Needing a Safe Pair of Hands

Functioning and Health-Related Quality of Life in Children with Congenital Hand Differences

Monique Saskia Ardon

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Betrouwbare Handen

Het functioneren en gezondheidsgerelateerde kwaliteit van leven van kinderen met een aangeboren handaandoening

Proefschrift

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Chapter 1

General Introduction

Our hands are extensively used in everyday activities and are the primary means of interaction with our environment. We use our hands for eating, bathing, gesturing and in childhood they are one of our instruments to discover the world. Especially in the developing child, hands are of great importance. When hand function in children is compromised, it may cause problems in participating in activities at home, with friends or at school. A difference in hand function in the developing child may be caused by a hand trauma or a congenital malformation, also called a congenital difference. In this thesis, we will focus on congenital hand differences.

Hand function is complex and needs a long developmental period to perfect the sophisticated interaction between the brain, the hands and sensory organs, thereby creating a hand skilled in performing daily activities. Therefore, parents of a new-born child with a diagnosed congenital hand difference have many questions. Their main concern is about the child's future functioning and well-being. Physicians and therapists working with these children and their parents experience the necessity for sound information about aetiology, treatment options and psychosocial support.

This thesis developed out of the recognition that there is a need for evidence-based information on the future functioning and well-being of these children and a need for knowledge on the most important factors that influence the functioning of these children.

Congenital Hand Differences

Children with congenital hand differences (CHD) are born with a disorder of the upper limb. In contrast with the status of a child's hand following trauma, the hand's anatomy of a child with a CHD is already different at birth. While there still is a lack of generally-accepted nomenclature, the disorder is also referred to as congenital anomalies or malformations. Since these terms are more reckoned to be negative terms, in this thesis we will use the phrase "congenital hand differences".[1]

The prevalence of CHD is estimated at 16 per 10,000 live births, but this number varies within different populations and ethnic groups[2-3] In approximately 75-80% of cases the difference is unilateral and associated anomalies are seen in up to 53% of cases. While associated musculoskeletal defects are found most frequently, several other congenital associated abnormalities exist that affect other systems, such as defects in head and neck, cardiovascular, gastrointestinal and genitourinary-tract systems[2-3]

The cause of the CHD is in 20 % genetic of origin and in 20 % the difference is caused by environmental factors, however in 60 % of all cases the precise cause remains unknown.[4] The upper limb difference can either be isolated (confined to the upper limb, possibly bilateral) or part of a syndrome. Although occasionally a genetic cause is found for an

isolated difference, most differences that are genetically based are part of a syndrome.

Upper-limb differences are mostly isolated and in most cases there are no other affected family members, suggesting that most of these differences are caused by vascular problems during embryogenesis, either from vasoconstriction, haemorrhage, thrombosis or embolization especially when transverse terminal defects are present.[2]

Classification of CHD is necessary to enable comparison of diagnosis and treatment, but is also difficult. The currently most commonly-used classification of congenital differences of the upper limb is based on the Swanson classification,[5] later modified by the Congenital Malformations Committee of the International Federation of Societies for Surgery of the Hand (IFSSH) in 1983 (Table 1).[3] This classification scheme consists of 7 main categories.[5] Most differences can be classified using this system[6], but in case of more than one type of differences within the same limb, classification may be difficult. Failures of differentiation and duplications are the most common differences.[7]

Table 1. Modified Swanson Classification

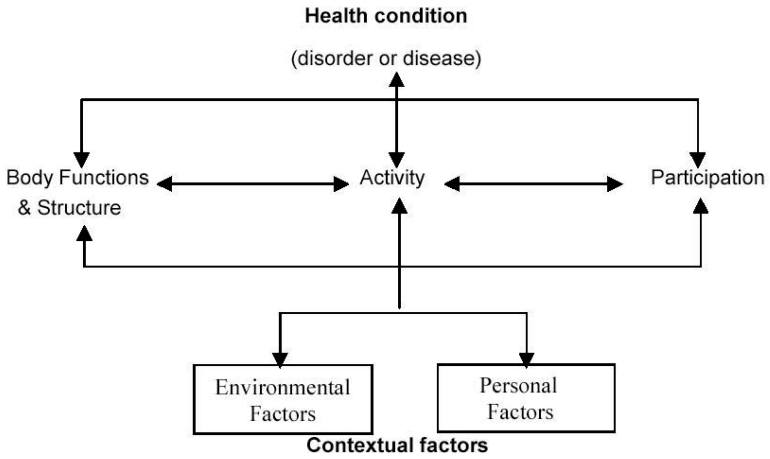
I	Failure of formation of parts (arrest of development)	
	A	Transverse arrest (common levels are upper third of forearm, wrist, metacarpal, phalangeal)
	B	Longitudinal arrest (including phocomelia, radial/ulnar club hands, typical cleft hand, atypical cleft hand otherwise referred to as part of the spectrum of symbrachydactyly)
II	Failure of differentiation of parts	
	A	Soft tissue involvement
	B	Skeletal involvement
	C	Congenital tumorous conditions (includes radio-ulnar synostosis, symphalangism (stiff PIPJs with short phalanges), camptodactyly, arthrogryposis, syndactyly)
III	Duplication	
IV	Overgrowth	
V	Undergrowth (thumb hypoplasia, Madelung's deformity)	
VI	Congenital constriction band syndrome	
VII	Generalised skeletal abnormalities	

Classifications can be useful to analyse groups of patients and to obtain a diagnosis. However, when using this diagnosis in everyday management of congenital hand differences, we should be aware that diagnosis does not predict function or direct treatment. Regardless of diagnosis, each child should be analysed and treated as an individual. To do so, it is important to monitor a child on all levels of functioning, which is best described with the framework of the World Health Organization International Classification of Functioning, Disability and Health – Child and Youth version (ICF-CY)

International Classification of Functioning, Disability and Health - Child and Youth Version

The International Classification of Functioning, Disability and Health - Child and Youth version (ICF-CY) is built from a bio-psychosocial model.[8-9] It captures the complexity of disability that takes into account both the medical and social aspects of the individual and society. The ICF-CY is designed for use with children and youth and allows for coding of more developmental aspects of functioning than the adult version. A child's functioning and disability, including its participation, is considered to arise from the interaction among health conditions, contextual or environmental factors, and personal factors. The ICF-CY provides a model of functioning and disability in which the interactions among these concepts are visualized (Figure A).

Figure A.



According to the ICF-CY model, functioning is classified as body functions, activities and participation. The ICF-CY has 2 parts (Health condition and Contextual factors), each consisting of 2 separate components: (1) body functions and structure, and activity and participation; and (2) environmental and personal factors. The ICF-CY provides codes that represent categories to describe the child's integrity of body functions and structures, the ability to perform daily-life activities and the scope of the individual's participation, and environmental factors that facilitate or impede functioning and personal factors. Beside the levels of functioning, there is also the distinction between capacity and performance. Capacity reflects what a child can do, and performance what a child does do in daily life. [8-9]

Children with CHD might experience problems in all domains of the ICF-CY. Therefore, in this thesis, the ICF-CY is the core framework to evaluate functioning of these children on all these domains.

Health-Related Quality of Life

Issues on functioning of children with CHD should not only address physical functioning, but also well-being of the child. The World Health Organization (WHO) describes the impact of health on a child's well-being as an individual's quality of life associated with their physical, mental and social well-being and is called health-related quality of life (HRQoL). HRQoL is defined as the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, and concerns.[10] Over the years, HRQoL has developed as an important outcome measure in pediatrics. The WHO and the International Association for Child Psychology and Child Psychiatry recommended that children's quality of life measurements should be self-reported wherever possible and therefore HRQoL is increasingly measured from the child's point of view.[11-13] Age-specific questionnaires are available as well as parallel versions of the child's questionnaire for their parents, allowing comparison of both scores or can be used as an alternative if a child is unable or unwilling to score the questionnaires. At the beginning of this project, data were lacking on HRQoL in children with CHD.

Aims and Contents of This Thesis

In this thesis, we intended to gain insight in the impact of a CHD on a child's and adolescent's daily functioning and HRQoL. Furthermore, we studied whether daily functioning and HRQoL can be enhanced by trying to find modifiable factors that influence function and HRQoL. Knowledge of these factors can be used to optimize the selection of interventions, both from a surgical and rehabilitative point of view.

The sequence of chapters in this thesis is based on the order of the anamnesis as used when consulting children with their parents in the outpatient clinic. Mostly, parents' first questions aim at getting answers on quality of life and future functioning of their children. Therefore, we started this thesis with two chapters on HRQoL. The chapters on functioning follow the top-down procedure. Whereas parents mostly question the levels of activities and social participation, the congenital hand team tries to find modifiable factors at all levels that influence activities and social participation. Hand surgeons intervene at the level of body functions, while rehabilitation physicians and hand therapists have possibilities to intervene at all levels.

The first part of this thesis documents the HRQoL and its main determinants. The second part presents the outcome according to the basic ICF-CY framework. Following a top down procedure, we start with HRQoL of children with CHD, followed by HRQoL, participation and activities in children with Apert Syndrome. Subsequently, we describe functioning on the different ICF-CY levels, relations between these levels and associated factors of children with diverse forms of CHD.

Chapter 2 provides insight in the perceived HRQoL in children with congenital hand differences. We evaluate HRQoL using child self-reports and compare the outcome to reference values of healthy peers. Furthermore, we examine associations with patient characteristics and performance of daily activities. **Chapter 3** focuses on the parent-child agreement on HRQoL. In this chapter, we compare the outcome on child self-reports and parent-reports in order to investigate whether the parent-report is a good substitute in cases where the child is unable to fill out the child self-report.

Chapter 4 describes HRQoL and functioning on activity and social participation level of children and adults with Apert Syndrome. **Chapter 5** addresses the capacity of the hands in performing daily activities, which is called manual capacity. Moreover, it evaluates body functions of the upper limb (e.g. hand functions) and manual capacity. Additionally, we explore the associations of manual capacity with both severity of the CHD and hand functions. The limitations in performance of daily activities are described in **Chapter 6**. In this chapter, we investigate which hand functions and manual capacity influence performance of daily activities, especially bimanual performance. Additionally, we try to enhance the clinical applicability of the Prosthetic Upper extremity Functional Index (PUFI) questionnaire by investigating the possibility of reducing the number of items, while still getting sufficient information on bimanual performance.

Finally, **Chapter 7** discusses the main findings of this thesis; it discusses methodological strengths and limitations, followed by implications for clinical practice and suggestions for future research.

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Chapter 2

Low Impact of Congenital Hand Differences on Health-Related Quality of Life

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Arch Phys Med Rehabil 2012;93: 351-7.

Abstract

Objective: To evaluate health-related quality of life (HRQoL) and its determinants in children with congenital hand differences (CHDs).

Design: Survey.

Setting: Outpatient clinic of a university hospital.

Participants: Children (N =116; age range, 10–14y) with CHDs.

Interventions: Not applicable.

Main Outcome Measures: HRQoL evaluated by child self-reports of the Pediatric Quality of Life Inventory and compared with reference values of healthy peers. Multivariable regression analysis was performed to investigate determinants of HRQoL.

Results: All children with CHDs had scores similar to those of healthy peers, except for a lower score on social functioning in children aged 13 to 14 years. Higher ease of activity performance was related to higher HRQoL scores, and presence of comorbidity was related to lower scores on all HRQoL subdomains except for school functioning. Additionally, physical health was influenced by ethnicity, bilateral involvement, and previous surgery; emotional functioning by the number of affected digits; school functioning by age; and total HRQoL by bilateral involvement.

Conclusions: Children with CHDs report similar HRQoL as healthy peers. HRQoL decreased in the presence of comorbidity but increased with higher ease of activity performance. Scores on some subdomains were improved by the number of affected digits, but were reduced by age, ethnicity, bilateral involvement, and surgery. Although HRQoL is an important health outcome, it may not be sensitive to detect changes over time or changes after treatment in children with CHDs.

Key Words: Adolescent; Child; Female; Hand deformity, congenital; Male; Quality of life; Questionnaires; Rehabilitation.

Introduction

After congenital heart malformations, congenital differences of the upper limb are the most frequently seen malformation at birth, and their incidence is estimated at 16 per 10,000 live births.[1] Parents of a child with a diagnosed congenital difference of the upper limb are mainly concerned about the child's future functioning and well-being. In case of prenatal diagnosis, some parents even consider late termination of the pregnancy.[2] Therefore, both before and after delivery, physicians counselling these parents need to provide evidence based information on the future functioning and well-being of the child. Functioning and well-being are 2 different aspects of the total functioning of a human being. Functioning is described by the World Health Organization (WHO) in the International Classification of Functioning, Disability and Health (ICF) at 3 levels: body function and structures, activity, and participation.[3] Well-being can be expressed in terms of health-related quality of life (HRQoL), which the WHO has defined as the individual's perception of their position of life in the context of culture and value systems in which they live, and in relation to their goals, expectations, and concerns.[4]

A chronic health condition, such as a congenital hand difference (CHD), has various effects on a person's functioning and well-being. It is well established that the relation between functioning and well-being is not straightforward.[5] Therefore, it is important to examine the effect of a health condition on all aspects of functioning and well-being.[5] Functioning of children with a CHD has been extensively studied, but research on the child's HRQoL is scarce.[5-10] Sheffler et al[5] reported that HRQoL in children with unilateral below-the-elbow deficiency was in the range of healthy peers and was even higher on social functioning. To our knowledge, however, HRQoL of children with CHDs other than only unilateral below-the-elbow deficiency, as well as the variables that influence HRQoL, is unknown. Therefore, the aims of this cross-sectional study were (1) to explore generic HRQoL in children with a CHD by administering the Dutch version of the generic core scales of the Pediatric Quality of Life Inventory Scales (PedsQL) 4.0[11-13] to measure the impact of a CHD by comparing the results with those of healthy peers and with children with other health conditions; and (2) to explore the variables related to different domains of HRQoL. Based on our clinical experience and on previous literature, we hypothesized that children with CHDs would report a similar HRQoL as their health peers.

Methods

This study used data from a cross-sectional study on functioning and HRQoL of children with a CHD. The subjects were 10- to 14-year old children, because this is the age range for the average onset of puberty, and also because in the Netherlands, there is a transition in this age group from primary school to secondary school. All children had a CHD treated at our hospital. Children were excluded if they had a mental or developmental delay or insufficient knowledge of the Dutch language. From the remaining subjects we randomly selected children, and we stopped the inclusion when we reached 120 participants (response rate of 40%). We found no differences between participants and non-participants regarding sex, diagnosis, and severity of the CHD. Children and their parents received a letter concerning the purpose and procedure of the study. If they agreed to participate, various questionnaires were filled out and selected body functions (eg, mobility, strength, and sensibility) were assessed. The local medical ethics committee approved the study, and parents of all children gave their informed consent to participate, as did all children of 12 years and older.

Participants

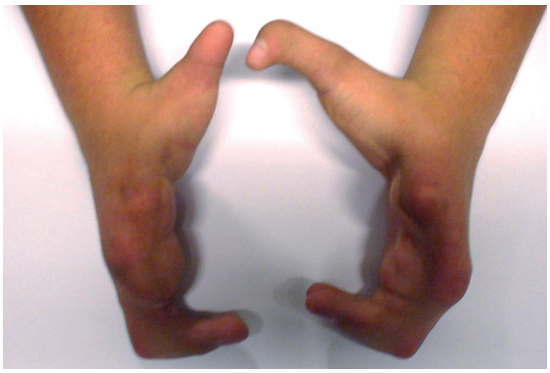
The questionnaires were completed by 116 of the 120 children. Each child's medical diagnosis was administered according to the International Federation of Societies for Surgery of the Hand (IFSSH) classification system. Since there is no established method for quantifying the severity of the CHD, we expressed this by means of bilateral involvement, number of affected digits per hand, and comorbidity.[14] Comorbidity was defined as the presence of any comorbidity not related to the hand problem, or the presence of syndromal differences related to the hand problem but in different body parts (eg, esophageal atresia, cardiac problems). Figure 1 presents examples of children participating in the study.

Outcome Measurement: HRQoL

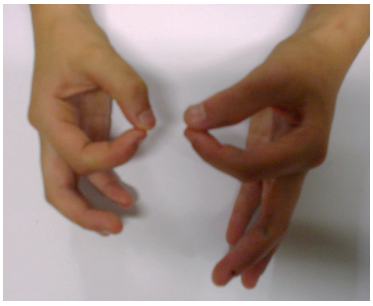
HRQoL was assessed using the PedsQL, a reliable and valid generic questionnaire.[11,13] The questionnaire consists of 23 questions and 4 generic core scales (8 on physical health, 5 on emotional functioning, 5 on social functioning, and 5 on school functioning). The psychosocial health score is an average of the emotional, social, and school functioning scores, and the total score is an average of the scores on all 4 generic core scales. Each question highlights an item on functioning that must be answered on a 5-point Likert scale to indicate the difficulties the child experiences with that item.[11] Answering options are never, almost never, sometimes, often, and almost always. Each answer is reversed and rescaled on a 0 to 100 scale. A score of 100 represents a maximum HRQoL score,

Figure 1. Four examples of children with a CHD in this study and the corresponding scores on the HRQoL measured with the PedsQL (score 0–100), and ease of activity performance measured with the PUFI (score, 0–100).

