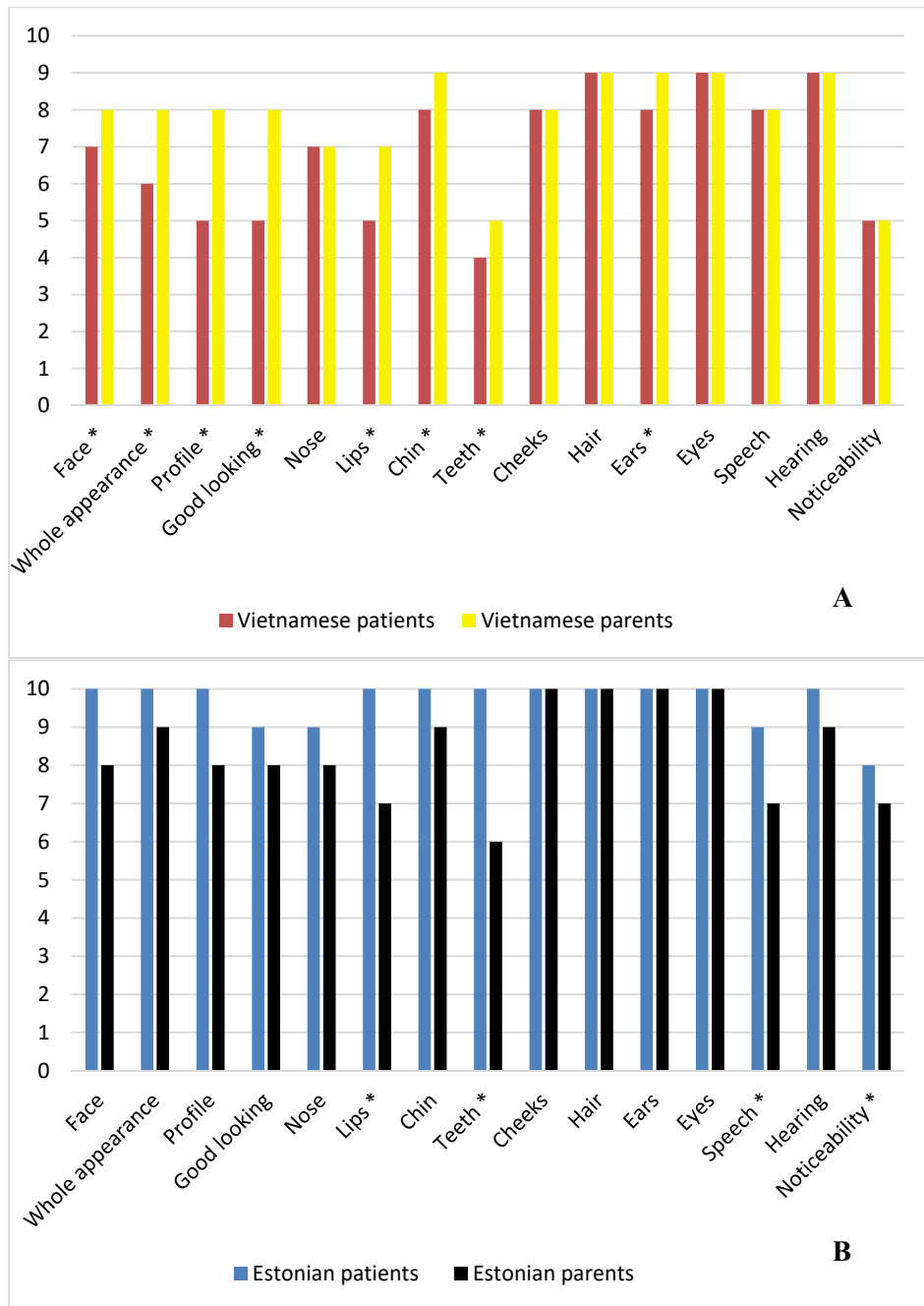


Figure 7. Median scores of each item of the CHASQ scored by (A) Vietnamese patients and their patients; (B) Estonian patients and their parents. The Wilcoxon test was used to compare the scores between the patients and their parents (* $p < 0.05$)

In both the Vietnamese and Estonian samples, no significant high or very high positive correlations were found between patients and their parents. In the Vietnamese sample, moderate and significant correlations were found in these items: face, nose, lips, teeth, and speech. In the Estonian sample, a moderate and significant correlation was found in only one item: nose (Table 11).

Table 11. The correlations between patients and their parent on the satisfaction of CHASQ items determined by Spearman's correlation coefficient (rho)

	Country	rho	p-value
Face	Vietnam	.64*	<.001
	Estonia	.28	.16
Whole appearance	Vietnam	.18	.36
	Estonia	.12	.54
Side view/Profile	Vietnam	.10	.60
	Estonia	.10	.61
Good-looking	Vietnam	.41	.03
	Estonia	.24	.23
Nose	Vietnam	.53*	<.01
	Estonia	.60*	<.01
Lips	Vietnam	.65*	<.001
	Estonia	.41	.03
Chin	Vietnam	.24	.21
	Estonia	-.00	.98
Teeth	Vietnam	.65*	<.001
	Estonia	.21	.29
Cheeks	Vietnam	.11	.57
	Estonia	.07	.75
Hair	Vietnam	.16	.41
	Estonia	-.02	.92
Ears	Vietnam	.28	.14
	Estonia	-.00	.99
Eyes	Vietnam	.32	.09
	Estonia	-.07	.73
Speech	Vietnam	.60*	<.01
	Estonia	.43	.03
Hearing	Vietnam	.48	.01
	Estonia	.15	.45
Noticeability	Vietnam	.10	.62
	Estonia	.44	.02

Bold formatting indicates significant correlations ($p < 0.05$).

An asterisk (*) indicates both moderate and significant correlations ($0.5 < \rho < 0.7$ and $p < 0.05$).

6. DISCUSSION

To the best of my knowledge, this is the first study to report different treatment outcome aspects of surgically treated patients with CL/P in Central Vietnam. The study investigated the patient's oral health, nasolabial aesthetics, speech, craniofacial morphology, maxillary arch dimensions, palatal dimensions, and upper airway structures. Moreover, we evaluated the patient's satisfaction with the treatment outcomes and maternal experiences of having a child with CL/P. The results rejected the null hypothesis that patients with CL/P in Central Vietnam had an acceptable or a moderate result for each treatment outcome, because only two outcomes (nasolabial aesthetics and satisfaction) were acceptable. The other outcomes on oral health status, speech, craniofacial morphology, maxillary arch dimensions, palatal dimensions, and upper airway structures were poor.

6.1. Oral health status (Paper I)

Patients with CL/P in our study demonstrated a very high level of dental caries experience. The level of caries was similar or even higher compared to other cleft populations (Besseling and Dubois, 2004; Al-Dajani, 2009; Britton and Welbury, 2010; Zhu et al., 2010; Xiao et al., 2015). Although the methods of control and prevention, as well as treatment for dental caries, are well-developed, individuals with CL/P still have a higher caries experience compared to the general population (Pinto et al., 2013; Antonarakis et al., 2013). A number of reasons have been proposed to explain the scenario of high caries experience in patients with CL/P: dry mouth because of mouth breathing habit, reduction of salivary secretion rate, longer clearance time of food, high levels of caries-associated micro-organisms, less natural cleansing of the teeth by the tongue and saliva due to crowding teeth, and enamel hypoplasia (Cheng et al., 2007; Zhu et al., 2010; Dahllof et al., 1989; Ahluwalia et al., 2004; Johnsen and Dixon, 1984). Additionally, parents might play a role in controlling caries. The parents tend to focus more on surgical procedures to correct the cleft rather than early dental care (Al-Dajani, 2009). Low socioeconomic status is a risk factor in the development of caries (Antonarakis et al., 2013). Misinformation or lack of education and prevention in oral health may contribute to the situation (Pinto et al., 2013).

Besides those reasons, there are several explanations for the very high caries experience in our study. Patients as well as their parents prioritized cleft surgery and paid little attention to oral health. The patients did not have a good practice of cleaning their teeth and did not have regular dental check-ups. Most of the parents in our study had a low or middle socioeconomic status. Their socioeconomic status was correlated with an increased risk of caries experience. Vietnamese parents usually underestimated the importance of maintaining healthy primary teeth because they think primary teeth will be replaced by

permanent teeth later in their life. Lastly, hidden sugar in Vietnamese dishes is a potential risk. Sugar is added not only to sweet dishes but also to other foods, such as savoury dishes and juices.

Patients in our study experienced gingivitis but not periodontitis. Previous research also showed that patients with CL/P have gingivitis more frequently than non-cleft individuals (Dahllof et al., 1989). The prevalence of gingivitis is around 80% (Fadeyibi et al., 2011; Lages et al., 2004; Ramstad, 1989). The major reason is the difficulty in cleaning teeth because of changes in the anatomy in the cleft region (Dahllof et al., 1989). The cleft deformity, surgical scars, or crowding can make it difficult to control plaque (Wong FWL and King, 1998; Stec-Slonicz et al., 2007). In our study, the patients reported brushing their teeth frequently; however, the gingival bleeding index was still high. We could infer that the patients did not perform a proper brushing technique to effectively remove plaque and achieve good oral health. The patients in our study did not receive presurgical orthopaedic appliances, orthodontic treatment, or bone grafting; therefore, those reasons could be ruled out.

6.2. Maternal experiences (Paper II)

In our study, the predominant feeling of the mothers of having a child with CL/P was sadness. The feelings of Vietnamese mothers were less extreme and aggressive compared to prior studies. It has reported that the mother usually feels shocked or surprised (Slutsky, 1969; Johansson and Ringsberg, 2004; McCorkell et al., 2012; Natsume et al., 1987; Vanz and Ribeiro, 2011). The difference in the feeling of the mothers in our study might be because of the following reasons. They might be aware of the CL/P from different resources; therefore, they were not shocked at the defect. They felt sad as a result of the disappointment of the defect and their inability to undo the defect. Due to a strong Buddhist influence in Vietnam, the mothers might also view the defect as bad karma and have a sympathetic attitude to the defect (Hutchinson et al., 2011). Finally, changes in the family planning policy in Vietnam might have eased the mother's initial feelings. Since the 1960s, the two-child policy was implemented to control the fertility rate in the chaos of the population explosion at that time. From the 2000s, the policy was changed into "each family should have two children" (Nam Phuong and Le Phuong, 2017). Since 2018, the Population Law stated: "couples will be self-determined about their child's birth, the distance between births, and the number of children" (N.Q., 2018).

Beliefs about the causes of CL/P are related to geographic location, and cultural attitudes (Mednick et al., 2013). "Unknown" is the most common response to causal attribution of CL/P by Vietnamese mothers. Beliefs were similar to people in Kenya, Russia, Cambodia, and Peru (Mednick et al., 2013); however, people in the UK reported "unknown" as the least common response (Nelson J et al., 2009). The difference might be due to the amount of prenatal counselling and education provided in developing and developed countries

(Mednick et al., 2013). Vietnamese mothers did not mention any supernatural causes or folk beliefs, which could be a positive effect of modernization. Some supernatural beliefs existed in other cultures such as “God’s will”, the punishment of sins in the past life, or witchcraft (Weatherley-White et al., 2005; Mzezewa and Muchemwa, 2010).

Vietnamese mothers had support from their husbands and/or other family members. They also did not hide their child with CL/P from the public. It was shown that mothers of a child with visible clefts perceived more social support than mothers whose child had less visible clefts (Sank et al., 2003). In some places, parents were anxious about exposing their child to new situations, or hide their child from the public for some time (Mzezewa and Muchemwa, 2010; Weatherley-White et al., 2005).

6.3. Nasolabial aesthetics (Paper III)

Changes in facial aesthetics, especially nasolabial aesthetics because of the cleft, could cause negative psychosocial consequences, difficulty in making friends, or problems in relationships with family and friends (Noor and Musa, 2007; Rankin and Borah, 2003). Thus, it is important to evaluate nasolabial aesthetics as one of the cleft treatment outcomes (Witt and Marsh, 1997). In our study, nasolabial aesthetics were considered to have a fair appearance (nasolabial scores: 2.9). Based on the five-point aesthetic index, our result was similar to other inter-centre studies: six European centres (nasolabial score: 2.8–3.4), Americleft (nasolabial score: 2.8–3.0), and Eurocleft (nasolabial score: 2.8–3.7) (Brattstrom et al., 2005; Asher-McDade et al., 1992; Mercado et al., 2011). Despite differences in the treatment protocols such as presurgical orthopaedic appliances, bone grafts, various methods and the timing of lip and palate surgery, number of surgeons, and surgeon experience and skill, our study produced a comparable overall nasolabial aesthetics with the aforementioned centres. It is possible that patients might not need many treatments to achieve acceptable nasolabial aesthetics.

Nasolabial aesthetics can be determined by an objective assessment or subjective assessment. Objective assessments of facial aesthetics are generally inadequate because they often rely on hard tissue analysis, neglect the harmony of the face, and are not grounded in socially accepted aesthetic standards (Alley and Hildebrandt, 1988; Vegter et al., 1997). Subjective assessment—human perception—on the other hand, can act as a reliable measurement as long as a group of raters is used to overcome potential subjectivity (Alley and Hildebrandt, 1988). In this study, we used a panel of five raters, three different subjective methods with reference photographs, and a descriptive note of the four nasolabial features to increase the reliability.

6.4. Nasalance scores (Paper IV, V)

Patients with CL/P who have speech problems may also have problems with psychosocial functioning, difficulties with specific communication tasks, and problems with social relationships (Feeney et al., 2012). They could experience social exclusion and have feelings of introversion and low self-esteem (Henningsson et al., 2008; Shapiro et al., 2015). Therefore, it is essential to evaluate the speech outcome of cleft treatment. It is the cornerstone to make a decision for surgical revision procedures (Bickham et al., 2017).

This study developed the standard passages for the Vietnamese language, established the normative nasalance scores, and introduced the speech outcomes of patients with CP±L in Vietnam. As the speech outcomes had shown, a high prevalence of hypernasality in the study was concerned.

Instrumental assessment using the Nasometer has been proven to be an objective tool to assess nasalance in patients with CP and to complement the auditory perceptual assessment of speech (Pegoraro-Krook et al., 2014; Swennen et al., 2004). Nasalance scores obtained by the Nasometer are language dependent; thus, normative nasalance scores have been developed for many languages (Brunnegard and van Doorn, 2009; D'Haeseleer et al., 2015; El-Kassabi et al., 2015; Ibrahim et al., 2012; Karakoc et al., 2013). Also, since the distribution of phonemes in each language is different, standard passages for each language are needed (Keuning et al., 2002).

To interpret the nasalance scores, a cut-off score is applied (Van Doorn and Purcell, 1998). The cut-off score is determined by assuming a limit of 2 standard deviations beyond the mean (Van Doorn and Purcell, 1998). Since the mean scores of nasalance scores are dependent on the language, the cut-off score is also language-specific, for example 27% in the Brazilian Portuguese language, 29% in the Finnish language, or 32% in the English language (Dalston et al., 1991; Pegoraro-Krook et al., 2014; Haapanen, 1994). As for the Vietnamese language, nasalance scores for oral stimuli above 24.7% are considered hypernasal. Nasalance scores for nasal stimuli below 38.5% are deemed as hyponasal. Applying those findings to the present study, we found that hypernasality occurred in 52.6% ($n = 20$) of the patients. The occurrence of hypernasality was much higher than in other cleft studies, such as 10.2%–17.6% in children with UCLP in the UK, 11% in children with CLP and 38% in children with CP in Finland (Haapanen, 1994; Sell et al., 2001; Sell et al., 2015). The reasons could be oronasal fistula, lacking speech therapy, or different surgical techniques. An oronasal fistula is recognized as a contributor to hypernasality (Sell et al., 2001). About two-thirds of patients in the UK study received speech therapy, whereas, in our study, the patients did not have speech therapy at all (Sell et al., 2001). The study in the UK also showed that the centralization of cleft services improved speech outcomes (Sell et al., 2015).

6.5. Craniofacial morphology and upper airway structures (Paper VI)

Children with CL/P in our study possessed maxillary retrognathia, vertical dysplasia in the maxilla, and class III malocclusion. Those characteristics were well-documented in previous studies (Chen et al., 2012; Naqvi et al., 2015; Ebin et al., 2010). It is generally accepted that the normal growth of the maxilla is inhibited by scar tissue resulting from cleft surgery (Naqvi et al., 2015). Children with CL/P also had a significant reduction in their cranial base angle and mandibular length. Differences in the size and angulation of the cranial base were more likely related to genetic factors rather than postoperative scarring (Ebin et al., 2010). The smaller mandible was presumably to fit with the smaller and retruded maxilla, although, in fact, most of the children with CL/P had a Class III malocclusion (Gopinath et al., 2017).

Children with CL/P had a smaller inferior oropharyngeal airway space and pharyngeal airway space (PAS) but not the nasopharyngeal airway or hypopharyngeal airway. Adults with CL/P had no significant differences in terms of pharyngeal dimensions compared to non-cleft adults. Our findings mirrored the results of previous studies (Aydemir and Toygar-Memikoğlu, 2014; Aras et al., 2012; Pimenta et al., 2015; Cheung and Oberoi, 2012). Several authors reported that juveniles (6–12 years) and adolescents (13–17 years) with CL/P had a reduced airway passage size, nasopharyngeal airway area, and PAS distance (Agarwal and Marwah, 2016; Aras and Dogan, 2017; Imamura et al., 2002). Adults with CL/P (17–45 years) had a significantly lower total and superior airway volume but not the inferior airway volume compared to controls (Shahidi et al., 2016).

In our study, the hyoid bone position was obtained and modified from the hyoid triangle suggested by Bibby and Preston (1981). The hyoid triangle determines the hyoid bone position in three dimensions, is independent of the cranial reference plane, and minimizes incorrectness derived from changes in head posture (Bibby and Preston, 1981). We found that the hyoid bone was positioned more anteriorly. That position might reflect a habitual adaption to airway obstruction in the pharyngeal airway space (Wermker et al., 2012; Aras and Dogan, 2017).

Although cone beam computed tomography (CBCT), or computed tomography (CT) scans have been intensively used in recent years to study the airway structures, we used lateral cephalograms due to following reasons. Cephalometry is available at most hospitals and/or cleft centres in Vietnam and has a lower cost than CBCT or CT scans. Since CBCT is not indicated as routine radiology for all patients, it is easier to use cephalograms to compare with control groups (Jakobsone et al., 2010; SEDENTEXCT, 2012). We were also aware of the shortcomings of lateral cephalograms, such as magnification errors, superimposition of bilateral structures, difficulties in landmark identification, and a two-dimensional interpretation of three-dimensional structures (Jakobsone et al., 2010).

6.6. Maxillary arch dimensions and palatal dimensions (Paper VI)

Patients with CL/P had a shorter arch length and narrower maxilla compared with those of the controls. This finding was in agreement with previous studies (Bittencourt Dutra Dos Santos et al., 2015; Gopinath et al., 2017; Ye et al., 2010; Kilpelainen et al., 1996). Children with CL/P had a more pronounced constriction in the anterior regions, i.e. canine and premolar regions, but not in the molar regions. However, adults with clefts had narrower arches in both anterior and posterior regions. As for the palate height and palate angle, the significant differences between the cleft and control groups disappeared in the adult group. It seemed that adults with clefts caught up with the development of the palate in adulthood. As in the child cleft group, the palate depth was decreased, and the palate was flattened.

There are some factors that might affect the dimensions of the maxilla in patients with clefts, including: genetic factors, the type and timing of surgery, the skill of the surgeon, and the type and extent of the cleft, high incidence of hypodontia, untreated caries in primary teeth, scars after cleft surgery, and abnormal positioning of the tongue (Gopinath et al., 2017; Heliövaara and Rautio, 2005; Heliövaara et al., 2014). Morphological changes in different regions of the hard palate might be a result of scarring, habitual position of the tongue, and orofacial function (Gopinath et al., 2017; Berwig et al., 2011).

In this study, to eliminate bias in evaluating the transverse dimensions of the maxilla due to improper tooth position, such as buccal tipping, we measured the transverse dimensions at two landmarks: the tip (i.e. maxillary arch dimensions) and the palatal gingival margin of the tooth (i.e. palatal dimensions). Thus, we could determine the dimensions of the dental arch as well as the size of the palate.

6.7. Patient satisfaction (Paper VII)

Since health care is shifting from a traditional paternalistic approach to a patient-centred approach, patient-reported outcomes are becoming more important because treatment is viewed from patient's perspective, and observer bias could be avoided (Black, 2013; Fix et al., 2018; Deshpande et al., 2011). However, validated cleft-specific instruments to collect patient-reported outcomes are scarce (Jones et al., 2014; Shaye, 2014; Wong Riff et al., 2017). The Cleft Hearing, Appearance, and Speech Questionnaire (CHASQ) was designed and validated specifically for patients with CL/P and their parents. The CHASQ has been used in daily practice in the UK for audit purposes (Cleft Psychology Special Interest Group (SIG), 2014). Because the CHASQ was developed in the English language, it was translated into Vietnamese and Estonian following a linguistically validated process (Mapi Research Institute, 2005).

The CHASQ score interpretation suggests score above 5.0 is within the norm. Vietnamese patients scored their satisfaction with facial features, hearing, and speech above 5.0 except for lips and teeth. Therefore, the patients were most satisfied with their appearance, hearing, and speech. It is worth noting that among facial features, patients were least satisfied with their lips. It shows the major influence of the cleft on the satisfaction towards the lip and nose (Gkantidis et al., 2013). Patients' satisfaction with teeth was low. It reflected the findings of a high prevalence of caries in Vietnamese patients with CL/P (Paper I). Also, patients did not receive orthodontic treatment, so they might not be satisfied with misaligned teeth (Noor and Musa, 2007).

Vietnamese patients rated their satisfaction significantly lower than Estonian patients in most of the items. Some speculations for this were low self-esteem, lack of information, and their overall standard of beauty. It has been shown that Asian people self-rated lower on self-esteem than Western people (Cai et al., 2007). Patients preferred knowing about their condition at an early age, i.e. before or during elementary school. Asian parents tend to hide information about CL/P from their child. The patients, consequently, did not fully understand their condition until adulthood (Omiya et al., 2014).

Agreement on the satisfaction with the outcomes of the cleft treatment between patients and parents was moderate in our study. Other studies also reported a low to fair/moderate agreement between patients and parents (Bjerke, 2016; Noor and Musa, 2007; Gkantidis et al., 2015). Experiences related to CL/P might be different between patients and parents; thus, they could influence patients and their parents' satisfaction differently and lead a low agreement between them (Gkantidis et al., 2013). Therefore, it is crucial to evaluate the patient's satisfaction and include patient's opinion in the treatment decision-making process, not just parents and/or physician's opinions (Noor and Musa, 2007).

The items of the CHASQ are related to facial features, hearing, and speech; they can be used to determine the satisfaction of patients and their parents with the cleft treatment outcomes. The CHASQ can be used to determine any significant differences between patients and parents in ratings of the features related to facial appearance, hearing, and speech. The CHASQ can also be used to determine any changes in the satisfaction of patients over time throughout the treatment process to discover if the patient might need psychological counselling.

6.8. Clinical suggestions

In Vietnam, information related to patients with CL/P is mostly collected from hospital registries. No national statistics about CL/P are available (Phan and Hoang, 2007). Therefore, it is necessary to establish a national cleft registry to record and monitor patients with CL/P (Al-Dajani, 2009). From the registry, a follow-up and recall system should be established. Also, it is important to

establish standards of record-taking with a list of the minimally required records and any additionally recommended records (American Cleft Palate-Craniofacial Association, 2017). The minimal records are models, lateral cephalograms, photos, speech, audiometry, and patient/parent satisfaction (American Cleft Palate-Craniofacial Association, 2017).

Patients who are operated on by charity operation teams usually pay attention to surgical procedures to correct the cleft. Oral health is often underscored and neglected. This study showed that patients were not satisfied with their teeth, and the caries experience was very high. Hence, it is crucial to promote awareness of oral health in the cleft population and integrate preventive dental regimens into the cleft protocol (Zhu et al., 2010; Wong FWL and King, 1998). Paediatric dentists and/or general dentists should be responsible and check the dental health of their patients to detect any dental problems at an early stage. Primary and secondary caries prevention should be implemented for patients with CL/P (Pinto et al., 2013; Dahllof et al., 1989). Preventive measures include education about oral hygiene maintenance, prophylaxis, fluoride application, and dietary advice (King et al., 2013). Dental education should be given not only to children but also to their parents and/or caregivers (Al-Dajani, 2009; Mutarai et al., 2008). Brushing techniques should be demonstrated to the patients, parents, and/or caregivers (Fadeyibi et al., 2011).