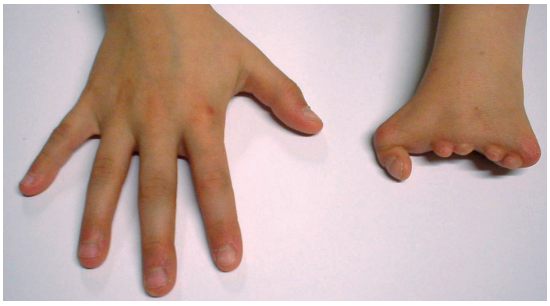
A 12-year-old boy with ulna dysplasia. PedsQL scores:47 (physical health), 65 (emotional), 70 (social), 65 (school), 67 (total psychosocial), and 60 (total HRQoL); PUFI score: 68.



A 14-year-old boy with ectrodactyly–ectodermal dysplasia–clefting syndrome. PedsQL scores: 72 (physical health), 85 (emotional), 90 (social), 60 (school), 78 (total psychosocial), and 76 (total HRQoL); PUFI score: 92.



A 13-year-old girl with former bifid thumb. PedsQL scores: 100 (physical health), 100 (emotional), 100 (social), 100 (school), 100 (total psychosocial), and 100 (total HRQoL); PUFI score: 100.



A 14-year-old girl with symbrachydactyly. PedsQL scores: 84 (physical health), 90 (emotional), 75 (social), 80 (school), 82 (total psychosocial), and 83 (total HRQoL); PUFI score: 91.

while 0 is the lowest possible HRQoL. In the present study, 2 age versions of the PedsQL were used: child self-report for ages 8 to 12 years and for ages 13 to 18 years. Examples of questions or statements are as follows: "It is hard for me to lift something heavy" (physical health); "I feel sad or blue" (emotional functioning); "I cannot do things that other kids my age can do" (social functioning); "I have trouble keeping up with my schoolwork" (school functioning).

Determinant Measurement: Covariates

The sociodemographic variables taken into account as possible covariates were the child's sex, age, and ethnicity. For ethnicity, if the child and both parents were born in the Netherlands, the child was designated as Dutch; if born in another country or in the Netherlands but both parents were born in another country, the child was designated as foreign; and if born in a foreign country but adopted by Dutch parents, the child was designated as an adoptive child. Other variables considered to be possible covariates of HRQoL were cosmesis, comorbidity (yes/no), activity performance, number of affected digits per hand (1–5), surgical intervention in the past (yes/no), and bilateral involvement (yes/no). Cosmesis of both hands was measured using a visual analogue scale, with (at the left end of the scale) "the ugliest hand" corresponding with a score of 0, and (on the right end) "the most beautiful hand" corresponding with a score of 10. All children were asked to give their opinion on both hands. In bilaterally affected children the lowest score was used for regression analysis. Activity performance was measured by means of the Prosthetic Upper Extremity Functional Index (PUFI), a questionnaire developed for children with transverse reduction limb deficiencies that has good validity and reliability when used for children with longitudinal radial deficiency.[8,15] The PUFI was originally used to evaluate 3 items: the extent to which a child actually uses the prosthesis for daily activities, the comparative ease of activity performance with and without the prosthesis, and the perceived usefulness of the prosthesis. Buffart et al[8] slightly changed the PUFI to enable assessment of children with hand differences other than transverse limb defects alone. For the present study we only assessed the ease of activity performance, which was scored on a 5-point ordinal scale ranging from "no difficulty'' to "cannot do.'' The older-child version of the PUFI (age, 7–18y) was used, which comprises 38 bimanual activities. The answers provide scaled sum scores ranging from 0 to 100 points, where higher scores indicate less difficulty with performance.

Statistical Analysis

For all children, levels of both total HRQoL and all subdomains were calculated. Also analyzed was whether the HRQoL of the children in the present study differed from that in healthy Dutch peers, using a 2-tailed independent-samples *t*-test and Levene's test for equality of variance. Ease of activity performance was selected as the main candidate determinant of HRQoL, together with several other likely covariates. Descriptive statistics were computed, and multivariable linear regression models were used to assess the relationship of each independent variable with both the PedsQL total score and subdomain scores. Statistical significance was set at α less than .05. Linear regression model assumptions were examined and satisfied. All data were analyzed using SPSS for Windows version 15.0.[a]

Results

Demographics

Table 1 presents demographic characteristics of the 116 children participating in the present study; their mean age was 11.8 ± 1.6 (range, 10–14) years; 53% were boys. Most children were unilaterally affected (67%) and had undergone surgery (65%). The majority had no comorbidity or syndromal correlated problems (78%) and were of Dutch origin (82%). According to the IFSSH classification, the diagnoses were almost equally represented in the groups of failure of formation (26%), failure of differentiation or separation of parts (23%), undergrowth (28%), and duplication (19%). One child had overgrowth, 3 had constriction ring syndrome, and none were classified with generalized skeletal abnormalities. The 5 most common diagnoses were radial polydactyly (15%), symbrachydactyly (15%), hypoplasia (10%), aplasia (9%), and syndactyly (8%). In 19% of the children the CHD was part of a syndrome; the syndromes present in 3 or more patients were ectrodactyly– ectodermal dysplasia–clefting syndrome and Poland's Syndrome.

Level of HRQoL

To illustrate individual scores on HRQoL reported by children with different types of CHD, the outcome of 4 children is shown in Figure 1. Table 2 presents the mean ± SD HRQoL scores of the study children and of healthy Dutch children.[16] Compared with healthy peers, the 42 boys and 35 girls of the group aged 10 to 12 years had (on average) similar scores on all subdomains. The 20 boys and 19 girls aged 13 to 15 years also had scores similar to their healthy peers, except for social functioning for which their scores were significantly lower (81.8 vs 90.0 in healthy peers; $P = .013$). Although overall mean scores were similar among study participants and healthy peers, for most scores variance was higher in the study group, indicating more extreme scores in these children. Table 3 shows the 5 items receiving the lowest scores, per age group. The items mentioned by participants are similar to those of healthy children, but with a slightly different order of importance. In the younger age group, the fifth item ("I cannot do things that other kids my age can do") is not mentioned by healthy peers. In the older age group, some children mentioned having difficulty with sleeping, which was not the case with their healthy peers.

Table 1. Characteristics of the 116 Participating Children

Characteristics	Values
Age in years:	11.8 ±1.6 (10 to 14)
Ease of activity performance (PUFI)	91.9 ± 10.6 (31.9 to 100)
	n (%)
Gender	
Boys	62 (53%)
Girls	54 (47%)
Affected side	
Unilateral	77 (67%)
Bilateral	39 (33%)
Number of affected digits	
1	36 (31%)
2	13 (11%)
3	14 (12%)
4	11 (10%)
5	42 (36%)
Surgical treatment	
None	41 (35%)
1 or more	75 (65%)
Comorbidity	
Not present	90 (78%)
Present	26 (22%)
Origin	
Dutch	95 (82%)
Foreign	17 (15%)
Adoptive child	4 (3%)
Diagnosis according to the IFSSH classification	
Failure of formation	30 (26%)
Failure of differentiation or separation of parts	27 (23%)
Duplication	22 (19%)
Overgrowth	1 (1%)
Undergrowth	33 (28%)
Congenital constriction ring syndrome	3 (3%)
Generalized skeletal abnormalities	0 (0%)
Five most common diagnoses	
Radial polydactyly	17 (15%)
Symbrachydactyly	17 (15%)
Hypoplasia	12 (10%)
Aplasia	10 (9%)
Syndactyly	9 (8%)
Syndromes	
Total	22 (19%)
Most frequent	
Poland	4 (3%)
EEC	4 (3%)

NOTE: Values are mean ± SD (range) or n (%)
Abbreviation: EEC, ectrodactyly-ectodermal dysplasia-clefting syndrome

Table 2. HRQoL scores per Subdomain and Age Group for Dutch Reference Values and Children With a CHD.

Age group (y)	Subdomain	Dutch reference Mean (SD)	CHD Mean (SD)	P* (t-Test for mean scores)	P* (Levene's Test for variation)
		n=219	n=77		
10-12	Physical Health	84.9 ± 9.3	87.1 ± 17.4	.294	<.001
	Emotional functioning	77.1 ± 13.7	76.0 ± 19.2	.650	<.001
	Social functioning	86.1 ± 12.3	85.6 ± 16.0	.781	.003
	School functioning	78.7 ± 12.0	78.6 ± 17.7	.977	<.001
	Psychosocial health	80.6 ± 10.3	80.1 ± 15.0	.771	.001
	Total Score	82.1 ± 8.9	82.4 ± 14.9	.853	<.001
		n = 106	n = 39		
13-14	Physical Health	87.3 ± 9.0	89.5 ± 11.1	.217	.347
	Emotional functioning	77.3 ± 16.0	74.9 ± 15.6	.424	.444
	Social functioning	90.0 ± 10.8	81.8 ± 18.9	.013	<.001
	School functioning	77.0 ± 12.6	74.4 ± 17.0	.375	.009
	Psychosocial health	81.4 ± 10.2	76.9 ± 14.0	.072	.048
	Total Score	83.5 ± 8.9	81.3 ± 11.6	.236	.135

NOTE. Values are mean ± SD as otherwise indicated.
*P-values are shown for the t-test comparing the mean scores between both groups
*P-values are shown for the Levene's test comparing the between-subject variation in both groups.

Table 3. The 5 Most Reported Problems per Age Group for Dutch Reference and Children With a CHD

Age group (y)	Dutch reference	Children with a CHD
10-12	1. I hurt or ache 2. I forget things 3. I feel angry 4. I have trouble sleeping 5. I feel sad or blue	1. I feel angry 2. I forget things 3. I feel sad or blue 4. I have trouble sleeping 5. I cannot do things that other kids my age can do
13-14	1. I forget things 2. It is hard to pay attention in class 3. I hurt or ache 4. I feel angry 5. I have trouble keeping up with my schoolwork	1. I forget things 2. I feel angry 3. It is hard to pay attention in class 4. I have trouble sleeping 5. I hurt or ache

Determinants for HRQoL

Table 4 presents the results of the regression analyses; only factors that made a significant contributor to the model ($P < .05$) are shown. Physical health score is negatively associated with the presence of comorbidity, bilateral involvement, previous surgery, and ethnicity (eg, on average foreign children score lower than Dutch and adoptive children), and is positively associated with the ease of activity performance. The low βvalue for ease of activity performance is due to its range (0 –100). For example, a child with a comorbidity on average scores 9.3 points lower on the domain of physical health than a child with no comorbidity, but a child with an ease of activity performance score of 93, on average scores 23 times .85 higher than a child with an ease of activity performance score of 70. Ease of activity performance is positively associated with all subdomains. Comorbidity is negatively associated with all subdomains, except for school functioning. Some covariates are associated with only 1 subdomain. For instance, ethnicity is associated only with physical health, age with school functioning, and the number of affected digits only with emotional functioning. Bilateral involvement influences physical health and total HRQoL.

Table 4. Determinants for the PedsQL Score with the Explained Variance (R^2) per Subdomain.

Outcome variable	R^2	Factors contributing to Model	β	SE	95% Confidence Interval	p
Physical Health	.54	Bilateral involvement	-6.8	2.2	-11.1 to -2.4	.003
		Comorbidity	-9.3	2.6	-14.4 to -4.3	<.001
		Foreign	-7.0	2.8	-12.5 to -1.5	.013
		Ease of activity performance	0.9	0.1	0.7 to 1.1	<.001
		Operative treatment	-4.4	2.1	-8.6 to -0.3	.037
Emotional functioning	.27	No. of affected digits	2.2	0.9	0.5 to 4.0	.013
		Comorbidity	-11.5	3.7	-18.9 to -4.2	.002
		Ease of activity performance	0.8	0.2	0.5 to 1.1	<.001
Social functioning	.26	Comorbidity	-13.9	3.5	-20.7 to -7.0	<.001
		Ease of activity performance	-0.5	0.1	0.3 to 0.8	<.001
School functioning	.14	Age	-1.9	0.9	-3.7 to -0.1	.041
		Ease of activity performance	0.6	0.2	0.3 to 0.9	<.001
Psychosocial health	.29	Comorbidity	-10.6	2.9	-16.4 to -4.9	<.001
		Ease of activity performance	0.7	0.1	0.4 to 0.9	<.001
Total Score	.44	Bilateral involvement	-4.4	2.2	-8.6 to -0.1	.043
		Comorbidity	-10.1	2.5	-14.9 to -5.3	<.001
		Ease of activity performance	0.7	0.1	0.5 to 0.9	.002

Discussion

This cross-sectional study on HRQoL using patient-reported data shows that children with CHDs report high HRQoL, as measured by the PedsQL. On average, their scores are similar to those of healthy peers, although variation in scores was higher in the CHD group. HRQoL was reduced by comorbidity and, in some subdomains, mean scores were reduced by increasing age, non-Dutch ethnicity, previous surgery, or when both hands were involved. HRQoL was increased by more ease of activity performance or more affected digits per hand. The main purpose of HRQoL assessment is to describe the impact of a disease relative to healthy peers, or relative to children with other health conditions. Table 5 shows the self-reported HRQoL of different groups: healthy children,[16] children with CHDs, children with a congenital below-the-elbow deficiency,[10] children with juvenile rheumatoid arthritis,[17] and children with upper extremity fractures.[18] Children with CHDs reported a similar HRQoL to that of healthy peers and peers with other upper extremity problems, but higher compared with children with juvenile rheumatoid arthritis. This comparison suggests that the impact of a CHD on HRQoL is, on average, relatively low, although HRQoL is more impaired if more body parts are affected.

Although on average, the impact of CHDs on HRQoL was relatively low, variation between subjects was higher in the CHD group compared with healthy peers, indicating that more children with CHDs could be at risk for an impaired HRQOL.

Varni et al[11] suggested that 1 SD below the mean in healthy children may be a clinically relevant reduction in HRQoL. Applying this threshold in our sample shows that, for example, 20.5% of the children with CHDs in the older age group were at risk for an impaired HRQoL, compared with 17.8% of the healthy children. The larger variation in the scores and the earlier reported relation between disease severity and HRQoL[17] indicate that it may be useful to screen individual children with CHDs for specific HRQoL problems, especially in children with comorbidity and who are bilaterally involved.

The high HRQoL in the present population may be related to Levine's disability paradox, which describes that many people with serious and persistent disabilities report that they experience good HRQoL, whereas most external observers believe that these individuals lead an undesirable daily existence.[19] Additionally, children with CHDs may experience little restrictions in their HRQoL and, therefore, report scores as high as healthy children.

While HRQoL is related to activity performance, high scores can be explained by the high activity level. In these children, high activity levels were found using questionnaires addressing daily activities,[7,20] and may be explained by the ability to adapt to their environment; this confirms our finding that bilaterally involved children (who have fewer options to use alternative strategies) had lower HRQoL scores. Finally, the high HRQoL could be related to the fact that the PedsQL is a generic measure allowing comparison

Table 5. Child Self-Report: means ± (SDs) for the PedsQL 4.0 Generic Core by Health Condition and Comparisons With Dutch Reference Values

	10-12 years old		13-14 years old				
Subdomain	**Healthy[16]**	**CHD**	**Healthy[16]**	**CHD**	**Below-elbow deficiency[10]**	**Juvenile rheumatoid arthritis[17]**	**Upper extremity fracture[18]**
Physical Health	84.9 ± 9.3	87.1 ± 17.4	87.3 ± 8.9	89.5 ± 11.1	88.6	70.9 ± 23.8	86.3
Emotional functioning	77.1 ± 13.7	76.0 ± 19.2	77.3 ± 15.9	74.9 ± 15.6	77.7	73.1 ± 22.9	79.5
Social functioning	86.1 ± 12.3	85.6 ± 16.0	90.0 ± 10.8	81.8 ± 18.9	83.1	78.6 ± 19.1	85.1
School functioning	78.7 ± 12.0	78.6 ± 17.7	77.0 ± 12.6	74.4 ± 17.0	49.6	74.3 ± 20.0	79.3
Psychosocial health	80.6 ± 10.3	80.1 ± 15.0	81.4 ± 10.2	76.9 ± 14.0	79.9	75.2 ± 17.1	81.3
Total Score	82.1 ± 8.9	82.4 ± 14.9	83.5 ± 8.9	81.3 ± 11.6	82.9	73.7 ± 17.8	82.6

with other patient groups, and the generic HRQoL may be high. We would suggest using a disease-specific instrument, if available, to have a complementary measurement on HRQoL. At present, however, there is no disease-specific tool for children with CHDs.