When cleft centres are about to open in Central Vietnam, postgraduate programmes should be adjusted to provide additional training on cleft care, especially for maxillofacial surgeons, paediatricians, orthodontists, and speech-language pathologists. Currently, in Central Vietnam, speech-language pathologists are scarce. There are some on-going courses to educate more speech-language pathologists for the region.

Cleft centres in Vietnam should improve and standardize cleft treatment protocols across the country to provide consistently superior outcomes. It facilitates the needs to compare the treatment outcomes between centres in Vietnam. Inter-centre comparisons could avoid the sampling bias and allow for direct comparison of the outcomes together with other major components of the treatment program (Shaw et al., 1992). It has also been proven that a centralized multidisciplinary cleft service improves treatment outcomes (Ness et al., 2015).

6.9. Research limitation

A major limitation of the study was the small sample size. Despite the effort to recall operated patients with CL/P, we could not establish a larger sample size. There were three main reasons: patients declined to be in the study; patient's contacts were unreachable; no cleft registry was available. Some patients refused to participate in the study because they desired more intervention, not just a check-up; the long travel distance from their place to the study site; no reimbursement for travel costs. It was good that we had announced the call for

the study on television, since it increased the total number of patients who we contacted via phone.

A sample size of 30 to 40 is recommended based on a 0.5 significant level and 80% power to enable significant power for sensitive and important outcome measures (Long et al., 2011). Although the sample size of our study was small, it still met the suggested minimum sample size. For that reason, our study represented a reliable and valid assessment of the outcomes in question.

Disregarding the small sample size, the frequency of CL/P by sex and laterality in our study was similar to those described in the literature. Males were shown to be more prone to CL±P, while females were more prone to CP. CL/P was usually unilateral and more favourable on the left side (Mossey and Modellb, 2012; Dixon et al., 2011). The most common cleft type was CLP (Mossey and Little, 2002). Similar findings were also ascertained by other research in Vietnam (Lam et al., 2010; Nguyen TD and Thai, 2004).

6.10. Future directions

In the future, a longitudinal study and large sample size are needed to evaluate the long-term outcomes of the cleft treatment. It would be good to revisit patients with CL/P in the region after 10 to 15 years to evaluate treatment outcomes to see if there are any changes in the outcomes. Also, future research could investigate other outcome domains that the current study did not touch, for example: feeding difficulties, psychological issues, or aspects related to the process of care or burden of treatment.

7. CONCLUSIONS

1. Patients with CL/P in Central Vietnam had a poor oral health status with a very high level of dental caries and signs of gingivitis but not periodontitis.
2. Mothers of patients with CL/P mostly had a feeling of sadness because of the condition of their child. They did not report any superstitious or folk beliefs in causal attribution to CL/P. Their life did not have any major changes because of the child with CL/P.
3. The patients had a fair appearance of nasolabial aesthetics regardless of the rating methods. Nasal symmetry was the least favourable feature among the four features assessed.
4. The study established normative nasalance scores for non-cleft Vietnamese-speaking children in the central regional dialect. The patients had a poor speech outcome with more than half of the patients having hypernasality.
5. Some patients had Class III malocclusion. The airway space was reduced in children with CL/P but not in adults with CL/P. The maxillary arch and palatal dimensions were reduced in children with CL/P in three dimensions. However, adults with CL/P had a similar size of the palate compared to the controls.
6. The patients and their parents were satisfied with the cleft treatment outcomes. The patients were less satisfied with features associated with having been born with a cleft. The agreement between the patients and parents ranged from low to moderate.

REFERENCES

- Agarwal A and Marwah N. (2016) Assessment of the Airway Characteristics in Children with Cleft Lip and Palate using Cone Beam Computed Tomography. *Int J Clin Pediatr Dent* 9: 5–9.
- Ahluwalia M, Brailsford SR, Tarelli E, et al. (2004) Dental caries, oral hygiene, and oral clearance in children with craniofacial disorders. *J Dent Res* 83: 175–179.
- Al-Dajani M. (2009) Comparison of dental caries prevalence in patients with cleft lip and/or palate and their sibling controls. *Cleft Palate Craniofac J* 46: 529–531.
- Al-Ghatam R, Jones TE, Ireland AJ, et al. (2015) Structural outcomes in the Cleft Care UK study. Part 2: dento-facial outcomes. *Orthod Craniofac Res* 18: 14–24.
- Alley TR and Hildebrandt KA. (1988) Determinants and consequences of facial aesthetics. In: Alley TR (ed) *Resources for ecological psychology. Social and applied aspects of perceiving faces*. Hillsdale, NJ, US: Lawrence Erlbaum Associates, Inc, 101–140.
- Allori AC, Kelley T, Meara JG, et al. (2017a) A Standard Set of Outcome Measures for the Comprehensive Appraisal of Cleft Care. *Cleft Palate Craniofac J* 54: 540–554.
- Allori AC, Mulliken JB, Meara JG, et al. (2017b) Classification of Cleft Lip/Palate: Then and Now. *Cleft Palate Craniofac J* 54: 175–188.
- American Cleft Palate-Craniofacial Association. (2017) The Americleft Project: Experiences and recommendations for establishing successful inter-center collaborative outcome study.
- American Cleft Palate-Craniofacial Association. (2018) Parameters For Evaluation and Treatment of Patients With Cleft Lip/Palate or Other Craniofacial Differences. *Cleft Palate Craniofac J* 55: 137–156.
- Anh Xuan. (2018) Tỷ lệ bao phủ bảo hiểm y tế đạt gần 87% [The coverage rate of health insurance reaches nearly 87%]. Available at: <http://www.nhandan.com.vn/xahoi/item/36887602-ty-le-bao-phu-bao-hiem-y-te-dat-gan-87.html>.
- Antonarakis GS, Palaska PK and Herzog G. (2013) Caries prevalence in non-syndromic patients with cleft lip and/or palate: a meta-analysis. *Caries Res* 47: 406–413.
- Antonelli PJ. (2002) Otolaryngologic Needs of Individuals with Oral Clefts. In: Wyszynski DF (ed) *Cleft Lip & Palate: From Origin to Treatment*. Oxford University Press, 397–407.
- Aras I and Dogan S. (2017) Comparative Evaluation of the Pharyngeal Airways and Related Soft Tissues of Unilateral and Bilateral Cleft Lip and Palate Patients With the Noncleft Individuals. *Cleft Palate Craniofac J* 54: 53–59.
- Aras I, Olmez S and Dogan S. (2012) Comparative evaluation of nasopharyngeal airways of unilateral cleft lip and palate patients using three-dimensional and two-dimensional methods. *Cleft Palate Craniofac J* 49: e75–81.
- Asher-McDade C, Brattstrom V, Dahl E, et al. (1992) A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 4. Assessment of nasolabial appearance. *Cleft Palate Craniofac J* 29: 409–412.
- Asher-McDade C, Roberts C, Shaw WC, et al. (1991) Development of a method for rating nasolabial appearance in patients with clefts of the lip and palate. *Cleft Palate Craniofac J* 28: 385–390; discussion 390–381.
- Aydemir H and Toygar-Memikoğlu U. (2014) Pharyngeal Airway Dimensions in Cleft Lip and Palate Patients Compared With Class I Subjects. *Turkish J Orthod* 27: 46–50.

- Bannister P, Lindberg N, Jeppesen K, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 3. Descriptive study of postoperative nursing care following first stage cleft closure. *J Plast Surg Hand Surg* 51: 21–26.
- Berkowitz S. (2013) The Effect of Clefing of the Lip and Palate and the Palatal Arch Form. In: Berkowitz S (ed) *Cleft Lip and Palate: Diagnosis and Management*. 3rd ed. Berlin, Heidelberg: Springer, 61–85.
- Berwig LC, Silva AM, Correa EC, et al. (2011) Hard palate dimensions in nasal and mouth breathers from different etiologies. *J Soc Bras Fonoaudiol* 23: 308–314.
- Besseling S and Dubois L. (2004) The Prevalence of Caries in Children With a Cleft Lip and/or Palate in Southern Vietnam. *Cleft Palate Craniofac J* 41: 629–632.
- Bibby RE and Preston CB. (1981) The hyoid triangle. *Am J Orthod* 80: 92–97.
- Bickham RS, Ranganathan K, Wombacher NR, et al. (2017) Speech Perceptions and Health-Related Quality of Life Among Children With Cleft Lip and Palate. *J Craniofac Surg* 28: 1264–1268.
- Bittencourt Dutra Dos Santos P, Janson G, Assis VH, et al. (2015) Association Between Dental Arch Widths and Interarch Relationships in Children With Operated Unilateral Complete Cleft Lip and Palate. *Cleft Palate Craniofac J* 52: e196–200.
- Bjerke SM. (2016) Informant agreement between children born with cleft lip and/or palate (CL/P) and their parents on the Strengths and Difficulties Questionnaire (SDQ). *Department of Psychology – Faculty of Health Sciences*. Norway: The Arctic University of Norway.
- Black N. (2013) Patient reported outcome measures could help transform healthcare. *BMJ* 346: f167.
- Bongaarts CA, Kuijpers-Jagtman AM, van 't Hof MA, et al. (2004) The effect of infant orthopedics on the occlusion of the deciduous dentition in children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 41: 633–641.
- Bongaarts CA, Prah-Andersen B, Bronkhorst EM, et al. (2009) Infant orthopedics and facial growth in complete unilateral cleft lip and palate until six years of age (Dutchcleft). *Cleft Palate Craniofac J* 46: 654–663.
- Bongaarts CA, Prah-Andersen B, Bronkhorst EM, et al. (2008) Effect of infant orthopedics on facial appearance of toddlers with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 45: 407–413.
- Bongaarts CA, van 't Hof MA, Prah-Andersen B, et al. (2006) Infant orthopedics has no effect on maxillary arch dimensions in the deciduous dentition of children with complete unilateral cleft lip and palate (Dutchcleft). *Cleft Palate Craniofac J* 43: 665–672.
- Brattstrom V, Molsted K, Prah-Andersen B, et al. (2005) The Eurocleft study: inter-center study of treatment outcome in patients with complete cleft lip and palate. Part 2: craniofacial form and nasolabial appearance. *Cleft Palate Craniofac J* 42: 69–77.
- Bressmann T, Sader R, Ravens-Sieberer U, et al. (1999) [Quality of life research in patients with cleft lip and palate: preliminary results]. *Mund Kiefer Gesichtschir* 3: 134–139.
- Britton KF and Welbury RR. (2010) Dental caries prevalence in children with cleft lip/palate aged between 6 months and 6 years in the West of Scotland. *Eur Arch Paediatr Dent* 11: 236–241.
- Broder HL, Smith FB and Strauss RP. (1994) Effects of visible and invisible orofacial defects on self-perception and adjustment across developmental eras and gender. *Cleft Palate Craniofac J* 31: 429–436.