The finding of a high HRQoL in this patient group (in line with the above-mentioned disability paradox) indicates that HRQoL should not be the goal of surgery, although it is difficult to state that in the children in our study group who underwent surgery this did not affect HRQoL. It also indicates that HRQoL cannot be used as a responsive measure to evaluate treatment outcome and that goals for surgery should be defined and measured at other levels, such as at the ICF levels of body functions and structures, activity, and participation.

Although the HRQoL was high in the CHD group, social functioning of the children in the older age group was significantly different from that of their healthy peers. It is known that children with congenital differences do not have a negative self-sense until they are older and able to perceive stigma. We tried to capture the transition into puberty phase in our age groups, and the influence on social functioning became evident in the older age group. It might be meaningful to find out in future studies how the change in social functioning evolves when the children move into adulthood.[21]

Having evaluated a relatively large number of determinants of HRQoL, it appeared that sex (as in most patient groups) had no effect on HRQoL.[17,22] In contrast to 1 study[23] reporting a significant impact of cosmesis on HRQoL in a specific CHD (ie, limb reduction deficiency), no effect was found in the present study. Also, previous surgery was found to reduce the score on the physical health domain, but did not meet the definition of a minimally clinically important difference on PedsQL scores.[11] HRQoL was reduced by a comorbidity, which may indicate that not the hand difference alone but also syndromal differences influence HRQoL. When informing parents, it could be mentioned that HRQoL is influenced not only by the hand problem but also by comorbidity. For clinical care this may imply that the treatment of children with CHDs and with comorbidities should preferably involve a multidisciplinary approach.

Some HRQoL subdomains were negatively associated with age (ie, having foreign parents, having bilateral involvement, or both). The effect of age did not meet the definition of a minimally clinically important difference.[11] On the other hand, the effect of ethnicity did meet this definition of a minimally clinically important difference for the physical health domain. Consequently, clinicians should be aware that children with CHDs of foreign parents may have a lower HRQoL and may require more specific interventions. In agreement with studies[24,25] in other patient groups, all subdomains of HRQoL were improved by a higher level of ease of activity performance. This may be due to the fact that, although HRQoL is not in the classification of functioning of the WHO, HRQoL measures encompass several of its components, especially those related to activity.[26,27]

On first sight it was surprising that emotional functioning scores were higher in children with more affected digits. However, this is in accordance with experiences in daily practice and could be the result of psychosocial adjustment,[28,29] where children with a mild difference sometimes have more problems with their difference, because their hand and hand function could be closer to a normal hand, whereas children with a severe difference accept that it will never be a normal hand.

In summary, the clinical impact of the determinants of HRQoL in children with CHDs is that therapeutic management should incorporate treatment strategies to reduce the influence of comorbidity. In addition, if a child is bilaterally affected, then therapy should focus on optimizing hand function of at least 1 of the affected hands.

Study Limitations

The present study has some limitations that need to be addressed. The cross-sectional nature of the study prevents drawing conclusions about cause and effects when studying determinants. In addition, the study population is highly heterogeneous, which allows for studying determinants for the group as a whole but does not allow making statements about subpopulations. While the heterogeneity and the fact that the study was performed in 1 institution in the Netherlands limit the generalizability of the results, our findings are in line with other studies[5,10,23] in HRQoL in similar populations. Another limitation of the present study is that, to our knowledge, there is no technique available to quantify disease severity. Although bilateral involvement, number of affected digits, and comorbidity were used as proxies, a more sensitive measure of severity may provide more insight into how CHDs influence HRQoL.

Conclusions

The present study shows that children with CHDs experience a level of HRQoL similar to that of healthy peers, except for social functioning, which was lower in the older age group. However, there is more variation within the CHD group. HRQoL is increased by more ease of activity performance and (on some subdomains) by more affected digits, but reduced by comorbidity, bilateral involvement, and ethnicity. Based on these findings, we can reassure parents that their child with a CHD will probably rate their own HRQoL as high as that of healthy peers. Finally, generic HRQoL outcome measures are helpful in measuring rehabilitation or psychosocial goals and interventions. Results are useful for counselling of parents and children. Furthermore, they enable comparisons across diseases, but may not be sensitive enough to detect changes over time or changes after treatment in children with CHDs.

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Chapter 3

Poor Agreement on Health-Related Quality of Life Between Children With Congenital Hand Differences and Their Parents

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Abstract

Objectives: To determine agreement between children with congenital hand differences (CHDs) and their parents on health-related quality of life (HRQoL) and to explore whether characteristic variables were associated with this agreement on different domains of HRQoL.

Design: Survey.

Setting: University hospital, outpatient clinic.

Participants: Children with CHD (age range, 10–14y; N = 106).

Interventions: Not applicable.

Main Outcome Measure: Agreement on HRQoL was determined by comparing child self-reports and parent proxy-reports of the Pediatric Quality of Life Inventory 4.0 generic core scales, in Dutch. Agreement was examined both at group level and individual level.

Results: On a group level, children scored the same as their parents on a scale of 0 to 100 (physical health, 89.1±14.1 vs 88.0±15.6; psychosocial health, 80.6±13.4 vs 79.0±14.5; and total HRQoL, 83.5±12.3 vs 82.0±13.6). On an individual level, however, scoring was subject to high variation, with children reporting both higher and lower scores than their parent proxy. There were no major determinants for agreement; we only found that agreement was higher on emotional functioning in children with more affected fingers and on social functioning in bilaterally involved children.

Conclusions: In terms of mean group scores, 10- to 14-year old children with CHD agree with their parents or proxy on the child's HRQoL. However, on an individual level, they disagree; on some subdomains limits of agreement are as large as 30 points on the 0 to 100 scale. Therefore, care should be taken in cases where are unable to complete the questionnaire in choosing the parents' score as a representative substitute for the child's score.

Key Words: Child; Female; Hand deformities, congenital; Male; Quality of life; Questionnaires; Rehabilitation.

Introduction

Congenital hand differences (CHDs) are not very common. Their prevalence is estimated at 16 per 10,000 live births, but varies within different populations and ethnic groups.[1] In frequency they are second to congenital heart malformations.[1]

The impact of health on a child's well-being is described by the World Health Organization (WHO) as health-related quality of life (HRQoL). HRQoL is defined as the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, and concerns.[2] HRQoL has developed as an important outcome measure in pediatrics. In a previous study, our group reported on HRQoL in children with a CHD that is comparable with that of their healthy peers.[3] The study also found that HRQoL decreased in the presence of comorbidity but increased with higher ease of activity performance and that the severity, age, ethnicity, and surgery were associated factors.[3] The WHO and the International Association for Child Psychology and Child Psychiatry recommended that children's quality of life measurements should be self-reported wherever possible.[2] In line with this and due to development of age-specific tools for children, HRQoL is increasingly measured from the child's point of view. A parallel version of the child's questionnaire for their parents allows comparison of both scores or can be used as an alternative if a child is unable or unwilling to score the questionnaires.[4-6] It is important to determine whether the proxy-report can be used interchangeably with the child's self-report and therefore can be used to assess the child's HRQoL when their self-report data cannot be obtained. In addition, while it has been shown that child characteristics such as age, sex, and severity of disease influence child-parent agreement,[7] to our knowledge, variables that influence agreement are not extensively studied in children with different kinds of CHD. Ylimaïnen,[5] Sheffler,[6] and colleagues found that children with below-the-elbow deficiency report better quality of life than their parents perceive. Sheffler[6] also found that factors influencing parent-child agreement on quality of life include age and use of a prosthesis.

The primary objectives of this cross-sectional study were to determine agreement between children 10 to 14 years old with a CHD and their parents and whether characteristic variables were associated with this agreement on different domains of HRQoL. We hypothesized that children and their parents would agree on all dimensions.

Methods

This study used data from a cross-sectional study on functioning and HRQoL of children with a CHD. We recently reported on the HRQoL scores and the determinants of HRQoL of the children in a cohort study.[3] The subjects were 10- to 14-year-old children with a CHD treated at our hospital and their parents. We were particularly interested in the parent-child agreement in this age range because in the Netherlands there is a transition from primary school to secondary school in this age range and parental control decreases when children attend secondary school. Also, the average onset of puberty is at this age when children start sharing less information with their parents, which may also affect agreement. Children were excluded if they had a mental or developmental delay or insufficient knowledge of the Dutch language. From this sample, we randomly selected 300 subjects using a computer-generated random sequence and we stopped the inclusion when we reached the amount of 120 participants (response rate of 40%). We found no differences between participants and non-participants regarding sex, diagnosis, and severity of the CHD. The local ethics committee approved the study, and children above 12 years of age and all parents gave their informed consent to participate.

Participants

The questionnaires on HRQoL were completed by 116 of the children of whom 106 had a corresponding parent-report. In this article, parents of adoptive children are also referred to as parents and therefore all parent-reports were filled out by 1 of the child's parents. Patient characteristics were administered and each child's medical diagnosis was registered according to the International Federation of Societies for Surgery of the Hand classification system.[8] We expressed severity of the CHD by means of bilateral involvement, number of affected digits per hand, and comorbidity. Comorbidity was defined as the presence of any comorbidity not related to the hand problem, or the presence of syndromal differences related to the hand problem but in different body parts (eg, esophageal atresia, cardiac problems).

HRQoL Measure

HRQoL was assessed by means of a generic questionnaire, Pediatric Quality of Life Inventory (PedsQL) 4.0 generic core scales, in Dutch, which has been proven to be reliable and valid.[9] The PedsQL consists of 23 items and 4 generic core scales: physical health (8), emotional functioning (5), social functioning (5), and school functioning (5). The psychosocial health score is calculated from emotional, social, and school functioning scores, and the total score is an average of the scores on all 4 generic core scales. A 5-point Likert scale is used to answer the questions (0 = never a problem, 1 = almost

never a problem, 2 = sometimes a problem, 3 = often a problem, and 4 = almost always a problem).[9] Each answer is reversed and rescaled on a 0 to 100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0), so higher scores indicate better HRQoL. Parent-reports and child self-reports are of parallel content. We used 2 different age versions of the PedsQL: for ages 10 to 12 years, parents and their children filled out parent-report and child self-report for ages 8 to 12 years. For age 13 to 14 years, children and their parents filled out reports for ages 13 to 18 years.

Determinant Measurement: Covariates

Subject characteristics that were determined as possible covariates for child-parent agreement were the child's sex, age, and ethnicity. Three ethnic groups were made based on the country of birth of the children and their parents: Dutch, foreign, and adoptive. Other variables that were taken into account as possible covariates of the child-parent agreement were unilateral or bilateral involvement, number of affected digits per hand, and comorbidity (yes/no).

Statistical Analysis

Levels of total HRQoL and subdomains (physical health, emotional functioning, social functioning, school functioning, and psychosocial functioning) were calculated for children and their parents. In order to compare differences between child self-report and parent-report, mean scores and SDs were summarized separately.

To assess whether children and their parents agreed on the level of HRQoL, we examined the relation between scores of parents and children on different levels. To determine whether the children's and parent's responses differed significantly when comparing the means of the groups, we performed a 2-tailed, paired-samples *t*- test at a criterion level of $P < .05$.

Agreement was also determined using intraclass correlation coefficients (ICCs). The ICC was estimated by a 2-way random effects model as a ratio of between-child/parent to total variance, where total variance includes variation between child/parent and within child/parent.[10-12]

We computed the means of the absolute within child/parent differences, the means of the differences (mean bias), and the SD of differences to assess the magnitude and range of individual differences between children's and parents' responses.[13]

In this calculation, a mean bias smaller than zero indicates that parents score higher than their children and a mean bias greater than zero indicates that children score higher than their parents.[13] Consecutively, the graphical method of Bland and Altman[13] plots was used to illustrate the differences in responses pairwise. Limits of agreement were

calculated as mean bias ± 1.96 times the SD of the difference. Mean bias and the limits of agreement levels were drawn as horizontal lines in the scatter plot. The Bland and Altman plot demonstrates not only the overall degree of agreement, but also whether the agreement is related to the underlying value of the item. For instance, parents of children with a low quality of life score may agree more closely with their children than parents of children with higher scores. Linear regression models were used to assess the relationship of each independent variable of interest with agreement on both the PedsQL total score and subdomain scores. Statistical significance was set at $\alpha = .05$. Linear regression model assumptions were examined and satisfied. All data were analyzed using SPSS for Windows version 17.0.[a]

Results

Demographics

The demographic characteristics of the 106 children participating in the study are presented in Table 1. The 5 most common diagnoses were: radial polydactyly (16%), symbrachydactyly (9%), aplasia (8%), and hypoplasia, including longitudinal radial deficiency (8%) and syndactyly (5%). The syndromes that were found 3 times or more were VATER/ VACTERL association (vertebral defects, anal defects, cardiac defects, esophageal defects, renal defects, limb defects), EEC syndrome (ectrodactyly-ectodermal dysplasia-clefting syndrome), Poland syndrome, and constriction ring syndrome.

Level of HRQoL and the Relation Between Children's and Parents' Reports

Agreement on group level, that is, the mean group scores of children and their parents divided for each subdomain, is presented in Table 2. On all subdomains and in the total score, scoring was not significantly different between children and their parents (see Table 2). ICC values were moderate and ranging from .60 on emotional functioning to .75 on physical functioning, but excellent on school functioning.

Although mean scores were highly similar on the group level, the means of the absolute differences (see Table 2) indicate a mean disagreement between parent and child of 6 to 9 points for different subdomains and total score. This relatively large disagreement was confirmed in the Bland and Altman plots (Figs 1–6). These plots show a mean near zero but a wide confidence interval on all subdomains, indicating that children and their parents tend to disagree, but without a consistent pattern of 1 rating higher than the other.

Table 1. Characteristics of Participating Children

Characteristics	Values
Age in years	11.8 ± 1.6 (10-14)
Sex	
Boys	56 (53)
Girls	50 (47)
Affected side	
Unilateral	71 (67)
Bilateral	35 (33)
Number of affected digits	
1	30 (28)
2	13 (12)
3	14 (13)
4	9 (9)
5	40 (38)
Surgical treatment	
None	40 (38)
1 or more	66 (62)
Comorbidity	
Not present	82 (77)
Present	24 (23)
Origin	
Dutch	86 (81)
Foreign	16 (15)
Adoptive child	4 (4)
Diagnosis according to the IFSSH classification	
Failure of formation	27 (25)
Failure of differentiation or separation of parts	24 (23)
Duplication	22 (21)
Overgrowth	1 (1)
Undergrowth	29 (27)
Congenital constriction ring syndrome	3 (3)
Generalized skeletal abnormalities	0 (0)

Abbreviation: IFSSH, International Federation of Societies for Surgery of the Hand.
NOTE. Values are mean ± SD (range) or n (%)

Table 2. PedsQL Scale Scores of the Difference Between Child and Parent-reports, ICC values, and Absolute Child-parent Differences

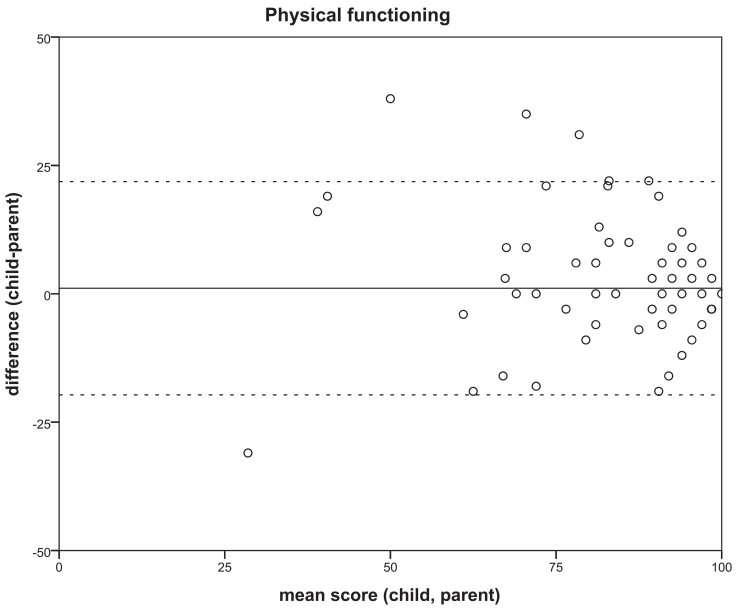
Sub domain	Child	Parent	P	ICC	Absolute Difference
Physical Health	89.05 ± 14.1	87.96 ± 15.6	.289	.75	6.66 ± 8.2
Emotional functioning	77.57 ± 16.3	76.84 ± 18.0	.629	.60	9.45 ± 12.2
Social functioning	85.52 ± 16.5	83.11 ± 18.2	.087	.66	9.01 ± 11.4
School functioning	78.63 ± 16.4	76.84 ± 18.6	.105	.79	7.45 ± 8.6
Psychosocial health	80.56 ± 13.4	78.95 ± 14.5	.126	.70	7.04 ± 8.2
Total Score	83.46 ± 12.3	82.03 ± 13.6	.120	.73	6.34 ± 7.1

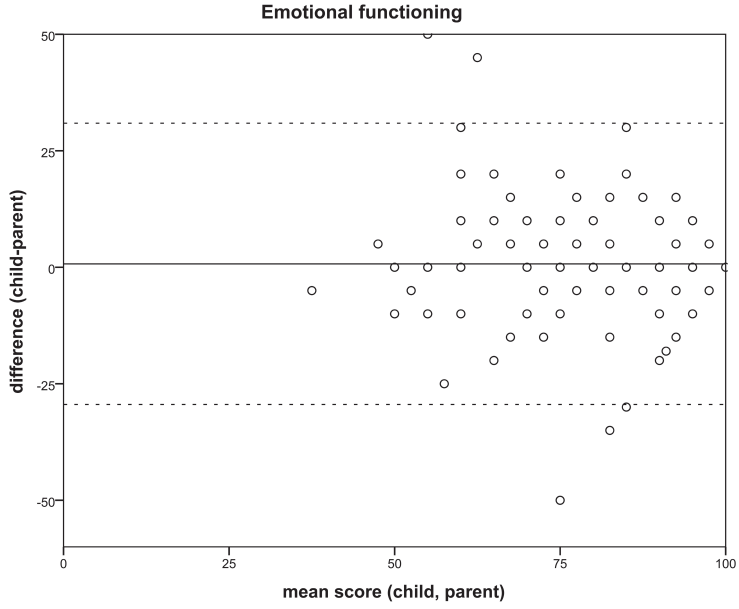
NOTE: Values are mean ± SD or as otherwise indicated

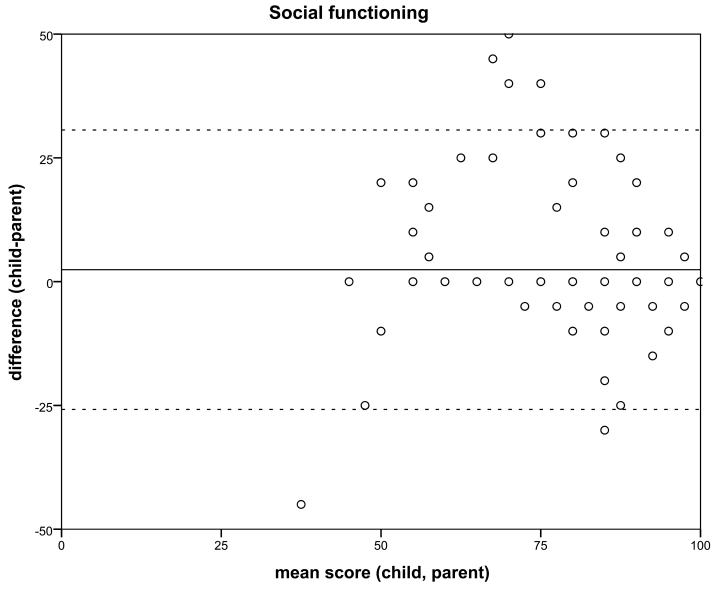
Determinants for Child-Parent Agreement

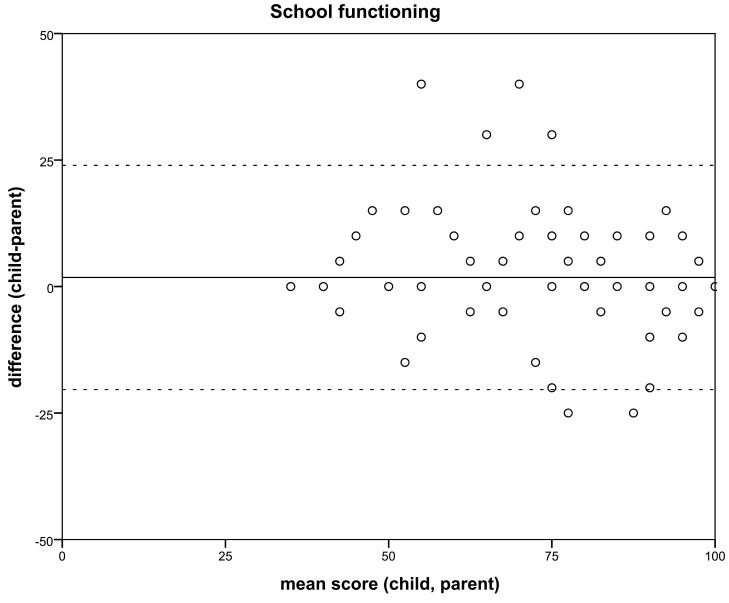
We found no determinants that influenced the agreement on total score and only 2 determinants that influenced agreement between children and their parents on 2 subdomains. The first significant determinant was the number of affected fingers on emotional functioning (β = 2.0; 95% confidence interval, 0.23–3.70; *P* = .027). Inspection of the data indicated that children with 1 or 2 affected digits (indicating a less severe CHD) scored lower than their parents on HRQoL, while children with 3 or more affected digits scored higher than their parents. The second determinant was bilateral involvement, which affected agreement level on social functioning (β= 6.4; 95% confidence interval, 0.34 –12.5; *P* = .038). Inspection of the data indicated that unilaterally affected children on average agree less with their parents on their social functioning. Disagreement mainly consisted of higher child ratings compared with their parents. None of the other covariates that were entered in the model were statistically significant at the level of .05.

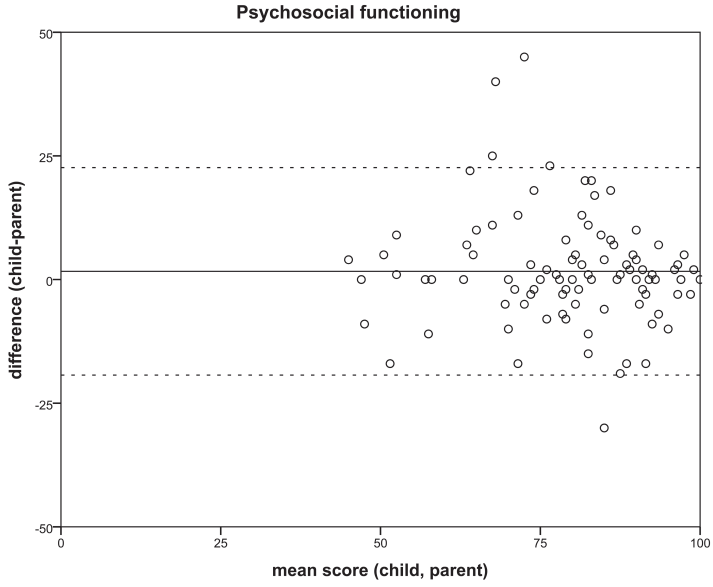
Figures 1-6. Bland and Altman plots

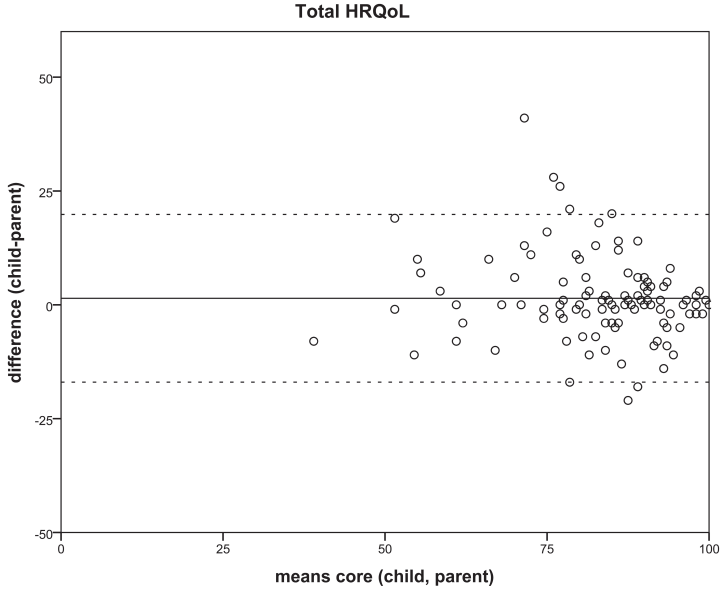





Social functioning
difference (child-parent)
mean score (child, parent)
50
25
0
-25
-50
0
25
50
75
100


School functioning
difference (child-parent)
mean score (child, parent)
50
25
0
-25
-50
0
25
50
75
100


Psychosocial functioning
difference (child-parent)
mean score (child, parent)
50
25
0
-25
-50
0
25
50
75
100


Total HRQoL
difference (child-parent)
means core (child, parent)
50
25
0
-25
-50
0
25
50
75
100

Discussion

In this study, which is a continuation of the report by our group,[3] on the level of HRQoL of children aged 10 to 14 years with different kinds of CHD, we measured child-parent agreement on HRQoL. The PedsQL, a generic HRQoL questionnaire, which is quick and simple to administer in clinical practice, was used.

We found that the mean scores of the children and their parents were not significantly different, although parents had a tendency to score lower on HRQoL of their children. However, when we determined agreement on the individual level, we found that children and their parents often disagree considerably. The disagreement occurred in both directions on all subdomains, without a consistent pattern of 1 rating higher than the other (see Table 2). Overall, we did not find that age, sex, and ethnicity significantly influenced the level of disagreement. However, we did find more agreement on social functioning in bilaterally affected children and their parents and on emotional functioning in children with more affected digits.

It has been previously reported that parents tend to score lower on HRQoL of children with a chronic health condition.[7] Although we also found this tendency in our data, on group level the child's and parents' scoring was not significantly different. In line with our findings, Upton et al[14] also found that most differences in mean scores on the child's HRQoL between children and their parent or proxy were small and not statistically different.

Although mean scores were not statistically different, when the scores were analyzed using ICCs, the child-parent agreement was only moderate. In addition, when absolute agreement is considered, using Norman et al's[15] definition of a clinically meaningful difference in HRQoL, the differences between the scores of children and their parents or proxy were clinically meaningful on all domains, except for the physical health score and school functioning score. The mean absolute difference was 6 to 9 points. However, in individual cases the difference added up to even 40 points on psychosocial functioning (see fig 5).

While agreement between parent and child reports of quality of life has been studied in pediatric populations with various health problems, research in this area has not often focused on children with CHD and musculoskeletal conditions.[5,6] Recent studies in children with congenital below-the-elbow deficiency also reported poor child-parent agreement. Whereas we found similar scores on group level and disagreement on individual level, recent studies found significant differences in the HRQoL scores between children and their parents. Sheffler et al[6] reported that parents scored lower only on social functioning scores, but Ylimaïnen et al[5] observed that parents not only scored significantly lower on total HRQoL, but also on all subdomains of older children. Parents also scored lower in their study on physical limitation for younger children and for girls, but also emotional

functioning of girls.[5,6] We are not aware of studies that have compared children's and parent's perspectives on HRQoL of children with various forms of CHD, other than congenital below-the-elbow deficiency alone.

To evaluate if there were important differences between subgroups of our study population, we investigated if there were factors that influenced the disagreement. We found that factors such as age, sex, and ethnicity did not have such an effect. In their review, Upton et al[14] reported that the effect of the child's age on disagreement is inconclusive. The effects differ from no effect on disagreement, to lower agreement between younger children and their parents. More disagreement in adolescents is also reported. Only 1 study[14] showed an effect of sex on agreement.

Knowing which factors influence child-parent agreement enables clinicians to comprehend each respondent's views on the child's HRQoL and better interpret parent-reports when children are unable to answer. Although we found that agreement was significantly higher on emotional functioning in children with more affected digits and on social functioning in bilaterally involved children, we consider this a result from multiple testing.

In clinical practice, decisions should be based on the opinion of either children or parents. Varni et al[16] showed that children as young as 5 years of age give reliable and valid self-reports of their HRQoL and Limbers et al[17] reported that children across age groups in their study interpreted items on the PedsQL 4.0 generic core scales in a similar manner regardless of their age. In addition, the WHO recommends that children's quality of life measurements should be subjective self-reported wherever possible.[2] Therefore, in line with this and based on the results of our study, we suggest using the child's self-report, except for cases where the child is mentally or otherwise insufficiently capable.

Study Limitations

A limitation of the study is that although we carefully selected a generic questionnaire to compare our results with those of children with other congenital or chronic health conditions, such a generic questionnaire may not be sensitive to the specific problems that children with CHD encounter in daily life. Another possible limitation is that we did not measure parental stress, which is considered to be associated with agreement on HRQoL.[18,19] The negative effect on scoring the child's HRQoL in parents with higher stress levels could explain some individual differences between child-parent scoring. In addition, although the age range was carefully chosen to study the effects of transition from child to teenager and from primary school to secondary school, the agreement between parents and children may be different for other age groups, limiting the generalizability of our results for the total population of children and teenagers with CHD.

A major strength of this study is the large study population of children with CHD, which allowed us to study the level of child-parent agreement as well as factors that influence this level of agreement.

Conclusions

The results of this cross-sectional study on child-parent agreement of 10- to 14-year-old children on HRQoL show that although the scores of children and their parents on the child's HRQoL are similar on a group level, they should not be used interchangeably, because on an individual level children and their parents disagree. Therefore, in clinical practice we advise making decisions based on 1 report, in most cases the child's self-report. In case of questions about the mental well-being of the child, the parent could be measured to obtain a complementary opinion.

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Chapter 4

The Impact of Apert Syndrome on Activity, Participation and Health-Related Quality of Life

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To be submitted

Introduction

Apert syndrome is a rare genetic condition affecting around 1 per every 65.000 live births, and occurs equally frequent among males and females, and has been linked to elevated paternal age.[14-16] The syndrome consists of craniosynostosis of the coronal sutures associated with cerebral anomalies, midface hypoplasia, acrobrachysyndactyly of all extremities and a low to near normal mental development.[15, 16]

The Apert hand is one of the most complex examples of congenital differences of the upper limb. Although treatment protocols have been optimized during the past decades, management is still difficult and many different approaches have been published.[17-20] Hand differences in Apert syndrome are most commonly described using Upton's classification.[21] Depending upon radiological examination of the syndactyly, the classification distinguishes three types. Type I indicates a complex syndactyly of the index, middle and ring fingers, a separate thumb and the separate little finger may either be connected with a membranous syndactyly or separate from the ring finger and is also referred to as "spade hand". Type II hands, also called "mitten or spoon hands" consist of complex syndactyly of the index finger through the little finger with an associated, incomplete syndactyly of the thumb. Type III hands, also known as "rosebud hands" consist of complex syndactyly of all fingers. In all types a brachyclinodactyly of the thumb is present. Furthermore, a synostosis between the fourth and fifth metacarpal bones could be present. **[22, 23]** Even though the descriptions per type of hand are clearly defined, classification of some hands in clinical practice is not always straightforward.

The Apert foot shows medial deviation of the great toe with fusion of its two phalanges, accompanied by minimal range-of-motion at the metatarsophalangeal joint. The midfoot and hindfoot will characteristically fuse in a supinated position. In most patients, a prominence is present of the third and fifth metatarsal heads with callus formation. Although the lower extremity deformities are progressive and lead to difficulty with alignment, painful stresses, and shoe wear, it has received less attention than the craniofacial and upper extremity anomalies.[24]

Although clinicians are increasingly interested in daily functioning and well-being of their patients, in current literature less emphasis is laid on this aspect than on the different impairments in body functions , which have been more extensively described.[25] Considering all malformations that are present in Apert Syndrome, it is not surprising that they have a large impact on daily functioning.

Daily functioning is best described using World Health Organization's (WHO) International Classification of Functioning (ICF)[26] and International Classification of Functioning for Children and Youth (ICF-CY).[9] It describes human functioning at three levels: body function and structure, activity and participation.[9, 26] Body functions are the

physiological and psychological functions. Activity refers to an individual's execution of a task or action in the current environment. For participation, the social context is added to an activity, referring to activities involved in a life situation.[9, 26]

Due to the severe limitations at the level of body functions and structure, it is clear that Apert syndrome will be accompanied by severe activity limitations and participation restrictions, and consequently, on quality of life (QoL). The WHO has defined QoL as the individual's perception of their position of life in the context of culture and value systems in which they live, and in relation to their goals, expectations, and concerns.[10] QoL can be divided in generic QoL and health-related QoL (HRQoL). Previous studies from our department focussing on HRQoL in children with craniosynostosis, investigated health-related problems and quality of life of 4-18 year old patients with Apert Syndrome. They found a lower quality of life in patients with Apert syndrome compared to other patients with other craniosynostosis and healthy peers, but did not relate their group to children with other upper- and lower limb impairments.[27, 28]

Therefore, the aim of the present study was to investigate daily functioning and QoL of patients with Apert Syndrome.

Methods

We performed a cross-sectional study in patients aged 6 years and older with Apert's Syndrome treated at our hospital. Questionnaires were send through regular mail to all eligible patients and their caregivers, asking them to complete questionnaires on upper- and lower limb functioning, participation, generic HRQoL, and health status. Table 1 presents an overview of the questionnaires that were used for the specific ages and purposes. In patients aged 6-16 year, a caregiver completed all questionnaires. Patients aged >16 years were asked to fill in the questionnaires themselves, but if they experienced difficulty completing the questionnaires, they could fill them out with help of a caregiver or let them be filled out by a caregiver alone.