- Brunnegard K and van Doorn J. (2009) Normative data on nasalance scores for Swedish as measured on the Nasometer: influence of dialect, gender, and age. *Clin Linguist Phon* 23: 58–69.
- Burdi AR and Silvey RG. (1969) Sexual differences in closure of the human palatal shelves. *Cleft Palate J* 6: 1–7.
- Cai H, Brown JD, Deng C, et al. (2007) Self-esteem and culture: Differences in cognitive self-evaluations or affective self-regard? *Asian J Soc Psychol* 10: 162–170.
- Cançado RH and Lauris JRP. (2014) Error of the method: what is it for? *Dental Press J Orthod* 19: 25–26.
- Chen ZQ, Wu J and Chen RJ. (2012) Sagittal maxillary growth pattern in unilateral cleft lip and palate patients with unrepaired cleft palate. *J Craniofac Surg* 23: 491–493.
- Cheng LL, Moor SL and Ho CT. (2007) Predisposing factors to dental caries in children with cleft lip and palate: a review and strategies for early prevention. *Cleft Palate Craniofac J* 44: 67–72.
- Cheung T and Oberoi S. (2012) Three Dimensional Assessment of the Pharyngeal Airway in Individuals with Non-Syndromic Cleft Lip and Palate. *PLoS ONE* 7: e43405.
- Christensen K, Juel K, Herskind AM, et al. (2004) Long term follow up study of survival associated with cleft lip and palate at birth. *BMJ* 328: 1405.
- Christensen K and Mortensen PB. (2002) Facial clefting and psychiatric diseases: a follow-up of the Danish 1936–1987 Facial Cleft cohort. *Cleft Palate Craniofac J* 39: 392–396.
- Clapp RW, Baraldi C, Grassman J, et al. (2014) On Agent Orange in Vietnam. *Am J Public Health* 104: 1860–1861.
- Cleft Psychology Special Interest Group (SIG). (2014) Cleft Hearing Appearance and Speech Questionnaire user guide.
- Cooper ME, Ratay JS and Marazita ML. (2006) Asian Oral-Facial Cleft Birth Prevalence. *Cleft Palate Craniofac J* 43: 580–589.
- Costigan CL and Cox MJ. (2001) Fathers' participation in family research: is there a self-selection bias? *J Fam Psychol* 15: 706–720.
- D'Haeseleer E, Bettens K, De Mets S, et al. (2015) Normative Data and Dialectical Effects on Nasalance in Flemish Adults. *Folia Phoniatr Logop* 67: 42–48.
- Dahlberg G. (1940) Statistical Methods for Medical and Biological Students. *Br Med J* 2: 358–359.
- Dahllof G, Ussisoo-Joandi R, Ideberg M, et al. (1989) Caries, gingivitis, and dental abnormalities in preschool children with cleft lip and/or palate. *Cleft Palate J* 26: 233–237; discussion 237–238.
- Dalston RM, Warren DW and Dalston ET. (1991) Use of nasometry as a diagnostic tool for identifying patients with velopharyngeal impairment. *Cleft Palate Craniofac J* 28: 184–188; discussion 188–189.
- Daskalogiannakis J, Mercado A, Russell K, et al. (2011) The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 3. Analysis of craniofacial form. *Cleft Palate Craniofac J* 48: 252–258.
- Davis JS and Ritchie HP. (1922) Classification of congenital clefts of the lip and palate: with a suggestion for recording these cases. *JAMA* 79: 1323–1327.
- De Ladeira PR and Alonso N. (2012) Protocols in cleft lip and palate treatment: systematic review. *Plast Surg Int* 2012: 562892.
- Deshpande PR, Rajan S, Sudeepthi BL, et al. (2011) Patient-reported outcomes: A new era in clinical research. *Perspect Clin Res* 2: 137–144.

- Devi ES, Sai Sankar AJ, Manoj Kumar MG, et al. (2012) Maiden morsel - feeding in cleft lip and palate infants. *J Int Soc Prev Community Dent* 2: 31–37.
- Dissaux C, Bodin F, Grollemund B, et al. (2015) Evaluation of 5-year-old children with complete cleft lip and palate: Multicenter study. Part 1: Lip and nose aesthetic results. *J Craniomaxillofac Surg* 43: 2085–2092.
- Dissaux C, Grollemund B, Bodin F, et al. (2016) Evaluation of 5-year-old children with complete cleft lip and palate: Multicenter study. Part 2: Functional results. *J Craniomaxillofac Surg* 44: 94–103.
- Dixon MJ, Marazita ML, Beaty TH, et al. (2011) Cleft lip and palate: understanding genetic and environmental influences. *Nat Rev Genet* 12: 167–178.
- Drake AF, Davis JU and Warren DW. (1993) Nasal airway size in cleft and noncleft children. *Laryngoscope* 103: 915–917.
- Ebin LE, Zam NM and Othman SA. (2010) Cephalometric analysis of Malay children with and without unilateral cleft lip and palate. *Aust Orthod J* 26: 165–170.
- EFY Việt Nam. (2014) *Quyền lợi hưởng thẻ BHYT đối với các đối tượng tham gia BHYT [Benefits of health insurance cards for subjects involved in health insurance]*. Available at: <https://baohiemxahoidientu.vn/bhxh/quyen-loi-huong-the-bhyt-doi-voi-cac-doi-tuong-tham-gia-bhyt.html>.
- El-Kassabi RM, Hassan S, Mesallam TA, et al. (2015) Standardization of nasalance scores in normal Saudi speakers. *Logoped Phoniatr Vocol* 40: 77–85.
- Fadeyibi IO, Sorunke ME, Onigbinde OO, et al. (2011) Oral Health Status of Individuals with Cleft Lip, Cleft Palate or Both in a Nigerian Population. *Maced J Med Sci* 4: 265–270.
- Farrington F. (2002) Pediatric Dental Care. In: Wyszynski DF (ed) *Cleft Lip & Palate: From Origin to Treatment*. Oxford University Press, 372–380.
- Feeney R, Desha L, Ziviani J, et al. (2012) Health-related quality-of-life of children with speech and language difficulties: a review of the literature. *Int J Speech Lang Pathol* 14: 59–72.
- Feragen KB, Rumsey N, Heliovaara A, et al. (2017a) Scandcleft randomised trials of primary surgery for unilateral cleft lip and Palate: 9. Parental report of social and emotional experiences related to their 5-year-old child's cleft diagnosis. *J Plast Surg Hand Surg* 51: 73–80.
- Feragen KB, Semb G, Heliovaara A, et al. (2017b) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 10. Parental perceptions of appearance and treatment outcomes in their 5-year-old child. *J Plast Surg Hand Surg* 51: 81–87.
- Feragen KB and Stock NM. (2016) A longitudinal study of 340 young people with or without a visible difference: The impact of teasing on self-perceptions of appearance and depressive symptoms. *Body Image* 16: 133–142.
- Fix GM, VanDeusen Lukas C, Bolton RE, et al. (2018) Patient-centred care is a way of doing things: How healthcare employees conceptualize patient-centred care. *Health Expect* 21: 300–307.
- Flynn T, Moller C, Jonsson R, et al. (2009) The high prevalence of otitis media with effusion in children with cleft lip and palate as compared to children without clefts. *Int J Pediatr Otorhinolaryngol* 73: 1441–1446.
- Fogh-Andersen P. (1942) *Inheritance of harelip and cleft palate*, Copenhagen, Denmark: NYT Nordisk Forlag.

- Fudalej SA, Desmedt D, Bronkhorst E, et al. (2017) Comparison of Three Methods of Rating Nasolabial Appearance in Cleft Lip and Palate. *Cleft Palate Craniofac J* 54: 400–407.
- Fukushiro AP and Trindade IEK. (2005) Nasal airway dimensions of adults with cleft lip and palate: Differences among cleft types. *Cleft Palate Craniofac J* 42: 396–402.
- Gkantidis N, Papamanou DA, Christou P, et al. (2013) Aesthetic outcome of cleft lip and palate treatment. Perceptions of patients, families, and health professionals compared to the general public. *J Craniomaxillofac Surg* 41: e105–110.
- Gkantidis N, Papamanou DA, Karamolegkou M, et al. (2015) Esthetic, Functional, and Everyday Life Assessment of Individuals with Cleft Lip and/or Palate. *BioMed Res. Int* 2015: 1–8.
- Gopinath VK, Samsudin AR, Noor S, et al. (2017) Facial profile and maxillary arch dimensions in unilateral cleft lip and palate children in the mixed dentition stage. *Eur J Dent* 11: 76–82.
- Goswami M, Jangra B and Bhushan U. (2016) Management of feeding Problem in a Patient with Cleft Lip/Palate. *Int J Clin Pediatr Dent* 9: 143–145.
- Gravel JS and Wallace IF. (2000) Effects of otitis media with effusion on hearing in the first 3 years of life. *J Speech Lang Hear Res* 43: 631–644.
- Haapanen ML. (1994) Cleft type and speech proficiency. *Folia Phoniatr Logop* 46: 57–63.
- Haque S and Alam MK. (2015) Common dental anomalies in cleft lip and palate patients. *Malays J Med Sci* 22: 55–60.
- Hasslof P and Twetman S. (2007) Caries prevalence in children with cleft lip and palate – a systematic review of case-control studies. *Int J Paediatr Dent* 17: 313–319.
- Hathaway R, Daskalogiannakis J, Mercado A, et al. (2011) The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 2. Dental arch relationships. *Cleft Palate Craniofac J* 48: 244–251.
- Heliövaara A, Kuseler A, Skaare P, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 6. Dental arch relationships in 5 year-olds. *J Plast Surg Hand Surg* 51: 52–57.
- Heliövaara A, Leikola J and Rautio J. (2014) Anterior Crossbite, Dental Arch Dimensions, and Later Need for Orthognathic Surgery in 6-Year-Old Children With Unilateral Cleft Lip and Palate. *Cleft Palate Craniofac J* 51: 579–584.
- Heliövaara A and Rautio J. (2005) Dental arches in six-year-old children with operated and unoperated submucous cleft palate and isolated cleft palate. *Acta Odontol Scand* 63: 123–126.
- Henningsson G, Kuehn DP, Sell D, et al. (2008) Universal parameters for reporting speech outcomes in individuals with cleft palate. *Cleft Palate Craniofac J* 45: 1–17.
- Hoang D and Nguyen KT. (2011) Volunteering in Nha Trang, Vietnam: senior medical students' perspectives of a surgical mission trip. *Yale J Biol Med* 84: 461–470.
- Hunt O, Burden D, Hepper P, et al. (2005) The psychosocial effects of cleft lip and palate: a systematic review. *Eur J Orthod* 27: 274–285.
- Hunt O, Burden D, Hepper P, et al. (2007) Parent reports of the psychosocial functioning of children with cleft lip and/or palate. *Cleft Palate Craniofac J* 44: 304–311.
- Hutchinson K, Wellman MA, Noe DA, et al. (2011) The psychosocial effects of cleft lip and palate in non-Anglo populations: a cross-cultural meta-analysis. *Cleft Palate Craniofac J* 48: 497–508.

- Huynh TTT and Hoang TH. (2007) Đặc điểm sọ mặt trẻ em 7–10 tuổi có khe hở môi-hàm ếch (Nghiên cứu trên phim đo sọ sau phẫu thuật) [Craniofacial morphology in children with unilateral cleft lip and palate from 7 to 10 years in cephalometric analysis]. *Tuyển tập công trình nghiên cứu khoa học Răng Hàm Mật [Collection of Scientific Research in Odonto-Stomatology]*: 37–48.
- Ibrahim HM, Reilly S and Kilpatrick N. (2012) Normative nasalance scores for the Malay language. *Cleft Palate Craniofac J* 49: e61–63.
- Imamura N, Ono T, Hiyama S, et al. (2002) Comparison of the sizes of adenoidal tissues and upper airways of subjects with and without cleft lip and palate. *Am J Orthod Dentofacial Orthop* 122: 189–194; discussion 194–185.
- IPDTC Working Group. (2011) Prevalence at Birth of Cleft Lip with or without Cleft Palate: Data from the International Perinatal Database of Typical Oral Clefts (IPDTC). *Cleft Palate Craniofac J* 48: 66–81.
- Jakobsone G, Neimane L and Krumina G. (2010) Two- and three-dimensional evaluation of the upper airway after bimaxillary correction of Class III malocclusion. *Oral Surg Oral Med Oral Pathol Radiol Endod* 110: 234–242.
- Jenny HE, Massenburger BB, Saluja S, et al. (2017) Efficacy of facilitated capacity building in providing cleft lip and palate care in low- and middle-income countries. *J Craniofac Surg* 28: 1737–1741.
- Jindal MK and Khan SY. (2013) How to feed cleft patient? *Int J Clin Pediatr Dent* 6: 100–103.
- Johansson B and Ringsberg KC. (2004) Parents' experiences of having a child with cleft lip and palate. *J Adv Nurs* 47: 165–173.
- Johnsen DC and Dixon M. (1984) Dental caries of primary incisors in children with cleft lip and palate. *Cleft Palate J* 21: 104–109.
- Jones T, Al-Ghatam R, Attack N, et al. (2014) A review of outcome measures used in cleft care. *J Orthod* 41: 128–140.
- Karakoc O, Akcam T, Birkent H, et al. (2013) Nasalance scores for normal-speaking Turkish population. *J Craniofac Surg* 24: 520–522.
- Karsten A, Marcusson A, Hurmerinta K, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 7. Occlusion in 5 year-olds according to the Huddart and Bodenham index. *J Plast Surg Hand Surg* 51: 58–63.
- Kaul R, Jain P, Saha S, et al. (2017) Cleft lip and cleft palate: Role of a pediatric dentist in its management. *Int J Pedod Rehabil* 2: 1–6.
- Kernahan DA and Stark RB. (1958) A new classification for cleft lip and cleft palate. *Plast Reconstr Surg Transplant Bull* 22: 435–441.
- Keuning KH, Wieneke GH, van Wijngaarden HA, et al. (2002) The correlation between nasalance and a differentiated perceptual rating of speech in Dutch patients with velopharyngeal insufficiency. *Cleft Palate Craniofac J* 39: 277–284.
- Kilpelainen PV, Laine-Alava MT and Lammi S. (1996) Palatal morphology and type of clefting. *Cleft Palate Craniofac J* 33: 477–482.
- King NM, Wong WL and Wong HM. (2013) Caries experience of chinese children with cleft lip and palate. *Cleft Palate Craniofac J* 50: 448–455.
- Konst EM, Prahl C, Weersink-Braks H, et al. (2004) Cost-effectiveness of infant orthopedic treatment regarding speech in patients with complete unilateral cleft lip and palate: a randomized three-center trial in the Netherlands (Dutchcleft). *Cleft Palate Craniofac J* 41: 71–77.
- Koo TK and Li MY. (2016) A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med* 15: 155–163.