Table 1. Questionnaires used in This Study per Age Group

Level	Participants	
	6-16 years	> 16 years
Upper-limb activities	Abilhand-kids	DASH
Lower-limb activities	LEFS	LEFS
Participation	CAPE	IPA
Generic HRQoL	CHQ-PF	SF-36
Health status	HUI-3	HUI-3

NOTE: Abilhand-kids = Abilhand-Kids- Cerebral Palsy, DASH = Disabilities of the Arm Shoulder and Hand, LEFS = Lower Extermity Functional Scales, CAPE = Children's Assessment of Participation and Enjoyment, IPA = Impact on Participation and Autonomy, CHQ-PF = Child Health Questionnaire Parent Form, SF-36 = Medical Outcomes Study 36-item Short-form Health survey, HUI-3 = Health Utilities Index Mark 3

Upper-limb Activities Questionnaires

We used the Abilhand-Kids- Cerebral Palsy version to assess the parent's perceptions of the child's difficulty in performing bimanual daily activities.[29, 30] This questionnaire is developed for children aged 6-15 years with cerebral palsy, measuring 21 items on a three level scale: impossible, difficult, easy. The raw scores are converted to a logit measure using an online Rasch analysis, ranging from −6.75 to 5.98 logits. Logits (log-odds units), are probability units that express the natural logarithm of the odds of success (i.e. the pass to fail probability ratio). At any given ability level, 1 logit difference between 2 patients indicates that their odds of successful achievement of any activity are 2.7:1 (i.e. e^1:1). Therefore higher values indicate higher ability.[31]

The Disabilities of the Arm Shoulder and Hand (DASH) outcome measure consists of 30 items and is designed to measure physical function and symptoms in patients with musculoskeletal disorders of the upper limb.[32,33] For each item, respondents were asked to provide their perceived difficulty in performing an activity on a five level scale: no difficulty, mild difficulty , moderate difficulty, severe difficulty and unable. Answers are transformed and provide a sum score ranging from 0-100, with higher scores indicating greater disability.[34]

Lower-limb Activities Questionnaires

The Lower Extremity Functional Scales (LEFS) is a region-specific, 20-item questionnaire designed to measure overall function of the lower extremities in patients with musculoskeletal conditions of the lower limb. For each item, respondents were asked to provide the perceived difficulty on a five level scale: extreme difficulty or unable to perform activity, quite a bit of difficulty, moderate difficulty, a little bit of difficulty and

no difficulty. The total raw score ranges from 0 to 80, and is transformed to a 0-1 scale by dividing by 80. Higher scores indicate better function.[35, 36]

Participation Questionnaires

The Children's Assessment of Participation and Enjoyment (CAPE) is a child self-report measure of participation in recreation and leisure activities. Since participation is multidimensional, it measures diversity (which activities does the child do), intensity (how often does a child do activities) and enjoyment (how much does the child enjoy the activity) of participation, but also assesses with whom and where activities are undertaken. The CAPE includes 55 informal and formal activities that can be organized into five activity types: recreational, active-physical, social, skill-based, and self-improvement. For each activity type a score can be obtained, as well as an overall participation score, a score for formal activities and a score for informal activities. Higher scores indicate more participation. If children were unable to answer the items alone, caregivers were asked to help them.

The "Impact on Participation and Autonomy" (IPA) is a generic outcome measure, evaluating the adult's perceived personal impact of chronic conditions on participation and autonomy.[37, 38] The IPA quantifies limitations in participation and autonomy. For this purpose it contains 32 items on five subscales, autonomy indoors, family role, autonomy outdoors, social life and relationships, and work and education. For each question there are 5 response options: very good, good, fair, poor, or very poor. The IPA also evaluates to which extent these limitations are experienced as a problem. This is examined with nine questions, covering nine different aspects of participation and autonomy. All scores of the subscales were added up and divided by the number of items answered. A sum score cannot be obtained if more than 25% of the answers were missing. Higher scores indicate more restrictions in participation and autonomy.[39]

Generic HRQoL Questionnaires

To examine generic HRQoL in children, we used the Child Health Questionnaire Parent Form (CHQ-PF50). This is a generic health questionnaire, measuring parental perception of their child's overall health and is appropriate caregivers of children aged 5 years and older.[27] The CHQ-PF50 consists of 50 items divided into 11 multi-item and 2 single-item scales, covering both physical and psychosocial aspects: physical functioning, role functioning emotional and/or behavioural, role functioning-physical, bodily pain, general behaviour, mental health, self-esteem, general health perceptions, parental impact-emotional (parent scale), parental impact-time, family activities, family cohesion, and change in health. Items were scored on 4- to 6-item Likert scales. These raw scores were

summed and rescaled to a 0–100 scale with higher scores indicating better functioning or well-being. In addition, physical and psychosocial summary scores were calculated.[40]

To assess generic HRQoL in adults, we used the Medical Outcomes Study 36-item Short-form Health survey (SF-36).[41, 42] This addresses eight domains: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, pain, mental health, vitality, and general health perception. All raw scores were converted to a 0 to 100 scale providing sum scores for each domain. Subsequently, summary scores were calculated for the physical and mental component. Higher domain and summary scores indicate higher levels of functioning or well-being.

Health Status Questionnaire

The Health Utilities Index Mark 3 (HUI3-15Q) is a utility or preference-based scoring system to measure health status.[43, 44] The HUI3 is a 15-item questionnaire, addressing eight attributes (vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain), which can be described at 5 or 6 levels. The attributes are weighted according to preferences obtained from a Dutch community sample. These attribute levels are used to determine single-attribute utility (SAU) scores and multi-attribute utility (MAU) scores. Level 1 represents no impairment, whereas higher levels represent more severe impairment. Attribute scores of 0.00 represent being dead and 1.00 living in perfect health. Therefore, negative scores indicate states described as worse than dead.[45]

Statistical Analysis

Descriptive statistics included median and interquartile ranges (IQR). Since we used different questionnaires for children than adults, we present the scores separately for the both age groups and for each type of hand per age group. The sizes of the subgroups did not allow statistical testing. Additionally, we compared our data to, if available, norm groups and to conditions of which data were available on the same outcome measurements. Since no data were available on Apert Syndrome studies, of the available conditions, for comparison with our group, we picked the best-suited group per outcome measure. Due to missing data on the type of hand of one child and seven adults, the number of participants of the total group and the sum of the subgroups per type are not equal. All analysis were performed using the IBM SPSS software package for Windows version 20.0

Results

Participants

We identified 63 patients, of whom 6 were too young to participate, 3 deceased and 5 were lost to follow up. Forty (82%) of the 49 eligible patients participated in the study; 24 adults and 16 children. Non-responders were not different regarding age (p = .76), gender (p = .12) and type of Apert (p = .39). For the adults, 46% was not able to work and only 17% lived independently or with a partner (Table 2). Only one child lived in an institution, all others lived with their parents. All patients had underwent surgery of their hands, 69% of the children and 50% of the adults was surgically treated at our centre.

Table 2. Characteristics of the Participants per Age Group

	Values	
	Age 6-16 y	**Age > 16 y**
Age (years)	12 ± 3.4	27.8 ± 8.8
Type Apert		
1	5 (31)	10 (42)
2	6 (38)	3 (13)
3	4 (25)	4 (17)
Missing	1 (6)	7 (29)
Sex		
Male	6 (38)	9 (38)
Female	10 (62)	15 (62)
Hand surgery		
All hand surgery performed in our centre	11 (69)	12 (50)
Surgery (partly) elsewhere	5 (31)	12 (50)
Work status		
Student	NA	1 (4)
Part-time or full-time job	NA	10 (42)
Unemployed	NA	2 (8)
Inability to work	NA	11 (46)
Housing		
Living together with partner	NA	1 (4)
Independently	NA	3 (13)
Institution	1 (5)	12 (50)
With parents	15 (79)	7 (29)
Missing	NA	1 (4)
Filled out questionnaires		
Independently	0	10 (42)
Father	1 (6)	4 (17)
Mother	15 (94)	7 (29)
Supervisor	0	3 (12)

NOTE: Values are mean ± SD (range) or n (%)

Level of Activities

Abilhand-Kids scores were comparable with scores of children with cerebral palsy, either acquired or congenital (Table 3a). Since no reference values of healthy peers were available, comparison with healthy peers was not possible. Our group scored 60% of the maximal scores. DASH scores were worse than those of patients with radial dysplasia after centralization of the wrist, and worse than those of healthy peers, but comparable to a large group of patients with injuries or clinical conditions of the upper limb.[33, 46, 47]

Table 3a. Results on Activities of the Upper Limb: Abilhand-Kids (< 16 y) and DASH(> 16 y)

Upper-limb activities	Measured value		Corrected for normvalues		
	Median	IQR	logits (Median)*	logits (IQR)	p
6-16 years (N = 16)					
Total	25	18 to 34	0.75	-0.45 to 3.29	.300**
Type 1 (N = 5)	23	19 to 33	1.38	-0.40 to 3.76	.897***
Type 2 (N = 6)	29	8 to 38	2.74	-1.43 to 3.73	
Type 3 (N = 4)	24	13 to 28	0.63	-1.23 to 1.07	
> 16 years					
Total (N = 22)	26	52 to 77	NA	NA	.680**
Type 1 (N =8)	29	18 to 57	NA	NA	.940***
Type 2 (N = 3)	32	2 to	NA	NA	
Type 3 (N = 4)	28	11 to 48	NA	NA	

*in logits, corrected for normvalues of cp-patients
** independent samples median test
*** independent Kruskall-Wallis test

Activity scores on functioning of the lower extremities, as measured with the LEFS, showed large variance within the group, from 35% to 97% of the maximum score of lower extremity functioning (Table 3b). The adults scored better than patients with hip or knee osteoarthrosis. For the children, no reference values were available.

The results on social participation, divided for each activity category, are displayed in Table 4. We found that the children with Apert Syndrome score similar to their healthy peers, regardless of the type of hand. Similar to the children, the adult group did not perceive large restrictions in participation: the scores were comparable to those of patients with spinal conditions (i.e. a traumatic or non-traumatic spinal cord injury; a spinal column fracture without neurological involvement; or a spinal degenerative disease) [48], but much better than patients with Rheumatoid Arthritis (RA).[49]

Table 3b. Results on Activities of the Lower Limb

Lower-limb activities	Measured value		
	Median	IQR	p
6-16 years			
Total (N = 15)	.78	.68 to .89	.566*
Type 1 (N =5)	.78	.61 to .90	.330**
Type 2 (N=5)	.88	.63 to .91	
Type 3 (N=4)	.69	.35 to .80	
> 16 years			
Total	.83	.65 to .96	.497*
Type 1 (N=10)	.77	.66 to .97	.976**
Type 2 (N=2)	.78	.56 to	
Type 3 (N=4)	.86	.35 to .97	

* independent samples median test
** independent Kruskall-Wallis test

Table 4a. Results on Participation of the Participants < 16 y: CAPE

	Median (IQR)	Mean (sd)	
		With physical disability	Without physical disability
Recreational activities			
Diversity			
Total (N=11)	8 (5 to 8)	6 ± 3	7 ± 2
Type 1 (N=3)	10 (4 to)		
Type 2 (N= 3)	6 (5 to)		
Type 3 (N=4)	9 (6 to 10)		
Intensity			
Total (N=11)	3.8 (2.3 to 4.8)	3.2 ± 1.3	3.4 ± 1.1
Type 1	4.8 (4.8 to)		
Type 2	2.8 (2.8 to)		
Type 3	3.9 (2.5 to 4.2)		
Enjoyment			
Total (N=11)	4.2 (3.8 to 4.6)		
Type 1	3.8 (3.8 to		
Type 2	4.6 (3.8 to)		
Type 3	4.2 (4.0 to 4.5)		
Active physical			
Diversity			
Total (N=11)	4 (2 to 5)	2.4 ± 1.5)	3.5 ± 1.7
Type 1	4 (3 to)		
Type 2	2 (0 to)		
Type 3	5 (2 to 5)		
Intensity			
Total (N=11)	1.2 (0.7 to1.5)	1.1 ± 0.7	1.6 ± 0.7
Type 1	1.5 (0.9 to)		
Type 2	0.7 (0.0 to)		
Type 3	1.3 (0.7 to1.8)		
Enjoyment			
Total (N=11)	4.1 (3.5 to 4.8)		
Type 1	4.0 (3.5 to)		
Type 2	4.7 (4.4 to)		
Type 3			
Social activities			
Diversity			
Total (N=11)	8 (6 to9)	4.3 ± 2.0	5.3 ± 2.0
Type 1	8 (8 to)		
Type 2	7 (1 to)		
Type 3	7 (4 to 8)		
Intensity			
Total (N=11)	2.8 (1.4 to 3.5)	2.4 ± 1.0	2.9 ± 1.0
Type 1	3.5 (2.8 to)		
Type 2	2.8 (0.4 to)		
Type 3	1.7 (1.1 to 3.0)		

Enjoyment			
Total (N=11)	4.3 (4.1 to 4.8)		
Type 1	4.4 (4.3 to)		
Type 2	5.0 (4.3 to)		
Type 3	4.1 (3.9 to 4.6)		
Skill-based activities			
Diversity			
Total (N=11)	3 (1 to 4)	1.5 ± 1.5	2.1 ± 1.5
Type 1	2 (1 to)		
Type 2	1 (0 to)		
Type 3	4 (2 to 5)		
Intensity			
Total (N=11)	1.2 (0.5 to 1.7)	0.9 ± 0.8	1.1 ± 0.8
Type 1	0.8 (0.5 to)		
Type 2	0.4 (0.0 to)		
Type 3	1.8 (1.1 to 2.3)		
Enjoyment			
Total (N=11)	4.5 (3.9 to 5.0)		
Type 1	4.5 (3.7 to)		
Type 2	4.5 (4.0 to)		
Type 3	4.5 (3.8 to 4.9)		
Self - employment activities			
Diversity			
Total (N=11)	4 (3 to 5)	3.1 ± 1.8	4.3 ± 2.0
Type 1	6 (5 to)		
Type 2	4 (1 to)		
Type 3	4 (3 to 4)		
Intensity			
Total (N=11)	2.1 (1.1 to 2.7)	1.7 ± 1.0	2.4 ± 1.1
Type 1	2.7 (2.7 to)		
Type 2	2.2 (0.6 to)		
Type 3	2.0 (0.9 to 2.1)		
Enjoyment			
Total (N=11)	3.8 (3.5 to 4.0)		
Type 1	3.8 (3.5 to)		
Type 2	4.0 (3.2 to)		
Type 3	3.6 (2.9 to 4.7)		
Formal activities			
Diversity			
Total (N=11)	3 (1 to 4)		
Type 1	3 (1 to)		
Type 2	0 (0 to)		
Type 3	4 (3 to 7)		

Intensity		
Total (N=11)	1.0 (0.3 to 1.2)	
Type 1	0.8 (0.3 to)	
Type 2	0.0 (0.0 to)	
Type 3	1.2 (0.9 to 1.9)	
Enjoyment		
Total (N=11)	4.3 (3.7 to 4.8)	
Type 1	4.3 (3.3 to)	
Type 2	4.0 (4.0 to 4.0)	
Type 3	4.5 (3.6 to 4.9)	
Informal activities		
Diversity		
Total (N=11)	23 (19 to 25)	
Type 1	25 (23 to)	
Type 2	23 (8 to)	
Type 3	21 (16 to 25)	
Intensity		
Total (N=11)	2.6 (2.1 to 3.3)	
Type 1	3.3 (2.6 to)	
Type 2	2.6 (1.1 to)	
Type 3	2.4 (2.0 to 2.6)	
Enjoyment		
Total (N=11)	4.0 (3.9 to 4.5)	
Type 1	4.0 (3.8 to)	
Type 2	4.8 (4.0 to)	
Type 3	4.1 (3.9 to 4.4)	
Total participation		
Diversity		
Total (N=11)	27 (23 to 28)	27.1 ± 5.8
Type 1	28 (24 to)	
Type 2	23 (8 to)	
Type 3	27 (20 to 28)	
Intensity		
Total (N=11)	1.9 (1.5 to 2.4)	
Type 1	2.4 (1.8 to)	
Type 2	1.4 (0.8 to)	
Type 3	1.9 (1.6 to 2.0)	
Enjoyment		
Total (N=11)	4.2 (3.9 to 4.5)	
Type 1	4.1 (3.8 to)	
Type 2	4.3 (4.0 to)	
Type 3	4.0 (3.9 to 4.5)	

Table 4b. Results on Participation of the Participants > 16 y: IPA

	Measured value	
	Median	**IQR**
Autonomy indoors		
Type missing (N = 6)	0.14	0.00 to 1.14
Total (N = 19)	0.29	0.00 to 1.14
Type 1 (N = 7)	0.29	0.14 to 1.14
Type 2 (N = 3)	0.42	0.14 to
Type 3 (N = 3)	1.14	0.00 to
Family role		
Type missing (N = 6)	0.78	0.57 to 1.18
Total (N = 19)	1.00	0.57 to 1.86
Type 1 (N = 7)	1.00	0.14 to 1.86
Type 2 (N =3)	1.00	0.85 to
Type 3 (N = 3)	2.00	0.00 to
Autonomy outdoors		
Type missing (N = 6)	0.40	0.20 to 1.65
Total (N = 19)	0.60	0.20 to 1.60
Type 1 (N = 7)	0.60	0.00 to 1.00
Type 2 (N = 3)	0.80	0.20 to
Type 3 (N = 3)	1.60	0.00 to
Social life		
Type missing (N = 6)	1.07	0.54 to 1.50
Total (N = 19)	1.14	0.57 to 1.29
Type 1 (N = 7)	1.14	0.57 to 1.29
Type 2 (N = 3)	1.14	0.29 to
Type 3 (N = 3)	1.00	0.29 to
Work & education		
Type missing (N = 3)	1.17	0.50 to
Total (N = 8)	1.08	0.88 to 1.29
Type 1 (N = 4)	1.08	1.00 to 2.54
Type 2 (N = 1)	0.83	0.83 to
Type 3 (N = 0)		

In Table 5a the results on generic HRQoL or health profile are described. For all types, children's summary scores on psychosocial functioning and family activities were comparable with healthy peers, only family activities in children with type 3 hands were lower. Even so, parents of children with type 1 hands scored lower on their child's physical functioning and perceived limitations on social roles both physical and emotional/ behavioral.