- Kuijpers-Jagtman AM, Nollet PJ, Semb G, et al. (2009) Reference photographs for nasolabial appearance rating in unilateral cleft lip and palate. *J Craniofac Surg* 20: 1683–1686.
- Lages EM, Marcos B and Pordeus IA. (2004) Oral health of individuals with cleft lip, cleft palate, or both. *Cleft Palate Craniofac J* 41: 59–63.
- Lam HP, Nguyen BD and Tran TT. (2010) Đặc điểm tình hình khe hở môi hàm ếch tại 32 tỉnh thành phía Nam từ 2007–2010 [Descriptive of non-syndromic cleft lip and palate in 32 cities of southern Vietnam from 2007 to 2010]. *Tuyển tập công trình nghiên cứu khoa học Răng Hàm Mặt [Collection of Scientific Research in Odonto-Stomatology]*: 81–89.
- Le D-C, Kubo T, Fujino Y, et al. (2010) Health Care System in Vietnam: Current Situation and Challenges. *Asian Pacific Journal of Disease Management* 4: 23–30.
- Lohmander A, Persson C, Willadsen E, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 4. Speech outcomes in 5-year-olds - velopharyngeal competency and hypernasality. *J Plast Surg Hand Surg* 51: 27–37.
- Long RE, Jr., Hathaway R, Daskalogiannakis J, et al. (2011) The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 1. Principles and study design. *Cleft Palate Craniofac J* 48: 239–243.
- Lorot-Marchand A, Guerreschi P, Pellerin P, et al. (2015) Frequency and socio-psychological impact of taunting in school-age patients with cleft lip-palate surgical repair. *Int J Pediatr Otorhinolaryngol* 79: 1041–1048.
- MacLean JE, Hayward P, Fitzgerald DA, et al. (2009) Cleft lip and/or palate and breathing during sleep. *Sleep Med Rev* 13: 345–354.
- Mapi Research Institute. (2005) Linguistic validation of a Patient Reported Outcomes Measure.
- Marcusson A, Paulin G and Ostrup L. (2002) Facial appearance in adults who had cleft lip and palate treated in childhood. *Scand J Plast Reconstr Surg Hand Surg* 36: 16–23.
- Mars M, Asher-McDade C, Brattstrom V, et al. (1992) A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 3. Dental arch relationships. *Cleft Palate Craniofac J* 29: 405–408.
- McCorkell G, McCarron C, Blair S, et al. (2012) Parental experiences of cleft lip and palate services. *Community Pract* 85: 24–27.
- Mednick L, Snyder J, Schook C, et al. (2013) Causal attributions of cleft lip and palate across cultures. *Cleft Palate Craniofac J* 50: 655–661.
- Mercado AM, Russell KA, Hathaway RR, et al. (2011) The Americleft study: an inter-center study of treatment outcomes for patients with unilateral cleft lip and palate part 4. Nasolabial aesthetics. *Cleft Palate Craniofac J* 48: 259–264.
- Millard T and Richman LC. (2001) Different cleft conditions, facial appearance, and speech: relationship to psychological variables. *Cleft Palate Craniofac J* 38: 68–75.
- Molsted K, Asher-McDade C, Brattstrom V, et al. (1992) A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 2. Craniofacial form and soft tissue profile. *Cleft Palate Craniofac J* 29: 398–404.
- Molsted K, Brattstrom V, Prah Andersen B, et al. (2005) The Eurocleft study: inter-center study of treatment outcome in patients with complete cleft lip and palate. Part 3: dental arch relationships. *Cleft Palate Craniofac J* 42: 78–82.
- Molsted K, Humerinta K, Kuseler A, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 8. Assessing naso-labial appearance in 5-year-olds - a preliminary study. *J Plast Surg Hand Surg* 51: 64–72.

- Mossey PA and Castillia EE. (2003) Craniofacial anomalies and associated birth defects. In: Mossey PA and Castillia EE (eds) *Global registry and database on craniofacial anomalies: report of a WHO Registry Meeting on Craniofacial Anomalies*. Geneva: World Health Organization, 15–33.
- Mossey PA and Little J. (2002) Epidemiology of Oral Clefts: An International Perspective. In: Wyszynski DF (ed) *Cleft Lip & Palate: From Origin to Treatment*. Oxford University Press, 127–158.
- Mossey PA, Little J, Munger RG, et al. (2009) Cleft lip and palate. *Lancet* 374: 1773–1785.
- Mossey PA and Modellb B. (2012) Epidemiology of Oral Clefts 2012: An International Perspective. In: Cobourne MT (ed) *Cleft Lip and Palate: Epidemiology, Aetiology and Treatment*. Switzerland: Karger, 1–18.
- Mutarai T, Ritthagol W and Hunsrisakhun J. (2008) Factors influencing early childhood caries of cleft lip and/or palate children aged 18 to 36 months in southern Thailand. *Cleft Palate Craniofac J* 45: 468–472.
- Mutthineni RB, Notalapati R and Kasagani SK. (2010) Comparison of oral hygiene and periodontal status in patients with clefts of palate and patients with unilateral cleft lip, palate and alveolus. *J Indian Soc Periodontol* 14: 236–240.
- Mzezewa S and Muchemwa FC. (2010) Reaction to the birth of a child with cleft lip or cleft palate in Zimbabwe. *Trop Doct* 40: 138–140.
- N.Q. (2018) *Từ 2018, sinh con thứ 3 trở lên sẽ không bị phạt [From 2018, giving birth to the third child and above will not be fined]*. Available at: <https://vtc.vn/tu-2018-khong-con-bi-phat-khi-sinh-con-thu-3-d378226.html>.
- Nackashi JA, Dedlow ER and Dixon-Wood V. (2002) Health Care for Children with Cleft Lip and Palate: Comprehensive Services and Infant Feeding. In: Wyszynski DF (ed) *Cleft Lip & Palate: From Origin to Treatment*. Oxford University Press, 303–318.
- Nagarajan R, Savitha VH and Subramaniyan B. (2009) Communication disorders in individuals with cleft lip and palate: An overview. *Indian J Plast Surg* 42: S137–143.
- Nagato N, Tsuyoshi K and Le H. (1998) Letter To The Editor. *Cleft Palate Craniofac J* 35: 183.
- Nahai FR, Williams JK, Burstein FD, et al. (2005) The Management of Cleft Lip and Palate: Pathways for Treatment and Longitudinal Assessment. *Semin Plast Surg* 19: 275–285.
- Nam Phuong and Le Phuong. (2017) *Nửa thế kỉ Việt Nam thay đổi chính sách “sinh để có kế hoạch” (Half a century of policy changes of "planned birth" in Vietnam)*. Available at: <https://vnexpress.net/projects/nua-the-ky-viet-nam-sinh-de-co-ke-hoach-nhu-the-nao-3618539/index.html>.
- Naqvi ZA, Shivalinga BM, Ravi S, et al. (2015) Effect of cleft lip palate repair on craniofacial growth. *J Orthod Sci* 4: 59–64.
- Natsume N, Suzuki T and Kawai T. (1987) Maternal reactions to the birth of a child with cleft lip and/or palate. *Plast Reconstr Surg* 79: 1003–1004.
- Nelson J, O’Leary C and Weinman J. (2009) Causal attributions in parents of babies with a cleft lip and/or palate and their association with psychological well-being. *Cleft Palate Craniofac J* 46: 425–434.
- Nelson P, Glenny AM, Kirk S, et al. (2012) Parents' experiences of caring for a child with a cleft lip and/or palate: a review of the literature. *Child Care Health Dev* 38: 6–20.

- Ness AR, Wills AK, Waylen A, et al. (2015) Centralization of cleft care in the UK. Part 6: a tale of two studies. *Orthod Craniofac Res* 18: 56–62.
- Nguyen CT and Nguyen BH. (2007) Đánh giá kết quả điều trị khe hở môi toàn bộ một bên theo phương pháp R.SONG [Treatment outcome of R.SONG surgical method to treat complete unilateral cleft lip]. *Y học Việt Nam [Vietnam Medicine]* 2: 78–83.
- Nguyen CU. (1999) Một số nhận xét về dị tật khe hở môi & hàm ếch qua 443 ca đã được phẫu thuật tại Khoa RHM BV Nguyễn Đình Chiểu Tỉnh Bến Tre [Assessment of 443 operated cleft lip and palate cases in Nguyen Dinh Chieu Hospital, Faculty of Odonto-Stomatology, Ben Tre Province]. *Tuyển tập công trình nghiên cứu khoa học Răng Hàm Mặt [Collection of Scientific Research in Odonto-Stomatology]*: 122–125.
- Nguyen HL. (2006) Trẻ dị tật bẩm sinh khe hở môi - vòm miệng tại Thừa Thiên Huế: thực trạng và các vấn đề [Cleft lip and palate children in Thua Thien Hue Province: facts and problems]. *Y học thực hành [Practical Medicine]* 10: 9–11.
- Nguyen TD and Thai QM. (2004) Tình hình phẫu thuật tạo hình khe hở môi tại Bệnh viện tỉnh Khánh Hòa trong 10 năm [Assessment of cleft lip surgery at a hospital in Khanh Hoa Province in 10 years (1991–2000)]. *Tuyển tập công trình nghiên cứu khoa học Răng Hàm Mặt [Collection of Scientific Research in Odonto-Stomatology]*: 236–242.
- Nguyen TTC. (2012) Đánh giá chức năng phát âm của bệnh nhân khe hở môi vòm miệng sau phẫu thuật 6 tháng tại bệnh viện Việt Nam-Cuba năm 2012 [Evaluation of speech function of cleft lip and palate patients 6 months after operation at Vietnam-Cuba Hospital in 2012]. Hanoi University.
- Nguyen VT. (2013) Nghiên cứu đặc điểm lâm sàng và đánh giá kết quả phẫu thuật tạo hình khe hở môi trên một bên theo phương pháp Millard [Study of clinical characteristics and evaluation of surgical outcome of repaired unilateral cleft lip using Millard method]. *Faculty of Odonto-Stomatology*. Hue University of Medicine and Pharmacy.
- Noor SN and Musa S. (2007) Assessment of patients' level of satisfaction with cleft treatment using the Cleft Evaluation Profile. *Cleft Palate Craniofac J* 44: 292–303.
- Noverraz RL, Disse MA, Ongkosuwito EM, et al. (2015) Transverse dental arch relationship at 9 and 12 years in children with unilateral cleft lip and palate treated with infant orthopedics: a randomized clinical trial (DUTCHCLEFT). *Clin Oral Investig* 19: 2255–2265.
- Omiya T, Ito M and Yamazaki Y. (2014) Disclosure of congenital cleft lip and palate to Japanese patients: reported patient experiences and relationship to self-esteem. *BMC Res Notes* 7: 924.
- Paradowska-Stolarz A and Kawala B. (2014) Occlusal Disorders among Patients with Total Clefts of Lip, Alveolar Bone, and Palate. *Journal of Biomedicine and Biotechnology* 2014: 6.
- Paul T and Brandt RS. (1998) Oral and dental health status of children with cleft lip and/or palate. *Cleft Palate Craniofac J* 35: 329–332.
- Pegoraro-Krook MI, Marino VCdC, Silva L, et al. (2014) Correlação entre nasalância e nasalidade em crianças com hipernasalidade [Correlation between nasalance and nasality in children with hypernasality]. *Revista CEFAC* 16: 1936–1944.
- Perry J and Zajac DJ. (2016) Clefts of the lip and palate. In: Zajac DJ and Vallino LD (eds) *Evaluation and Management of Cleft Lip and Palate: A Developmental Perspective*. Plural Publishing Inc., 23–48.