Table 5a. Results on Child Health Questionnaire–Parent Form (CHQ-PF); Median and Inter Quartile Ranges (IQR) per Subdomain on Completed CHQ-PF Questionnaires (N = 13), Type 1 (N=5), Type 2 (N= 5), Type 3 (N=3)

	Median	IQR
Physical Summary score		
Total	48.3	35.6 to 53.4
Type 1	46.5	14.4 to 54.2
Type 2	50.4	41.0 to 53.4
Type 3	49.8	35.1 to
Psychosocial Summary score		
Total	47.7	42.1 to 51.7
Type 1	45.7	42.1 to 48.2
Type 2	50.7	45.0 to 53.2
Type 3	49.7	40.1 to
Physical Functioning		
Total	88.9	66.7 to100.0
Type 1	77.8	50.0 to 97.2
Type 2	88.9	75.0 to 97.2
Type 3	100.0	66.7 to
Role social limitations- Emotional/Behavioral		
Total		
Type 1	77.8	38.9 to100.0
Type 2	22.2	0.0 to72.2
Type 3	100.0	83.3 to 100.0
	77.8	55.6 to
Role social limitations-physical		
Total	100.0	66.7 to 100.0
Type 1	66.7	0.0 to 91.7
Type 2	100.0	83.3 to100.0
Type 3	100.0	66.7 to
Bodily Pain/discomfort		
Total	80.0	60.0 to 95.0
Type 1	80.0	50.0 to 95.0
Type 2	60.0	55.0 to 95.0
Type 3	80.0	70.0 to
General Behaviour		
Total	80.8	64.2 to 86.3
Type 1	80.8	64.2 to 88.3
Type 2	80.8	62.2 to 84.2
Type 3	80.8	60.0 to
Mental Health		
Total	70.0	67.5 to 87.5
Type 1	85.0	62.5 to 90.0
Type 2	70.0	60.6 to 72.5
Type 3	80.0	70.0 to

Self Esteem		
Total	70.8	64.6 to 72.9
Type 1	70.8	66.7 to 70.8
Type 2	70.8	62.5 to 77.1
Type 3	70.8	62.5 to
Change in Health		
Total	50.0	50.0 to 62.5
Type 1	50.0	50.0 to 62.5
Type 2	50.0	50.0 to 87.5
Type 3	50.0	50.0 to 50.0
General Health perceptions		
Total	47.5	40.8 to 77.9
Type 1	68.3	28.3 to 82.9
Type 2	47.5	40.8 to 67.5
Type 3	56.7	35.0 to
Parental impact Emotional		
Total	75.0	66.7 to 79.2
Type 1	66.7	66.7 to 69.2
Type 2	75.0	62.5 to 87.5
Type 3	75.0	58.3 to
Parental Impact Time		
Total	88.9	77.8 to 100.0
Type 1	77.8	55.6 to 88.9
Type 2	100.0	88.9 to 100.0
Type 3	81.5	44.4 to
Family Activities		
Total	87.5	66.7 to 100.0
Type 1	87.5	64.6 to 93.8
Type 2	87.5	64.6 to 98.0
Type 3	84.7	54.2 to
Family Cohesion		
Total	85.0	71.3 to 100.0
Type 1	85.0	71.3 to 100.0
Type 2	85.0	71.3 to 85.0
Type 3	85.8	57.5 to

Table 5b. Results on SF-36: Median and Inter Quartile Ranges on SF-36 per Subdomain and Subgroup: Total (N = 19), Type 1 (N = 8), Type 2 (N = 1) and Type 3 (N = 3)

	Median	IQR
Physical component summary		
Total	49.7	51.9 to 60.5
Type 1	49.7	42.6 to 52.0
Type 2	47.0	NA
Type 3	43.6	43.6 to
Mental component summary		
Total	58.4	43.6 to 53.8
Type 1	55.2	43.5 to 61.5
Type 2	60.0	NA
Type 3	60.1	60.1 to
Physical functioning		
Total	80.0	55.0 to 100.0
Type 1	77.5	56.3 to 88.8
Type 2	60.0	NA
Type 3	50.0	10.0 to
Role physical functioning		
Total	100.0	75.0 to 100.0
Type 1	100.0	37.5 to 100.0
Type 2	100.0	NA
Type 3	100.0	0 to
Bodily pain		
Total	90.0	84.0 to 90.0
Type 1	90.0	75.0 to 90.0
Type 2	90.0	NA
Type 3	90.0	62 to
General health perceptions		
Total	70.0	60.0 to 90.0
Type 1	67.5	60.0 to 82.5
Type 2	75.0	NA
Type 3	70.0	55.0 to
Vitality		
Total	75.0	60.0 to 90.0
Type 1	72.5	52.5 to 91.3
Type 2	65.0	NA
Type 3	60.0	60.0 to
Social functioning		
Total	100.0	75.0 to 100.0
Type 1	81.3	75.0 to 100.0
Type 2	100.0	NA
Type 3	100.0	87.5 to

Role functioning: emotional		
Total	100.0	100.0 to 100.0
Type 1	100.0	75.0 to 100.0
Type 2	100.0	NA
Type 3	100.0	33.3 to
Mental health		
Total	88.0	72.0 to 96.0
Type 1	76.0	56.0 to 95.0
Type 2	88.0	NA
Type 3	88.0	80.0 to

Parents of all children scored their child's self-esteem lower than healthy peers. They also scored lower on emotional parental impact, which was more apparent in parents with children with type1 hands and impact on parental time, especially in type 1 and 2 hands compared to parents of healthy children. For general health, parents scored their child lower than healthy peers, but especially in children with type 2 hands. Even so, children with type 2 hands scored worse on pain and mental health. In contrast, family cohesion is higher in all children with Apert Syndrome compared with healthy peers. All adults in our study sample experienced more limitations on physical functioning, but experienced less pain and felt less limited in roles due to physical problems, or due to emotional problems than the Dutch norm group (Table 5b).[41] Social functioning and mental health were comparable in type 1, but higher in type 2 and 3. Patients with type 1 and 3 hands scored lower on general health, as did type 2 and 3 on vitality.

Table 6 present the results on health status as measured with HUI3. Hearing and ambulation are comparable for all types for both children and adults. Children with type 3 score less on vision, speech, cognition, and multi-attribute in comparison with the other types and adults. Even so, scores on cognition are lower in children type 1 and adults type 1 and 2. Although both children and adults perceive problems with dexterity, children score less than adults. For the adults, scores of the type 2 adults are lower on speech and of the type 3 adults on pain. Type 1 children score less on HUI3 multi-attribute.

Table 6. Results on Health Status as Measured with HUI3

	6-16 years Median (IQR)		16 years Median (IQR)
Vision		Vision	
Total (N = 14)	0.95	Total (N=24)	0.95 (0.95 to 1.00)
Type 1 (N = 5)	0.95 (0.95 to 1.00)	Type 1 (N=10)	0.95 (0.73 to 1.00)
Type 2 (N = 5)	0.95 (0.95 to 0.98)	Type 2 (N=3)	0.95 (0.95 to)
Type 3 (N = 4)	0.77 (0.43 to 0.99)	Type 3 (N=4)	0.98 (0.95 to 1.00)
Hearing		Hearing	
Total	1.00	Total	1.00 (1.00 to 1.00)
Type 1	1.00 (1.00 to 1.00)	Type 1	1.00 (0.71 to 1.00)
Type 2	1.00 (0.93 to 1.00)	Type 2	1.00 (1.00 to 1.00)
Type 3	1.00 (0.90 to 1.00)	Type 3	1.00 (0.90 to 1.00)
Speech		Speech	
Total	0.82	Total	0.91 (0.67 to 1.00)
Type 1	0.82 (0.41 to 0.91)	Type 1	1.00 (0.78 to 1.00)
Type 2	0.82 (0.75 to 1.00)	Type 2	0.67 (0.67 to)
Type 3	0.67 (0.48 to 0.78)	Type 3	0.82 (0.71 to 0.96)
Ambulation		Ambulation	
Total	1.00	Total	1.00 (1.00 to 1.00)
Type 1	1.00 (1.00 to 1.00)	Type 1	1.00 (0.96 to 1.00)
Type 2	1.00 (0.92 to 1.00)	Type 2	1.00 (0.83 to)
Type 3	1.00 (0.87 to 1.00)	Type 3	1.00 (0.75 to 1.00)
Dexterity		Dexterity	
Total	0.36	Total	0.67 (0.36 to 0.83)
Type 1	0.36 (0.08 to 0.92)	Type 1	0.67 (0.36 to 0.83)
Type 2	0.36 (0.36 to 0.75)	Type 2	0.67 (0.36 to)
Type 3	0.36 (0.21 to 0.59)	Type 3	0.60 (0.36 to 0.83)
Emotion		Emotion	
Total	1.00	Total	1.00 (0.93 to 1.00)
Type 1	1.00 (0.96 to 1.00)	Type 1	1.00 (0.91 to 1.00)
Type 2	1.00 (1.00 to 1.00)	Type 2	1.00 (0.91 to)
Type 3	1.00 (0.93 to 1.00)	Type 3	1.00 (0.93 to 1.00)
Cognition		Cognition	
Total	0.86	Total	0.86 (0.86 to 1.00)
Type 1	0.86 (0.78 to 1.00)	Type 1	0.86 (0.86 to 1.00)
Type 2	1.00 (0.59 to 1.00)	Type 2	0.86 (0.86 to)
Type 3	0.86 (0.86 to 0.97)	Type 3	1.00 (0.78 to 1.00)
Pain		Pain	
Total	1.00	Pain	1.00 (0.92 to 1.00)
Type 1	1.00 (0.74 to 1.00)	Total	1.00 (0.92 to 1.00)
Type 2	1.00 (0.85 to 1.00)	Type 1	1.00 (1.00 to 1.00)
Type 3	1.00 (0.94 to 1.00)	Type 2	0.89 (0.77 to 1.00)
		Type 3	
HUI 3 multi-attribute		HUI 3 multi-attribute	
Total	0.45	Total	0.60 (0.44 to 0.80)
Type 1	0.39 (0.21 to 0.83)	Type 1	0.59 (0.38 to 0.67)
Type 2	0.61 (0.42 to 0.78)	Type 2	0.57 (0.41 to)
Type 3	0.41 (0.16 to 0.61)	Type 3	0.52 (0.40 to 0.79)

NOTE: abbreviation IQR: Inter Quartile Ranges

Discussion

In this study on functioning and HRQoL of children and adults with Apert Syndrome, we found that on upper-extremity functioning, children scored 60% of maximal scores and their scores were comparable with scores of children with cerebral palsy. Adults scored worse than both healthy peers and patients with radial dysplasia after centralization of the wrist. Considering lower-extremity functioning, the adult group showed large variance within the group, but scored better than patients with hip or knee osteoarthrosis. For social participation, children scored similarly to healthy peers and even so, the adult group did not perceive large restrictions in participation. For HRQoL, parents of all children experience more limitations on their child's self-esteem and general health. Parents perceive a higher impact emotionally and on their time than parents of healthy peers, but family cohesion is higher in all children with Apert Syndrome. All adults experienced more limitations on physical functioning, but experienced less pain and felt less limited in roles due to physical problems, or due to emotional problems than the Dutch norm group. Furthermore, the results show that each type of hand has more or less impact when considering all subscales and domains.

Since children in our group scored only 60% of maximal scores for functioning of the upper extremity and adults scored worse than their healthy peers, we found that patients with Apert Syndrome are seriously limited in the performance of upper-limb daily activities. The results are confirmed by the outcome on dexterity of the health status. It seems that, despite of the fact that these children surgically treated at young age to enhance hand function and that they develop alternative strategies for performing daily activities, their upper-limb functioning is still poor. Since most daily activities involve the upper limb, it is worth the effort to study ways to enhance upper-extremity functioning in these patients.

In Apert Syndrome not only both hands are seriously affected, but also the feet have severe anomalies and may cause problems in daily functioning. We know from clinical practice, that the problems with functioning and complaints about feet evolve when children grow older. In contrast, our group does not report much problems. Since there was no disease-specific measure available for lower-extremity functioning in patients with Apert Syndrome, we choose the LEFS. Considering the outcome on this measure, the questionnaire might not be sensitive enough to detect problems in lower-extremity functioning in our group. On the other hand, the patients in our group might have learned to cope with their feet problems, but that is not consistent with experiences in daily practice.

Concerning social participation, in contrast to other groups of children with chronic physical conditions[50], our group of children scored similar to healthy peers. Leisure

activities, or "the time designated for freely chosen activities, performed when not involved in self-care or work or school"[51] are known to be important for children to explore their social, intellectual, emotional, communicative and physical potentials.[51] The high scores in our group imply that these children manage well to explore above mentioned potentials. This also means that they do not let their physical disabilities influence their social participation. Even so, the high scores on enjoyment on all activities in either category indicate that they really enjoy what they do.

We found that in our group only 17 % of the adults lived independently or with a partner. Even so, 54% of them were unemployed or unable to work .This might be a threat to social participation. Controversially, the adult group in our study did not experience major limitations in social participation. They scored better than patients with RA, which also highly affects both upper and lower extremities. The explanation might be found in the fact that, in contrast to RA, Apert Syndrome is a congenital syndrome. Adults born with this syndrome learn to cope with their limitations and from youth on they need to give a lot of effort to achieve their goals in life.

For HRQoL, we found that the parents of the children in our group reported child's summary scores on psychosocial functioning that were comparable with healthy peers. However, on some subdomains, scores were lower, mostly regarding general health, physical functioning and their child's self-esteem. Although we know from our previous study on HRQoL in children with CHD that parents tend to score lower on the child's HRQoL in children with more severe impairments and limitation[52], outcome in the child's group is confirmed by the data of the adult group. Adults, rating their own HRQoL, also report more limitations on general health and physical functioning.

Considering that having a child with a seriously limiting syndrome also has an effect on parents, we also measured parental impact and found that they report limitations on time and emotional impact. For emotional impact, Raposo-Amaral et al stated that the Apert patients acquired the necessary repertoire to manage aversive situations, including the presence of daily stigmatization given by means of bullying and teasing, but parents appeared to be much more affected by the stigma experience than the patients themselves.[53] Although not measured in our study, we hypothesized that visiting physicians more often than healthy peers and that the children are less independent in performing all daily activities may have caused the parental impact on time.

To our knowledge, this is the first study to map upper and lower extremity functioning, social participation and HRQoL in children and adults with Apert Syndrome. Besides describing the activity, participation and HRQoL of both children and adults with Apert Syndrome, we tried to distinguish scores on these items by taking into account the type of hand. From clinical practice, it is known that all three types have their own limitations and challenges to the hand surgeon and rehabilitation physician. In our group, we

did not find major differences between groups of hands. This may be caused by small group numbers, causing lack of power and therefore did not allow for statistical testing. Additionally, the cross-sectional design limits to make statements on causal relationships between the outcome measures.

Although we did not find major differences between the types of hand groups, there was a tendency to score with a wide range on some subdomains. Therefore, we still think it is worth the effort to measure all new-born children with Apert Syndrome on all levels of functioning and collect data to build a prospective cohort.

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Chapter 5

Relation between Manual Body Functions, Manual Capacity and Bimanual Performance using the PUFI in Children with CHD

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Abstract

Objectives: To assess aspects of hand function and manual capacity that influence bimanual performance in children with congenital hand differences (CHD), ranging from surgically corrected polydactyly or syndactyly to radial dysplasia. Secondly, to assess whether in this population the number of items on the Prosthetic Upper Extremity Functional Index (PUFI) can be reduced without losing information on bimanual performance.

Design: Cross-sectional design

Setting: University Hospital's Outpatient clinic

Participants and Methods: 10-14 year-old children with CHD (N= 106)

Interventions: Not applicable

Main outcome measures: Bimanual performance was evaluated with child self-reports on an adapted version of the PUFI, calculating ease of performance and actual use of the affected hand. Additionally, we assessed hand function and manual capacity.

Results: We found that the median score on ease of performance was high and that, on average, children used their affected hand actively in 97% of all activities. Manual capacity of the hand and lateral pinch strength of the dominant hand predict attainment of maximum PUFI scores. Non-maximum PUFI scores were predicted by opposition strength of the non-dominant hand and lateral pinch strength of the dominant hand. In addition, we found that in this patient group, only six items of the PUFI explain all variance in PUFI scores.

Conclusion: Children with a CHD generally have good bimanual performance and, on average, perform activities with active use of the affected hand. Therapy directed towards increasing manual capacity and finger muscle strength might assist to improve bimanual performance in children with CHD. Furthermore, we found that the number of items on the PUFI could be reduced from 38 to 6 items in children with CHD.

Introduction

Everyday functioning and development of children with congenital hand differences (CHD) is monitored through childhood and adolescence.[1] Upper limb functioning is commonly assessed using the framework of the World Health Organization's International Classification of Functioning, Disability and Health, Child and Youth version (ICF-CY), which describes the levels of 1) body function and structures, 2) daily activities, and 3) participation.[2] In children with CHD, impairments in body functions include, amongst other things, declined range of motion (ROM), muscle weakness and diminished coordination. Limitations in basic activities such as grasping, manipulating and releasing of objects, being essential components of most daily activities involving the upper limb, may result in limitations in daily activities and participation.

To obtain a complete representation of the child's limitation in daily activities, a distinction needs to be made between capacity and performance.[2] Capacity describes what a child can do in a standardized environment, while performance describes what a child does do in his or her current environment. What a child does do in daily activities is not only influenced by what he or she can do, but also by the physical and social context.[2] During hand activity, in literature capacity is mostly referred to as manual capacity or manual ability, while performance is commonly referred to as manual performance, either unimanual or bimanual.

In a previous paper we reported that children with CHD generally reach moderate to good manual capacity and that its relation with hand functions (at the ICF level of body function and structures) is more distinct in non-dominant hands than dominant hands.[3] In the present study, we broaden our focus towards activity performance of children with CHD. Limitations in activity performance generally become more evident in performing bimanual activities because unilaterally-affected children will perform unimanual activities with their unaffected hand [4] and bilaterally-affected children will choose their most able hand to perform the activity. However, since many daily tasks require cooperative use of both hands, bimanual performance can be regarded a more discriminative measure of limitations in performance of children with both unilateral and bilateral CHD.

While minimizing limitation in daily activities is a prominent goal in treating children with CHD, most surgical techniques intervene at the level of body functions of the upper limb, also referred to as hand functions, aiming to improve manual capacity and activity performance. This approach assumes relations between hand functions (e.g. strength and range of motion), manual capacity, and activity performance, but the nature of this relation and evidence for hand function variables predicting performance have scarcely been investigated.[5]

Therefore, the aim of the present study was to investigate the aspects of hand function and manual capacity that influence bimanual performance in children with CHD. Since Buffart et al. reported that the adapted Prosthetic Upper extremity Functional Index (PUFI) [5-8] has the most optimal reliability and validity to assess bimanual performance in children with CHD, we used this questionnaire to evaluate activity performance. The PUFI, however, is an extensive questionnaire consisting of 38 items. Although all items are used to evaluate performance and prosthetic use in children with an upper-limb reduction deficiency, it has never been investigated to what extent all items contribute to evaluate bimanual performance in children with CHD. Therefore, a second aim of this study was to evaluate the use of the PUFI in this population and specifically to investigate to what extent the extensive list of 38 items is needed to adequately assess bimanual performance in these patients, or whether there is a potential for decreasing the number of items.

Methods

Participants

Children (n=120) aged between 10-14 years were recruited from a database of children with a CHD treated at our hospital. Exclusion criteria were: cognitive or developmental delay and insufficient knowledge of the Dutch language. A total of 538 children (295 boys and 243girls) met these criteria and we randomly selected 300 participants using a computer generated random sequence. They were invited by mail and 120 were willing to participate in the study. We found no differences between participants and non-participants regarding gender, diagnosis, and severity of the CHD. Due to missing values on some outcome measures we were able to evaluate 106 of the children for the mentioned research purpose.

The medical ethics committee of our hospital approved the study and parents of all children gave their informed consent to participate as did all children above 12 years of age. Characteristics of the participating children are presented in Table 1.

Table 1. Characteristics of the 10-14 years-old Participating (N=106) and Non-Participating Children (N=194)

Characteristics	Values			
	Participants	Non-participants	PUFI score = 100	PUFI score < 100
Number (N)	106	194	28	78
Age in years:	11.8 ± 1.6	11.9 ± 1.7	11.8 ± 1.4	11.8 ± 1.7
Gender				
Boys	55	56	60	53
Girls	45	44	40	47
Affected side				
Unilateral dominant affected	8	*	10	6
non-dominant affected	61	*	61	62
Bilateral	31	*	29	32
Number of affected digits				
1	30	*	54	20
2	11	*	14	10
3	12	*	7	14
4	10	*	7	12
5	37	*	18	44
Surgical treatment				
None	38	*	14	86
1 or more	62	*	41	59
Diagnosis according to the IFSSH classification				
Failure of formation	25	24	4	33
Failure of differentiation or separation of parts	21	23	39	14
Duplication	21	22	32	17
Overgrowth	1	1	4	0
Undergrowth	29	27	21	32
Congenital constriction ring syndrome	3	3	0	4
Generalized skeletal abnormalities	0	0	0	0

NOTE: values are mean ± SD or %
* These data could not be retrieved validly from the patient files

Measurements

Bimanual performance of activities was assessed using the older-child version (ages ≥ 7 years) of the Prosthetic Upper Extremity Functional Index (PUFI).[6] This questionnaire, which was originally developed for children with transverse reduction limb deficiencies, was slightly adapted by Buffart et al to enable assessment and scoring of children with diverse forms of CHD and indicated good validity (construct validity: r = -.64) and reliability (test-retest reliability: ICC = .83) in children with longitudinal radial deficiency.[5,7,8] It evaluates to what extent a child actually uses the hand for 38 daily bimanual activities and is scored on a 5-point ordinal scale ranging from "active use of the hand" to "cannot do" (actual use). Additionally all 38 activities are scored on ease of activity performance , ranging from ''no difficulty'' to ''cannot do'' (ease of performance).[8] While the actual use can only be expressed as a proportion, the answers for ease of performance provide scaled sum scores ranging from 0 to 100 points where higher scores indicate more ease of performance. In line with previous research of Buffart et al[5]., we addressed ease-of-performance as the primary outcome measure. In bilaterally affected children, we asked the child to answer the questions for their most affected hand.

Manual capacity was tested according to Eliasson et al, evaluating 6 types of grip. (Table 2) [3, 9, 10] The test consists of 9 tasks that require handling objects with both grasp and pinch grip, scored on a 5-level ordinal scale. The scores range from 0 if the child cannot grip the object to 4 if the child can grip the object and completes the task with a normal grip and motion. All scores are added up and provide a sumscore between 0 and 36.

Hand function was assessed addressing joint mobility and muscle strength. We measured joint mobility with a finger goniometer to calculate the Total Active Range of Motion (TAROM) per hand,[11], and with the Pollexograph to measure thumb palmar abduction.[12, 13] We calculated the TAROM per hand as a sum of all individual fingers (MP-, PIP, and DIP joints) and the thumb (MP- and IP joint). We assessed grip and pinch strength (tip-tip pinch, tripod pinch and lateral pinch) with the Lode handgrip- and pinch grip dynamometer (Lode Medical Technology, Groningen, The Netherlands) and thumb opposition strength with the Rotterdam Intrinsic Hand Myometer (RIHM). For muscle strength, the mean of 3 maximum voluntary contractions was recorded. All dynamometer measurements were found to be reliable in children,[14, 15] and have previously been used in children with CHD.[16] An experienced hand therapist (MA), familiar with this type of measurements in this patient group for over 10 years performed all measurements (e.g. PUFI, manual capacity, joint range and muscle strength measurements).

Table 2. Manual Capacity; Tasks and Scoring system

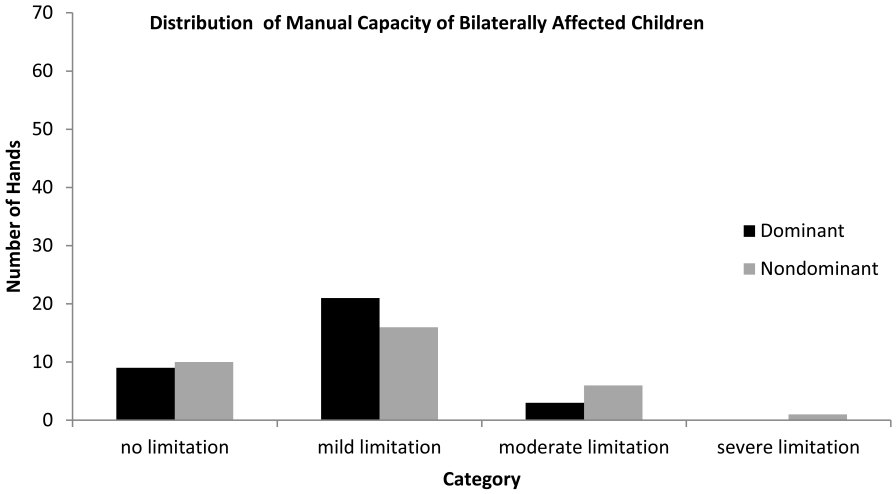
Grip	Task
Transverse grasp	Grasp a 2.5 cm diameter horizontal bar in mid-air and place it on the table
Transverse grasp	Move a 2.5 cm diameter vertical bar from one pegboard position to another
Transverse grasp	Lift a glass and pretend to drink
Diagonal grasp	Hold a knife and cut paste into pieces
Five-finger pinch	Pull a sleeve on and off the unaffected arm
Tripoid pinch	Unscrew a 2 cm diameter cap from a toothpaste tube
Tripoid pinch	Unscrew a 7 cm diameter lid from a jar
Lateral pinch	Grasp a vertically oriented plate (5 x 5 x 1 cm) in mid-air and place it on a table; requiring supination of the forearm
Pinch	Pick up a small cube and touch the chin with it
Score	**Judgement of grips**
0	Cannot grip the object
1	Grips object but cannot complete task
2	Grips object using an awkward grip and motion but completes task
3	Grips object using a slightly deviant grip and motion but completes task
4	Grips object using normal grip and motion and completes task

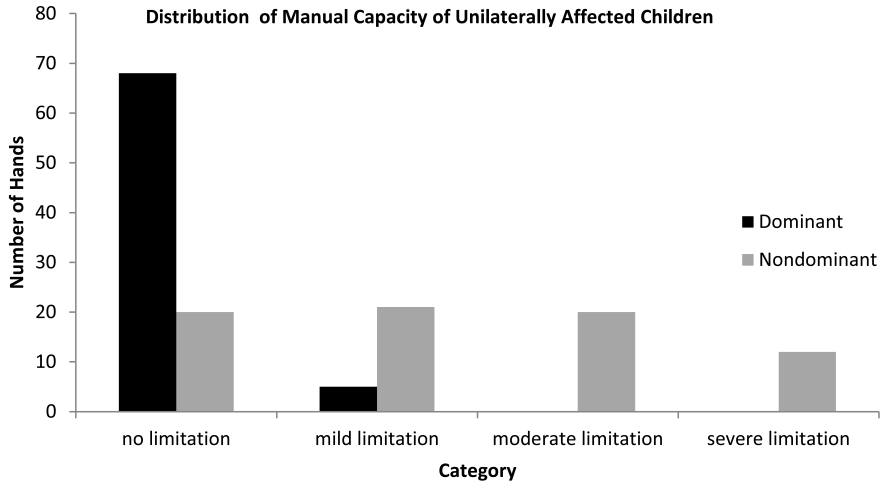
Statistical Analysis

Results on centrality and spread of PUFI, manual capacity and hand functions are displayed (Table 3 & 4). In addition, the percentage of the reference value is given for manual capacity, grip, pinch and opposition strength.[17, 18] Frequency tables on manual capacity are presented separately for unilaterally and bilaterally affected children (Figures 1a and 1b).

The distribution of all PUFI scores was skewed to the left, which is typical for the bounded responses. Twenty-eight children scored maximally on the PUFI while the remaining part was normally distributed. To account for this, we built separate models to identify factors associated with bimanual performance. Three models (Table 5) were constructed to determine predictors of maximal PUFI scores versus non-maximal PUFI scores. In this binary logistic regression analysis original PUFI scores were transformed in 1 (PUFI = 100; n = 28) and 0 (PUFI score < 100; n = 78) and we modeled to which extent PUFI scores were determined by hand functions (hand function model), manual capacity (manual capacity model) or manual capacity and hand functions combined in 1 model (combined model). Consecutively, the same models were constructed to analyze the

Figure 1a-1b.





subgroup of original PUFI scores < 100 (n = 78) using simple linear regression analysis with the same covariates. All models were built following the stepwise forward procedure.

In all models, we corrected for severity of the CHD using covariates of unilateral or bilateral affected and the number of affected digits per hand (1-5). Except for the PUFI questionnaire, all measurements were taken for both hands separately, referred to as dominant and non-dominant hand.

Due to the maximal score on a large amount of the 38 items of the PUFI, we decided to analyze the possibility to reduce the amount of items to the most discriminating. To achieve this we built a regression tree using recursive partitioning for the PUFI response. We have applied ANOVA as a splitting method with a complexity parameter (cp=0.5) to prune off the irrelevant splits. We used rpart package in R. All other statistical analyses were performed using the IBM SPSS software package for Windows version 20.0.

Table 3. Performance of Functional Activities

	Median (IQR)	Range (Min-Max)
Ease of performance	95 (87 to100)	32 to 100
Method of use of affected hand %		
active	97 (80 to100)	10 to 100
passive	0 (0 to 4)	0 to 67
forearm, elbow, trunk	0 (0 to 0)	0 to 34
one-handed	0 (0 to 0)	0 to 27
some help	0 (0 to 0)	0 to 14
cannot do	0 (0 to 0)	0 to 59

NOTE: IQR = Inter Quartile Ranges

Results

Median PUFI score on ease of performance was high (Table 3); approximately 96% of all activities could be performed independently, while only 1% of the activities were performed with help of someone else and 3% of the activities could not be performed. Children in our group scored high on ease of performance and, on average, the children perform 97% bimanual activities with active use of the affected hand.

Table 5 displays the results of the regression models predicting the maximum and non-maximum PUFI scores. Only factors significantly contributing to the model ($p< 0.05$) are shown. In the regression model with manual capacity, manual capacity of the non-dominant hand significantly contributed to predicting the maximal PUFI score (OR = 1.14). In the regression model using hand functions (range of motion and strength variables) as predictors, only grip strength (OR = 1.03) was associated with attainment of a maximum PUFI score. The OR of 1.03 means that the odds of scoring 100 on the PUFI's ease of performance scale were 1.03 times higher ($e^{0.029}$) for a child who, at a given level of all other covariates we controlled for in the logistic regression models, scored 1 unit higher on the scale of grip strength. When both hand function measures and manual capacity scores were entered into the model (model 3), manual capacity of the non-dominant hand (OR = 1.02) as well as lateral pinch strength (OR = 1.15) of the dominant hand predicted maximum PUFI score.

Table 4. Results of Manual Capacity and Body Functions Assessment

	Median (IQR*)	Possible range
Manual capacity		
D	36 (35 to 36)	0 to 36
ND	28 (17 to 36)	0 to 36
Hand Functions	Mean (SD)	% of reference[13,17,18] Mean (SD)
Mobility (degrees)		
TAROM		
D	911 ± 344	NA**
ND	745 ± 508	
Palm abd		
D	42 ± 19	89 ± 39
ND	35 ± 23	71 ± 47
Strength (Newton)		
Grip		
D	165 ± 84	87 ± 37
ND	90 ± 71	49 ± 36
Tip-tip		
D	31 ± 16	73 ± 33
ND	20 ± 16	47 ± 36
Tripod		
D	42 ± 20	75 ± 32
ND	22 ± 22	40 ± 39
Key		
D	51 ± 25	79 ± 33
ND	31 ± 26	48 ± 39
Opposition		
D	54 ± 19	85 ± 28
ND	36 ± 27	59 ± 43

NOTE: *Inter Quartile Ranges
** Not applicable since no reference values are available

Table 5. Logistic Regression Models Identifying Predictors of Maximum and Non-Maximum PUFI Scores

Model	Variables in the model	Nagelkerke R^2	Variables contributing to the model	β	SE	OR (95% CI OR)	P
Hand functions model	Hand functions*(dom+non-dom) Severity**	.235	Grip strength non-dom	.029	.007	1.03 (1.01 to 1.05)	<.001
Manual capacity model	Manual capacity (dom+non-dom) Severity**	.267	Manual capacity non-dom	.128	.036	1.14 (1.06 to 1.22)	<.001
Combined model	Hand functions* (dom+non-dom) Manual capacity (dom+non-dom) Severity**	.322	Lateral pinch strength dom Manual capacity non-dom	.018 .137	.009 .036	1.02 (1.00 to 1.04) 1.15 (1.07 to 1.23)	.038 <.001

* hand functions variables included in the model were TAROM, thumb palmar abduction, grip pinch, tip-tip pinch, tripod pinch and key pinch strength
** severity of disease was expressed by number of affected digits and unilateral or bilateral involvement

Table 6. Linear Regression Models Identifying Predictors of Spread in Non-Maximum PUFI Scores.