- Peter JP, Chinsky RR and Fisher MJ. (1975) Sociological aspects of cleft palate adults. III. Vocational and economic aspects. *Cleft Palate J* 12: 193–199.
- Peterson-Falzone SJ, Trost-Cardamone J, Karnell MP, et al. (2017) *The Clinician's Guide to Treating Cleft Palate Speech*, Missouri (MO): Elsevier.
- Pham GK. (2010) *Quy hoạch tổng thể phát triển hệ thống y tế Việt Nam giai đoạn đến năm 2010 và tầm nhìn đến năm 2020 [Master plan to develop health system in Vietnam to 2010 and vision to the year 2020]*. Available at: <http://www.nhandan.com.vn/phapluat/item/8961602-.html>.
- Phan QD and Hoang TH. (2007) Tình hình dị tật bẩm sinh khe hở môi-hàm ếch tại bệnh viện Từ Dũ và Hùng Vương [Situation of congenital birth defect, cleft lip and cleft palate, at Tu Du and Hung Vuong Hospitals]. *Tuyển tập công trình nghiên cứu khoa học Răng Hàm Mất [Collection of Scientific Research in Odonto-Stomatology]*: 93–100.
- Phares V, Lopez E, Fields S, et al. (2005) Are fathers involved in pediatric psychology research and treatment? *J Pediatr Psychol* 30: 631–643.
- Pimenta LA, De Rezende Barbosa GL, Pretti H, et al. (2015) Three-dimensional evaluation of nasopharyngeal airways of unilateral cleft lip and palate patients. *Laryngoscope* 125: 736–739.
- Pinto E, Pinto E, Soares S, et al. (2013) A critical review of dental caries in individuals with cleft lip. *World J. Dent* 4: 272–275.
- Posnick JC and Ricalde P. (2004) Cleft-orthognathic surgery. *Clin Plast Surg* 31: 315–330.
- Posnick JC and Ruiz RL. (2002) Staging of Cleft Lip and Palate Reconstruction: Infancy through Adolescence. In: Wyszynski DF (ed) *Cleft Lip & Palate: From Origin to Treatment*. Oxford University Press, 319–353.
- Prahl C, Kuijpers-Jagtman AM, van't Hof MA, et al. (2001) A randomised prospective clinical trial into the effect of infant orthopaedics on maxillary arch dimensions in unilateral cleft lip and palate (Dutchcleft). *Eur J Oral Sci* 109: 297–305.
- Prahl C, Kuijpers-Jagtman AM, Van 't Hof MA, et al. (2003) A randomized prospective clinical trial of the effect of infant orthopedics in unilateral cleft lip and palate: prevention of collapse of the alveolar segments (Dutchcleft). *Cleft Palate Craniofac J* 40: 337–342.
- Prahl C, Kuijpers-Jagtman AM, Van 't Hof MA, et al. (2005) Infant orthopedics in UCLP: effect on feeding, weight, and length: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 42: 171–177.
- Prahl C, Prahl-Andersen B, Van't Hof MA, et al. (2008) Presurgical orthopedics and satisfaction in motherhood: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 45: 284–288.
- Prahl C, Prahl-Andersen B, van 't Hof MA, et al. (2006) Infant orthopedics and facial appearance: a randomized clinical trial (Dutchcleft). *Cleft Palate Craniofac J* 43: 659–664.
- Ramstad T. (1989) Periodontal condition in adult patients with unilateral complete cleft lip and palate. *Cleft Palate J* 26: 14–20.
- Ramstad T, Ottem E and Shaw WC. (1995) Psychosocial adjustment in Norwegian adults who had undergone standardised treatment of complete cleft lip and palate. II. Self-reported problems and concerns with appearance. *Scand J Plast Reconstr Surg Hand Surg* 29: 329–336.
- Rankin M and Borah GL. (2003) Perceived functional impact of abnormal facial appearance. *Plast Reconstr Surg* 111: 2140–2146; discussion 2147–2148.

- Rautio J, Andersen M, Bolund S, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 2. Surgical results. *J Plast Surg Hand Surg* 51: 14–20.
- Reid J, Kilpatrick N and Reilly S. (2006) A prospective, longitudinal study of feeding skills in a cohort of babies with cleft conditions. *Cleft Palate Craniofac J* 43: 702–709.
- Sakano N. (2015) Introduction of regional health information network in Vietnam. *FUJITSU Sci. Tech. J.* 51: 84–89.
- Sandy J, Kilpatrick N and Ireland A. (2012) Treatment outcome for children born with cleft lip and palate. *Front Oral Biol* 16: 91–100.
- Sank JR, Berk NW, Cooper ME, et al. (2003) Perceived social support of mothers of children with clefts. *Cleft Palate Craniofac J* 40: 165–171.
- SEDENTEXCT. (2012) *Radiation Protection N° 172 Cone beam CT for dental and maxillofacial radiology (Evidence-Based Guidelines)*: Energy.
- Sell D, Grunwell P, Mildinhall S, et al. (2001) Cleft lip and palate care in the United Kingdom--the Clinical Standards Advisory Group (CSAG) Study. Part 3: speech outcomes. *Cleft Palate Craniofac J* 38: 30–37.
- Sell D, Mildinhall S, Alberty L, et al. (2015) The Cleft Care UK study. Part 4: perceptual speech outcomes. *Orthod Craniofac Res* 18: 36–46.
- Semb G, Brattstrom V, Molsted K, et al. (2005) The Eurocleft study: intercenter study of treatment outcome in patients with complete cleft lip and palate. Part 4: relationship among treatment outcome, patient/parent satisfaction, and the burden of care. *Cleft Palate Craniofac J* 42: 83–92.
- Shahidi S, Momeni Danaie S and Omidi M. (2016) Comparison of the Pharyngeal Airway Volume between Non-Syndromic Unilateral Cleft Palate and Normal Individuals Using Cone Beam Computed Tomography. *J Dent (Shiraz)* 17: 268–275.
- Shapiro DN, Waljee J, Ranganathan K, et al. (2015) Using the Patient Reported Outcomes Measurement Information System to Evaluate Psychosocial Functioning among Children with Craniofacial Anomalies. *Plast Reconstr Surg* 135: 1673–1679.
- Sharma RK and Nanda V. (2009) Problems of middle ear and hearing in cleft children. *Indian J Plast Surg* 42: S144-S148.
- Shaw WC, Asher-McDade C, Brattstrom V, et al. (1992) A six-center international study of treatment outcome in patients with clefts of the lip and palate: Part 1. Principles and study design. *Cleft Palate Craniofac J* 29: 393–397.
- Shaye D. (2014) Update on outcomes research for cleft lip and palate. *Curr Opin Otolaryngol Head Neck Surg* 22: 255–259.
- Silverstein LB. (2002) Fathers and families. In: McHale JP and Grolnick WS (eds) *Retrospect and Prospect in the Psychological Study of Families*. Mahwah, NJ: Lawrence Erlbaum Associates, 35–64.
- Sinko K, Jagsch R, Prechtl V, et al. (2005) Evaluation of esthetic, functional, and quality-of-life outcome in adult cleft lip and palate patients. *Cleft Palate Craniofac J* 42: 355–361.
- Sitzman TJ, Allori AC and Thorburn G. (2014) Measuring outcomes in cleft lip and palate treatment. *Clin Plast Surg* 41: 311–319.
- Slifer KJ, Beck M, Amari A, et al. (2003) Self-Concept and Satisfaction With Physical Appearance in Youth With and Without Oral Clefts. *Children's Health Care* 32: 81–101.

- Slutsky H. (1969) Maternal reaction and adjustment to birth and care of cleft palate child. *Cleft Palate J* 6: 425–429.
- Smallridge J, Hall AJ, Chorbachi R, et al. (2015) Functional outcomes in the Cleft Care UK study--Part 3: oral health and audiology. *Orthod Craniofac Res* 18: 25–35.
- Stanier P and Moore GE. (2004) Genetics of cleft lip and palate: syndromic genes contribute to the incidence of non-syndromic clefts. *Hum Mol Genet* 13: R73–81.
- Stec-Slonicz M, Szczepanska J and Hirschfelder U. (2007) Comparison of caries prevalence in two populations of cleft patients. *Cleft Palate Craniofac J* 44: 532–537.
- Stock NM and Feragen KB. (2016) Psychological adjustment to cleft lip and/or palate: A narrative review of the literature. *Psychol Health* 31: 777–813.
- Swanson JW, Yao CA, Auslander A, et al. (2017) Patient Barriers to Accessing Surgical Cleft Care in Vietnam: A Multi-site, Cross-Sectional Outcomes Study. *World J Surg* 41: 1435–1446.
- Swennen GR, Grimaldi H, Upheber J, et al. (2004) Nasalance measures in German-speaking cleft patients. *J Craniofac Surg* 15: 158–164; discussion 164.
- Takashima K, Wada K, Tra TT, et al. (2017) A review of Vietnam's healthcare reform through the Direction of Healthcare Activities (DOHA). *Environ Health Prev Med* 22: 74.
- Tillman KK, Hakelius M, Hoijer J, et al. (2018) Increased Risk for Neurodevelopmental Disorders in Children With Orofacial Clefts. *J Am Acad Child Adolesc Psychiatry* 57: 876–883.
- Uslu-Akcam O. (2017) Pharyngeal airway dimensions in skeletal class II: A cephalometric growth study. *Imaging Sci Dent* 47: 1–9.
- Van Doorn J and Purcell A. (1998) Nasalance levels in the speech of normal Australian children. *Cleft Palate Craniofac J* 35: 287–292.
- Vanpoelvoorde L and Shaughnessy MF. (1991) Parental Reactions to Cleft Palate Children. *Journal of Special Education* 15: 276–283.
- Vanz AP and Ribeiro NR. (2011) Listening to the mothers of individuals with oral fissures. *Rev Esc Enferm USP* 45: 596–602.
- Vegter F, Mulder JW and Hage JJ. (1997) Major residual deformities in cleft patients: a new anthropometric approach. *Cleft Palate Craniofac J* 34: 106–110.
- Vu TBH, Nguyen XN and Hoang CC. (2004) Mẫu câu âm thay thể của người bị khe hở vòm miệng [Articulation errors of cleft palate children]. *Nghien cuu y hoc [Medical research]* 28: 54–58.
- Warren DW, Hairfield WM, Dalston ET, et al. (1988) Effects of cleft lip and palate on the nasal airway in children. *Arch Otolaryngol Head Neck Surg* 114: 987–992.
- Waylen A, Ness AR, Wills AK, et al. (2015) Cleft Care UK study. Part 5: child psychosocial outcomes and satisfaction with cleft services. *Orthod Craniofac Res* 18: 47–55.
- Weatherley-White RC, Eiserman W, Beddoe M, et al. (2005) Perceptions, expectations, and reactions to cleft lip and palate surgery in native populations: a pilot study in rural India. *Cleft Palate Craniofac J* 42: 560–564.
- Wermker K, Jung S, Joos U, et al. (2012) Nasopharyngeal Development in Patients with Cleft Lip and Palate: A Retrospective Case-Control Study. *Int J Otolaryngol* 2012: 458507.
- Whitehill TL. (2001) Nasalance measures in Cantonese-speaking women. *Cleft Palate Craniofac J* 38: 119–125.
- Wilhelmsen HR and Musgrave RH. (1966) Complications of cleft lip surgery. *Cleft Palate Journal* 3: 223–231.

- Willadsen E, Lohmander A, Persson C, et al. (2017) Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 5. Speech outcomes in 5-year-olds - consonant proficiency and errors. *J Plast Surg Hand Surg* 51: 38–51.
- Williams AC, Bearn D, Mildinhal S, et al. (2001) Cleft lip and palate care in the United Kingdom--the Clinical Standards Advisory Group (CSAG) Study. Part 2: dento-facial outcomes and patient satisfaction. *Cleft Palate Craniofac J* 38: 24–29.
- Witt PD and Marsh JL. (1997) Advances in assessing outcome of surgical repair of cleft lip and cleft palate. *Plast Reconstr Surg* 100: 1907–1917.
- Wong FK and Hagg U. (2004) An update on the aetiology of orofacial clefts. *Hong Kong Med J* 10: 331–336.
- Wong FWL and King NM. (1998) The Oral Health of Children with Clefts—A Review. *Cleft Palate Craniofac J* 35: 248–254.
- Wong Riff K W Y, Tsangaris E, Goodacre T, et al. (2017) International multiphase mixed methods study protocol to develop a cross-cultural patient-reported outcome instrument for children and young adults with cleft lip and/or palate (CLEFT-Q). *BMJ Open* 7.
- World Health Organization. (2013) Oral health surveys. Basic methods, 5th ed.
- Worldometers. (2019) *Viet Nam Population*. Available at: <http://www.worldometers.info/world-population/vietnam-population/>.
- Xiao WL, Zhang DZ and Xu YX. (2015) The caries prevalence of oral clefts in eastern China. *Int J Clin Exp Med* 8: 16322–16327.
- Yao CA, Swanson J, Chanson D, et al. (2016) Barriers to Reconstructive Surgery in Low- and Middle-Income Countries: A Cross-Sectional Study of 453 Cleft Lip and Cleft Palate Patients in Vietnam. *Plast Reconstr Surg* 138: 887e-895e.
- Ye B, Ruan C, Hu J, et al. (2010) A comparative study on dental-arch morphology in adult unoperated and operated cleft palate patients. *J Craniofac Surg* 21: 811–815.
- Zeytinoğlu S, Davey MP, Crerand C, et al. (2016) Fathers of children born with cleft lip and palate: Impact of the timing of diagnosis. *Fam Syst Health* 34: 150–158.
- Zhu WC, Xiao J, Liu Y, et al. (2010) Caries Experience in Individuals With Cleft Lip and/or Palate in China. *Cleft Palate Craniofac J* 47: 43–47.
- Ziak P, Fedeles J, Jr., Fekiacova D, et al. (2010) Timing of primary lip repair in cleft patients according to surgical treatment protocol. *Bratisl Lek Listy* 111: 160–162.
- Zimmerman MA, Salem DA and Notaro PC. (2000) Make room for Daddy II: The positive effects of fathers' role in adolescent development. In: Taylor RD and Wang MC (eds) *Resilience across contexts* Mahwah, NJ: Lawrence Erlbaum Associates, 233–253.

APPENDICES

Appendix A: Speech stimuli

A1. Oral stimuli

A1.1. Oral words

Hoa, Phở, Trê, Quýt, Pa-tê, Tai, Gà, Đò, Voi, Thỏ, Rỗ, Bò, Xe, Dao, Sữa, Gió, Chó, Khế, Ly

A1.2. Oral sentences

Pa pa	Lí la lí lắ
Bà Bắ bị bắ	Thỏ thích thờ
Tí tập tạ	Rú ra rú rít
Đu đu đò	Chú chích chò
Con cò có cái cò cao	Tre trúc trờ trụi
Gà gò gáy	Khúc kha khúc khích
Xôi xúc xích	Hà hả hê
Phì phà phì phò	Dao dây dưa
Vũ về vôi vĩa	Su sửa số sách

A2. Oro-nasal stimuli

Quê hương là chùm khế ngọt
Cho con trèo hái mỗi ngày
Quê hương là đường đi học
Con về rợp bướm vàng bay
Quê hương là con diều biếc
Tuổi thơ con thả trên đồng
Quê hương là con đò nhỏ
Êm đềm khua nước ven sông

A3. Nasal stimuli

Nu na nu nóng
Hỏi han mọi người
Mênh mông sông nước
Ngày tháng năm
Mình muốn tắm mưa
Nói chuyện lan man
Nhấn nhủ nhau nói năng nhẹ nhàng

7. Chin:

Very happy ☺ ☹ Very unhappy

10 5 0

8. Teeth:

Very happy ☺ ☹ Very unhappy

10 5 0

9. Cheeks:

Very happy ☺ ☹ Very unhappy

10 5 0

10. Hair:

Very happy ☺ ☹ Very unhappy

10 5 0

11. Ears:

Very happy ☺ ☹ Very unhappy

10 5 0

12. Eyes:

Very happy ☺ ☹ Very unhappy

10 5 0

13. How happy are you with your speech?

Very happy ☺ ☹ Very unhappy

10 5 0

14. How happy are you with your hearing?

Very happy ☺ ☹ Very unhappy

10 5 0

15. Overall how noticeable do you feel your cleft is to other people?

Not at all noticeable ☺ ☹ Very noticeable

10 5 0

Appendix C: The Vietnamese version of the CHASQ

Tên	Ngày sinh	Ngày lập phiếu

Một số bạn trẻ nói với chúng tôi là họ rất hài lòng về khả năng nghe, về bên ngoài và cách phát âm của họ, trong khi đó một số khác cảm thấy ít hài lòng hơn. Bạn cảm thấy khả năng nghe, về bên ngoài và cách phát âm của bạn như thế nào? Không có câu trả lời đúng hay sai. Vui lòng đánh dấu chọn (✓) vào một ô cho mỗi câu hỏi.

Mức độ hài lòng của bạn với:

1. Gương mặt của bạn

Rất hài lòng	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không hài lòng
		10	5	0

2. Toàn bộ vẻ bên ngoài của bạn:

Rất hài lòng	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không hài lòng
		10	5	0

3. Mặt nhìn nghiêng:

Rất hài lòng	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không hài lòng
		10	5	0

4. Bạn nghĩ mình đẹp trai/đẹp gái đến mức nào?

Rất đẹp	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không đẹp chút nào
		10	5	0

Bạn thấy những phần này trên khuôn mặt bạn như thế nào?

5. Mũi:

Rất hài lòng	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không hài lòng
		10	5	0

6. Môi:

Rất hài lòng	😊	<input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	☹️	Không hài lòng
		10	5	0

7. Cảm:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

8. Răng:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

9. Má:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

10. Tóc:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

11. Tai:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

12. Mắt:

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

13. Mức độ hài lòng của bạn về cách phát âm của mình?

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

14. Mức độ hài lòng về khả năng nghe của bạn?

Rất hài lòng ☺ ☹ Không hài lòng
10 5 0

15. Nhìn chung, bạn thấy mức độ chú ý của mọi người với khe hở của bạn như thế nào?

Không chú ý ☺ ☹ Rất chú ý
10 5 0

Appendix D: The Estonian version of the CHASQ

Nimi	Sünniaeg	Täitmise kuupäev

Mõned noored ütlevad, et nad on rahul oma kuulmise, välimuse ja kõnega, teised aga ei ole nii rahul.
Kuidas sina tunned?
Ei ole õigeid ega valesid vastuseid.
Palun märgi iga küsimuse juures rist vastavasse kasti.

Palun hinda oma rahulolu:

1. Näo välimusega:

Väga rahul ☺ ☹ Ei ole üldse rahul

10 5 0

2. Välimusega üldiselt:

Väga rahul ☺ ☹ Ei ole üldse rahul

10 5 0

3. Profiiliga (külgsaatega):

Väga rahul ☺ ☹ Ei ole üldse rahul

10 5 0

4. Kui hea Sa enda arvates välja näed?

Väga kena ☺ ☹ Ei ole üldse kena

10 5 0

Palun hinda oma rahulolu:

5. Ninaga:

Väga rahul ☺ ☹ Ei ole üldse rahul

10 5 0

6. Huultega:

Väga rahul ☺ ☹ Ei ole üldse rahul

10 5 0

7. Lõuaga:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

8. Hammastega:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

9. Põskedega:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

10. Juustega:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

11. Kõrvadega:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

12. Silmadega:

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

13. Kui rahul oled Sa oma kõnega?

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

14. Kui rahul oled Sa oma kuulmisega?

Väga rahul ☺ ☹

10 5 0

Ei ole üldse rahul

15. Mis Sa arvad, kui märgatav on Sinu lõhe teistele inimestele?

Ei märgata üldse ☺ ☹

10 5 0

Väga märgatav

SUMMARY IN ESTONIAN

Esimene huule- ja suulõhedega patsientide ravitulemuste uuring Kesk-Vietnamis

Sissejuhatus

Huule- ja/või suulaelõhe on üks sagedasemaid kaasasündinud väärarenguid. Huule- ja suulaelõhede klassifikatsiooni alusel jaotatakse lõhed kolmeks suureks haigusfenotüübiks: huulelõhe (CL); huule- ja suulalelõhe (CLP) ja isoleeritud suulaelõhe (CP). Huule- ja/või suulaelõhe esinemissagedus on keskmiselt 1/700 elussünni kohta. Vietnamis esineb huule- ja/või suulaelõhe 1/677 elusünni kohta.

Suulõhega sündinud lapsed vajavad ravi erinevate spetsialistide poolt ja seda erinevatel vanuseperioodidel sünnist kuni täiskasvanuks saamiseni, tihti peale ka kauem. Seetõttu tuleb ravi kaugtulemusi hinnata erinevast perspektiivist. Vietnamis on enamikul patsientidest tervisekindlustus, kuid paljud patsiendid loodavad ikkagi rahvusvaheliste abiorganisatsioonide missioonidele, mitte ei kasuta riigimeditsiini võimalusi. Eeltoodu on ka põhjuseks, miks suulõhede ravi Vietnamis ei ole kooskõlas rahvusvaheliselt kasutuses olevate protokollidega. Kesk-Vietnamisse teevad missioone erinevad rahvusvahelised abiorganisatsioonid (Chonbuk Ülikooli operatsioonimeeskond, Operation Smile, Smile Train, Interplast, Global Care Korea) ja selliseid missioone on tehtud juba pikka aega. Sellisel kujul suulõhede ravi on suunatud pigem kirurgilistele sekkumistele ning pikemat aega nõudvad sekkumised nagu kõneravi ja hambumusanomaaliade ravi ei ole tagatud. Patsientide järelkontroll on sellise korralduse juures kaootiline ning ravi (kaug) tulemusi reeglina hinnatud ei ole.

Uurimustöö eesmärgid

1. Selgitada välja hammaste tervise olukord (kaariese esinemine ja parodonti seisund) huule- ja suulaelõhega patsientidel
2. Uurida huule- ja suulaelõhega sündinud lapse ema tundeid ja suhtumist lõhega lapse sünni; uskumusi ja kultuurilisi eripärasid ning elukorralduse muutust lõhega lapse sünni järgselt.
3. Hinnata huule- ja suulaelõhega patsientide nasolabiaalset esteetikat.
4. Luua normpatsientide nasaleerituse normid vietnami keele jaoks ning uurida vietnami keelt kõnelevate huule- ja suulaelõhega patsientide kõnekvaliteeti.
5. Selgitada välja huule- ja suulaelõhega patsientide kraniofatsiaalne morfoloogia, hambakaarte mõõtmed, kõvasuulae- ning ülemiste hingamisteede struktuuride parameetrid.
6. Uurida huule- ja suulaelõhega patsientide ning nende vanemate/hooldajate rahulolu ravitulemustega.

Uuringu metoodika

Uurimusse kaasati 81 huule- ja suulaelõhega patsienti. Erinevates uuringutes kasutati erinevaid kontrollgruppe. Nasolabiaalse esteetika hindamisel kasutati kontrollgrupina 33 Eestis ravitud huule- ja suulaelõhega patsiendi andmeid. Nasaalsuse normide väljatöötamisel vietnami keele jaoks uuriti 102 last, kellel

ei olnud suulõhe diagnoosi. Lõualuude morfoloogia ja ülemiste hingamisteede struktuuride uuringus kasutati kontrollgrupis 24 ilma suulõhe diagnoosita vietnamlase andmeid. Ravitulemuste hindamisel kasutati kontrollgrupina 27 Eesti huule- ja suulaelõhega patsienti

Hammaste kariosse seisundi määramiseks kasutati dmft/DMFT indeksi. Parodontaalse ravivajaduse hindamiseks kasutati kahte näitajat: veritsust sondeerimisel ja igemetasku seisundit.

Suulõhega sündinud lapse ema tunnete, uskumuste, teadmiste ja pere elukorralduse muutuste hindamiseks kasutati avatud küsimustega küsimustikku.

Nasolabiaalset esteetikat hindas 5 spetsialisti: näo- ja lõualuude kirurg, hambaarst, orthodontia resident, 2 ortodonti. Hindamiseks kasutati kolme eri meetodit: viie punkti esteetilist indeksit, *visuaal analoog skaalat (VAS)* ja referentsväärtuste meetodit.

Nasaleerituse normide välja töötamiseks koostati vietnami keele spetsiifikat arvestav testmaterjal, mis koosnes kolmest stiimulite grupist: (1) oraalsed, (2) oro-nasaalsed ja (3) nasaalsed stiimulid. Nasaleerituse aste määrati nasomeetriga (Nasometer II (model 6450) (PENTAX Medical, Montvale, NJ), kasutades spetsiaalset tarkvara Nasometer™ (PENTAX Medical, Montvale, NJ). Patsientidele esitati järelekordamiseks kõnelisi stiimuleid, patsient kordas talle esitatud kõnelist stiimulmaterjali kaks korda. Keskmist nasaleerituse väärtust ja standardhälvet kasutati andmete analüüsil.

Näo- ja lõualuude piirkonna luuliste struktuuride ning ülemiste hingamisteede morfoloogia hindamiseks kasutati kolju külgülesvõtteid. Kolju külgülesvõtted tehti aparaadiga Galileos (Dentsply Sirona, Germany) järgmiste seadetega: 9.4 sekundit, 60–84 kV ja 10–15 mA sõltuvalt soost, vanusest ja kehakujust. Kolju külgülesvõtetelt teostati tsefalomeetriline analüüs kasutades Dolphin Imaging tarkvara (Dolphin Imaging & Management Solutions, USA). Hambakaared skaneeriti intraoraalse skänneriga TRIOS® 3 Color Pod (3Shape, Denmark), mille tulemusena valmisid digitaalsed mudelid. Mudelanalüüsi käigus mõõdeti ülakaare dimensioonid ja suulae morfoloogia. Patsientide ja vanemate ravitulemustega rahulolu uurimiseks kasutasime Cleft Hearing, Appearance and Speech Questionnaire (CHASQ) küsimustikku. Küsimustik tõlgiti reeglite kohaselt eesti ja vietnami keelde.

Tulemused

Kesk-Vietnamis esines kaariest 87,2% huule- ja suulaelõhega patsientidest. dmft/DMFT indeksi järgi on see väga kõrge hambakaariese esinemise näitaja. Suulõhe diagnoosiga lastel vanuses ≤ 5 aastat oli indeks suuruseks 7.4 ± 6.6 . Vahelduvas hammaskonnas, vanuses 6–12 aastat oli dmft/DMFT indeks 9.0 ± 5.1 ja 1.6 ± 1.8 . Huule- ja suulaelõhega patsientidel vanuses ≥ 13 aastat oli DMFT 6.7 ± 5.0 . Olulisi seoseid ei leitud hambakaariese esinemise osas suulõhe klassifikatsioonist, vanusegrupist ja soost lähtuvalt ($p > 0.05$) väljaarvatud seos DMFT indeksi erinevuses vanusegruppides 6–12 ja ≥ 13 eluaastat ($p < 0.05$). Huule- ja suulaelõhega patsientidest 60%-l täheldati veritsust igemevaio sondeerimisel ja 5.3% (vanus > 15 aastat, $n = 19$) uuritavatest diagnoositi

igemetasku sügavusega 3.5–5 mm. Igemevao sondeerimisel ilma veritusetahammaste arv oli keskmisel 18.5 ± 5.2 ja veritsusega 2.7 ± 3.7 .

Suulõhega lapse sünni järgselt oli ema emotsionaalseks reaktsiooniks kurbus. Peaaegu pooled emadest ei osanud märkida põhjust, mis oleks võinud mängida rolli huule- ja suulaelõhe tekkes (47.4%). Ülejäänud emad pakusid suulõhe tekkepõhjusteid järgmiselt: terviserike (27.6%), ravimid (11,8%), keemikaalid (3,9%), pärilikkus (9,2%). Suuremal osal emadest oli olemas tugivõrgustik perekonna või abikaasa näol (92.1%). Umbes 40% suulõhega laste emadest ei tundnud, et nad oleksid pidanud tegama muudatusi oma igapäevaelus. Teine osa emadest, aga tõi esile järgmisi kitsaskohti: rahalised raskused, depression või raskused igapäevaeluga hakkama saamisel. Suurem osa emadest ei varjanud oma last teiste eest (78.9%).

Vietnamlastest koosnevas uuringugrupis, kasutades viie punkti esteetika-indeksit, hinnati nina sümmeetriat kõige madalamalt (2.7 ± 0.9), samas ees- talstest koosnevas uuringugrupis hinnati kõige madalamalt nasolabiaalset profiili (2.7 ± 1.0). Kahe uuringugrupi vahel ei leitud nasolabiaalse esteetika osas suuri erinevusi ($p > 0.05$) välja arvatud nina sümmeetrilisus. Kasutades erinevaid hindamismeetodeid nasolabiaalse esteetika määramiseks oli mõlemas opereeritud huule- ja suulaelõhega patsientide uuringugrupis hindamistulemused sarnased.

Nasaleerituse aste vietnami keelt kõnelevatel normlastel oli: 13,1% oraalsete, 30,7% oro-nasaalsete ja 56,9% nasaalsete stiimulite puhul. Sugude vahelised erinevused puudusid ($p < 0.05$).

Nasaleerituse aste vietnami keelses huule- ja suulaelõhede grupis oli: 30,2% oraalsete, 42,8% oro-nasaalsete ja 58,7% nasaalsete stiimulite puhul. Üle pooltel siia gruppi kuuluvatest patsientidest esines hüpernasaalsus (52,6%). Täiskasvanud suulõhega patsientidel oli tunduvalt kõrgem nasaleerituse aste kõigi kolme stimuli puhul ($p < 0.05$).

Huule- ja suulaelõhega laste näo- ja lõualuude ehituses olid järgmised tähelepanekud: teravam koljupõhimiku nurk, lühem koljupõhimik, lühem ja tagumise asetusega ülalõug, skeletaalne klass III suhe, lühem näo eesmise osa pikkus ja lühem alalõualuu pikkus. Samal uuringugrupil hinnati ka ülemiste hingamisteede struktuure ning leiti: eesmise asetusega keeleluu, väiksem suu- neelu ruum, väiksem keelepära tagune piirkond ja lühem pehme suulagi. Näo- ja lõualuude morfoloogia uuring täiskasvanute grupis näitas kolmanda klassi skeletaalset suhet, divergeeruvat skeletaalset mustrit, lühemat eesmist kolju- põhimikku ja lühemat ülalõualuu pikkust. Ülemiste hingamisteede mõõtmised täiskasvanud suulõhega patsientide grupis näitasid rohkem taga pool asetsevat keeleluud ja lühemat pehmet suulage.

Huule- ja suulaelõhega laste uuringugrupis olid ülalõualuu parameetrid vähenenud kõigis kolmes tasapinnas. Ülakaar ja ka suulagi olid kitsad, hambakaar ja suulagi olid lühenenud. Esimese jäävmolaari kohalt aga puudus erinevus hambakaare ja suulae laiuse osas kontrollgrupiga. Täiskasvanute uuringugrupis olid märgatavad erinevused hambakaare ja suulae laiuste osas ning hambakaare ja suulae pikkuses. Suulae sügavus ja nurgad ei erinenud kontrollgrupist.

Patsientide rahulolu CHASQ küsimustiku erinevate näitajate osas oli üle normväärtuste. Rahulolu huulte ja hammastega oli normist madalama hinnanguga vietnamlastest koosnevas uuringugrupis, kusjuures eestlastest koosnevas uuringugrupis ei olnud ükski näitaja normväärtustest väiksem. Võrreldes mõlemat gruppi, siis vietnamlased hindasid kõikide näitajate osas rahulolu madalamalt kui eestlastest uuritavad ($p < 0.05$) väljaarvatud kõnega rahulolu.

Vanemate rahulolu oli kõikide CHASQ küsimustiku näitajate osas normväärtustest kõrgem. Vietnamlastest vanemate rahulolu oli kõrgem kui nende lastel ($p < 0.05$), eestlastest lapsevanemate rahulolu erinevate näitajate osas oli aga nende lastest madalam ($p < 0.05$). Mõlemas uuringugrupis ei olnud tugevalt positiivset korrelatsioonseost vanemate ja laste hinnangute vahel. Vietnamlastest koosnenud uuringugrupis leiti positiivne korrelatsioonseos järgmiste näitajate osas: nägu, nina, huuled, hambad ja kõne. Eestlastest koosnenud uuringugrupis oli positiivne korrelatsioonseos ainult ühe näitaja osas, milleks oli nina.

Järeldused

1. Kesk-Vietnami huule- ja suulaelõhega patsientidel oli halb suutervis, väga suur hambakaarise esinemissagedus, esines gingiviiti age ei esinenud parodontiiti. Seos leiti hambakaarise esinemise ja vanemate *sotsiaalökonoomiline* staatuse vahel.
2. Suulõhega lapse sünni järgselt oli ema emotsionaalseks reaktsiooniks kurbus. Lõhe tekkes ei omistatud tähtsust üleloomulikele jõududele ega uskumustele. Suulõhega lapse sünn ei toonud kaasa suuri elumuutusi.
3. Sõltumata hindamismeetodist olid nasolabiaalse esteetika hindamistulemused sarnased. Nina sümmeetriat hinnati kõige kriitilisemalt.
4. Uuringu käigus töötati välja nasaleerituse normid vietnami keele Kesk-Vietnami murdele. Lähtuvalt nasaleerituse normidest ei olnud huule- ja suulaelõhega patsientide kõnekvaliteet hea. Rohkem kui pooltel uuritavatest esines hüpernasaalsus.
5. Osadel huule- ja suulaelõhega uuritavatest esines Angle III klassi hambumusanomaalia. Suulõhega laste uuringugrupis olid ülemiste hingamisteede suurus ning ülakaare ja suulae mõõtmed vähenenud kõigis kolmes tasapinnas. Täiskasvanud suulõhega patsientide suulae mõõtmed olid sarnased kontrollgrupi uuritavatega.
6. Nii suulõhega uuritavad kui ka nende vanemad olid rahul ravitulemustega. Suulõhega uuritavate rahulolu oli väiksem näitajatega mis on iseloomulikud just lõhe olemasolule. Hinnangute sarnasus suulõhega uuritavate ja nende vanemate vahel oli madalast keskmiseni.

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Publications:

1. Van Thai Nguyen, Hong Loi Nguyen, Toai Nguyen, Triin Jagomägi. Oral health status of patients with repaired cleft lip and palate in Central Vietnam. *Oral Health & Preventive Dentistry*. [Accepted].
2. Van Thai Nguyen, Triin Jagomägi. Maternal experiences of having a child with a cleft. *J Otol Rhinol*. 2018 7:3. doi: 10.4172/2324-8785.1000343
3. Van Thai Nguyen, Toai Nguyen, Triin Jagomägi. Nasolabial aesthetics of patients with repaired unilateral cleft lip and palate: A comparison of three rating methods in two countries. *J Craniomaxillofac Surg*. 2018 Aug;46(8): 1385–1389. doi: 10.1016/j.jcms.2018.05.029. Epub 2018 May 18.
4. Van Thai Nguyen, Lagle Lehes, Thi Thuy Hang Truong, Thi Van Anh Hoang, Triin Jagomägi. Normative nasalance scores for Vietnamese-speaking children. *Logoped Phoniatr Vocol*. 2017 Oct 26:1–7. doi: 10.1080/14015439.2017.1389985. [Epub ahead of print]

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- Erasmus+ projekt HI3 (2018–2020) “Health Innovation, Implementation and Impact (HI3)—A functional training program on how to implement sustainable change in the health care system on a clinical level”
- COST Action CA16234 (2017–2021) “European Cleft and Craniofacial Initiative for Equality in Care (ECCE)”
- EduShare (2016–2019) “Joint capacity building in biomedical higher education through adopting international academic standards and transferring technology between European and Vietnam universities—EDUSHARE”
- COST Action IS1210 (2013–2017) “Appearance Matters: Tackling the Physical and Psychosocial Consequences of Dissatisfaction with Appearance”

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1. Van Thai Nguyen, Hong Loi Nguyen, Toai Nguyen, Triin Jagomägi. Oral health status of patients with repaired cleft lip and palate in Central Vietnam. *Oral Health & Preventive Dentistry*. [Accepted].
2. Van Thai Nguyen, Triin Jagomägi. Maternal experiences of having a child with a cleft. *J Otol Rhinol*. 2018 7:3. doi: 10.4172/2324-8785.1000343
3. Van Thai Nguyen, Toai Nguyen, Triin Jagomägi. Nasolabial aesthetics of patients with repaired unilateral cleft lip and palate: A comparison of three rating methods in two countries. *J Craniomaxillofac Surg*. 2018 Aug;46(8): 1385–1389. doi: 10.1016/j.jcms.2018.05.029. Epub 2018 May 18.
4. Van Thai Nguyen, Lagle Lehes, Thi Thuy Hang Truong, Thi Van Anh Hoang, Triin Jagomägi. Normative nasalance scores for Vietnamese-speaking children. *Logoped Phoniatr Vocol*. 2017 Oct 26:1–7. doi: 10.1080/14015439.2017.1389985. [Epub ahead of print]

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