Model	Variables in the model	R^2	Variables contributing to the model	β	SE	P
Hand functions model	Hand functions*(dom+non-dom) Severity**	.191	Opposition strength non-dom Lateral pinch strength dom	.090 .086	.027 (.037 to .144) .034 (.018 to .155)	.001 .014
Manual capacity model	Manual capacity (dom+non-dom) Severity**	-	No variables	-	-	-
Combined model	Hand functions* (dom+non-dom) Manual capacity (dom+non-dom) Severity**	.191	Opposition strength non-dom Lateral pinch strength dom	.090 .086	.027 (.037 to .144) .034 (.018 to .155)	.001 .014

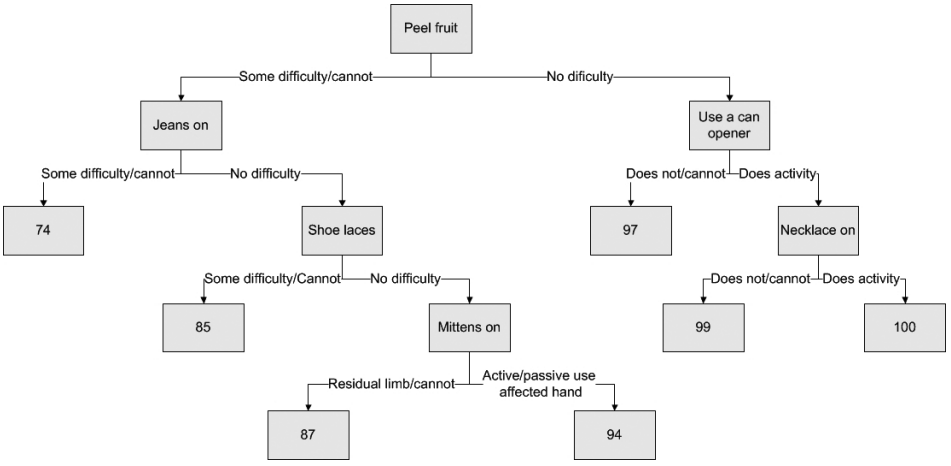
NOTE: * hand functions variables included in the model were TAROM, thumb palmar abduction, grip pinch, tip-tip pinch, tripod pinch and key pinch strength
** severity of disease was expressed by number of affected digits and unilateral or bilateral involvement

The regression model predicting the spread in non-maximum PUFI scores based on manual capacity scores did not reveal contributing factors, while the regression model with hand functions solely and combined with manual capacity gave similar results (Table 6).

In both models, opposition strength of the non-dominant hand (β=.090) together with lateral pinch strength of the dominant hand (β=.086) explained 19 % of the variance in non-maximum PUFI scores, whereas manual capacity did not contribute significantly to the last model. A β of .090 means that, among the subgroup of children who do not achieve maximum scores on the PUFI, but who are at the same level with respect to all covariates controlled for in the regression model, a one-unit difference in the affected hand's opposition strength is associated with a PUFI score that is 0.09 points higher.

The regression tree for PUFI items is displayed in Figure 2, showing that only six items on the PUFI explain all variance in scoring. The items were peeling fruit, putting on a pair of jeans, using a can opener, tying shoelaces, putting on mittens and putting on a necklace.

Figure 2.



Discussion

In this study, we describe bimanual performance measured with the child-version of the PUFI in children with CHD. The children scored high on ease of performance; on average they performed 97% of the bimanual activities with active use of the affected hand. We also investigated whether bimanual performance is predicted by hand functions (e.g. mobility, strength), manual capacity (the ability to handle objects with grasp and pinch grips), or both. Due to a skewed distribution of the outcome, we differentiated between predicting maximal PUFI score versus non-maximal PUFI score, followed by predicting spread in the non-maximal PUFI group. Overall, when combining both models, bimanual performance was predicted by two measures of muscle strength (e.g. opposition strength of the non-dominant hand and lateral pinch strength of the dominant hand) and by manual capacity of the non-dominant hand. Secondly, we evaluated whether all 38 PUFI items are relevant in a group of children with different CHD. We found only six discriminating items, indicating that for future use in this patient group the number of PUFI items could be reduced.

Despite the PUFI having the most optimal reliability and validity to assess bimanual performance in children with CHD[5-8], the relatively high scores found in this study may suggest that this measure is not sensitive enough to detect problems with bimanual activities in children with different kinds of CHD. The high scores may result from a lack of sensitivity, but may also indicate that children with CHD in this age-group do not feel many restrictions in performing their daily activities.

We found that manual capacity of the non-dominant hand was associated with the attainment of maximal scores on bimanual performance, which is comparable to the results of Sakzewski et al. in cerebral palsy (CP) children and may have implications for intervention strategies in training children with CHD.[19] Currently, in rehabilitation, two contrasting intervention strategies for enhancing use of an affected hand in daily activities exist: constrained induced movement therapy (CIMT)[20, 21] (i.e. forced use of the affected hand) and bimanual intensive therapy (BIT).[22] Recently Dong et al. reported that CIMT improved unimanual capacity of the impaired arm more than BIT, but that children may improve more in both bimanual performance and self-determined overall life goals following BIT.[23] Therefore therapists already use a combination of CIMT and BIT to improve arm function for children with unilateral CP. The findings in this study suggest that it may be valuable to further study the use and effectiveness of these interventions in children with CHD.

Bimanual activity performance was also predicted by grip- and opposition strength of the non-dominant hand and lateral pinch strength of the dominant hand in children who were not scoring a perfect 100 on the PUFI. Although grip strength of the non-dominant

hand accounted for 24% of the variance in the first model, it was not a significant contributor in the final model when manual capacity was added. Similarly, Sakzewski et al, found no relation between weakened strength and bimanual performance in hemiplegic children with CP.[19] In contrast, Arnould et al did find a relation between grip strength of the non-dominant hand and activity performance in children with CP.[19, 24]

The association of opposition strength of the non-dominant hand with non-maximal scoring on bimanual performance underlines the importance of opposition strength in children with CHD. In this patient group, hand surgeons perform opponens plasties which are known to increase opposition strength in thumbs with weakened or lacking opposition strength. [25, 26] Our finding is in line with a study in children with Charcot-Marie-Tooth disease. In this study an association was demonstrated between gain in opposition strength and gain in manual capacity and performance.[27]

We found that bimanual activity performance was predicted by variables from both the dominant hand and the non-dominant hand, which underlines that bimanual daily activities require different roles for each hand. Therefore, in children with CHD, each hand may be a limiting factor. In children with CP, Arnould et al also found in children that different qualities of movement are addressed in the dominant hand and non-dominant hand in bimanual activities. They stated that "the achievement of manual activities requires a highly dexterous dominant hand and a strong and an enough dexterous non-dominant hand to ensure adjustable stabilization of the objects".[24] This is in accordance with our results that hand strength and manual capacity of the non-dominant hand did predict bimanual performance in our group. In contrast with CP, children with CHD showed sufficient levels of dominant hand's manual capacity, which therefore, did not predict bimanual performance in children with CHD.

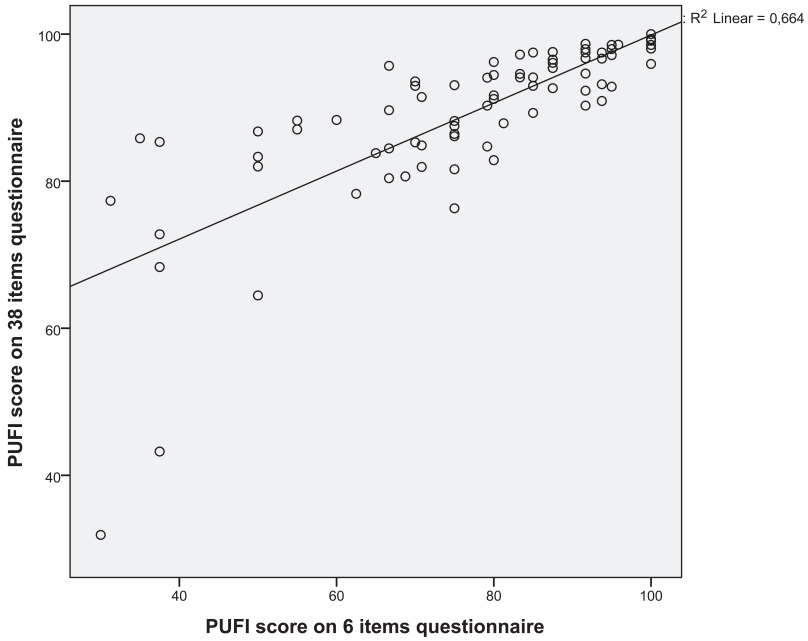
Despite of a maximal unimanual capacity in both hands, some children in our group did not score maximal on bimanual performance. This suggests that not only capacity or hand function determines bimanual performance. It supports the ICF-CY theory that relations between function and activities are not straightforward and that also personal factors as well as environmental factors play a role.[2] Since the child's personal factors (e.g. motivation and adaptability) and factors concerning school, familial and social environment were not studied, future research on the influence of these factors is still needed.

A second aim of our study was to assess whether the all 38 items of the PUFI are relevant to measure bimanual performance in children with CHD. We found only six discriminating items, indicating that for future use in this patient group the number of PUFI items could be reduced. The PUFI was originally constructed and validated for children with transversal reduction deficiencies, but also adapted and found reliable for children with CHD.[5, 7] Children in our group, that consisted of CHD of different severities,

however, scored relatively high on bimanual performance. We would like to emphasize, therefore, the regression tree that indicated that only 6 items were relevant was built with data from the children with generally high performance. In children with more activity limitations, the full PUFI may still be required to capture the complexity of their functional limitations.

In our group, we found that the number of PUFI items can be reduced to six, since only these six items discriminate between performance levels in children with CHD. This improves clinical applicability, since children need less time to fill out the questionnaire. In order to improve the clinical applicability and interpretation of the results on the PUFI, a future Rasch analysis of the items using a larger group of children with CHD would be beneficial. As a first indication that a reduced item – PUFI and the full PUFI are comparable, we found that the outcome on the old and new scores correlate well (Figure 3: R = .81, R^2 = .66).

Figure 3. Correlation between PUFI Score on 38-item Questionnaire and the 6-items Questionnaire



In this study, bimanual performance was measured performing activities with both hands simultaneously. To date, it is uncommon in rehabilitation medicine to focus on multitasking with two hands, while bimanual activities may be the primary activities that differentiate children with two unimpaired hands from children with either unilateral or bilateral CHD. In performing bimanual activities, children with CHD have developed alternate strategies and can choose the acting hand and stabilizing hand depending on the activity. However, when both hands are supposed to be occupied with two different tasks, such as holding a mobile telephone with one hand and opening the door with the other hand, both hands need to be acting hands. Hypothesizing that in these situations children with CHD are in disadvantage, simultaneous task performance might need to be addressed more extensively in future studies.

Limitations of our study also need to be addressed: the age range of 10-14 years limits the generalizability of our results. However, at the same time, this range was carefully chosen because this is the average onset of puberty and also because in the Netherlands there is a transition in this age group from primary school to secondary school. In addition, due to the cross-sectional design of our study, statements on causality between for instance, opposition strength and bimanual performance, cannot be made and should be confirmed in longitudinal studies or randomized clinical trials.

Conclusions

In conclusion, the present study showed that children with a CHD generally have good bimanual performance and that, on average, activities are performed with active use of the affected hand. Bimanual performance is associated with manual capacity and muscle strength. Non-maximal scores on bimanual performance are predicted by opposition strength of the non-dominant hand and lateral pinch strength of the dominant hand, suggesting that for improvement of bimanual performance, intervening at these items would be most beneficial. Furthermore, we found that the number of items of the PUFI questionnaire could potentially be reduced, since we found that variation in scores can be explained by only six items in children with CHD.

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Chapter 6

Stronger Relation between Impairment and Manual Capacity in the Non-Dominant Hand than the Dominant Hand in Congenital Hand Differences; Implications for Surgical and Therapeutic Interventions

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Abstract

Objectives: To evaluate manual activity capacity (i.e. activity capacity to perform hand activities) and its relation with body functions of the hand and forearm in children with congenital hand differences (CHD)

Methods: We assessed 10-14 year-old children with CHD (N = 106) using a functional handgrips test. Measurements of body functions included joint mobility and muscle strength. Patient characteristics were hand dominance and severity.

Results: We found a stronger relation between body functions and manual activity capacity in non-dominant hands than dominant hands. Dominant hands scored significantly higher on manual activity capacity than non-dominant hands that were similarly impaired at body functions level. Severity of the CHD and body functions had only small effects on manual activity capacity.

Conclusion: The relation between body functions and manual activity capacity is stronger in non-dominant hands than dominant hands, indicating that improvement in body functions lead to larger changes in manual activity capacity in the non-dominant hand. This may suggest that in bilaterally affected children surgery should be done at the non-dominant hand first since this hand would benefit most from surgery-induced body functions improvement.

Introduction

The impact of a congenital hand difference (CHD) on a child's functioning can be described at different levels of functioning.[1] The World Health Organization's International Classification of Functioning, Disability, and Health for Children and Youth (ICF-CY) distinguishes three domains: body functions, activity and participation.[2] Children with a CHD can experience impairments in body functions of the hand and forearm, further referred to as body functions, such as restricted joint mobility, sensation and grip strength, and may be restricted in activities. A child's activity, which the ICF-CY defines as the execution of a task or action by an individual, can be described by the two qualifiers of capacity and performance.[2] 'Capacity' is defined as what a child can do in a standardized environment, and 'performance' is what a child actually does do in daily life. Impairments in body functions can lead to restrictions in capacity to perform daily activities that require the use of the upper limbs.[3] While capacity reflects the child's ability to execute a task, performance is additionally influenced by the child's environment, which can facilitate or hamper performance.[2] In general, rehabilitation interventions as well as surgical interventions in children with CHD aim to improve body functions with the ultimate goal to improve manual activity capacity, also referred to as dexterity or manual ability. For example, hand surgeons perform muscle tendon transfers to enhance strength for specific movements or perform osteotomies to improve alignment of bones and joint movements. Even so, strength training and splinting therapy aim to improve muscle strength and joint mobility. However, the relationship between body functions and manual activity capacity to perform tasks is not straightforward and therefore it is difficult to state whether these interventions lead to the intended improvement of manual activity capacity.[4,5]Although body functions in children with CHD are well studied, the key components of the domain of body functions determining manual activity capacity of these children are largely unknown.[6-8] For example, many surgical interventions aim at strengthening the thumb, since it is assumed that the presence of a thumb accounts for at least 40% of the usefulness of the total hand.[9] However, objective data are lacking to support which muscle functions are most important for manual activity capacity and which levels of joint mobility and muscle strength are needed for manual activity capacity. Understanding the relation between body functions and manual activity capacity is essential for developing and selecting appropriate intervention strategies in children with CHD. Therefore, the aim of the present study was to disentangle the relationship between body functions and manual activity capacity in children with CHD.

Materials and Methods

This study used data from a cross-sectional study on functioning and health-related quality-of-life of children with a CHD. The Medical Ethical Committee of our hospital approved the study and parents gave their informed consent to participate, as did all children above 12 years of age.

Participants

Participants in this study sample were recruited from a database of children with a CHD treated at our hospital. Inclusion criteria were: age 10-14 years, no cognitive or developmental delay, and sufficient knowledge of the Dutch language. We selected a heterogeneous group of CHD patients to ensure that we had a relatively large variation in both body functions and manual activity capacity that would allow for investigating their interrelations. Three hundred participants were randomly selected using a computer generated random sequence. We evaluated 120 participants and we found no differences between participants and non-participants regarding gender, diagnosis, and severity of the CHD. Children and their parents received a letter concerning the purpose and procedure of the study. When they agreed to participate, a measurement session was planned and inform consent forms were signed. Due to time burden, some children did not participate in all measurements and we had missing values on some outcome measures (in 5 children we missed measurements on manual activity capacity, in 4 children on strength, in 1 child both on manual activity capacity and strength, in 2 on Kapandji and in 2 on palmar abduction) Therefore, we were able to evaluate 106 of the children for the mentioned research purpose. Characteristics of the participating children are presented in Table 1.

Manual Activity Capacity

Since there is currently no available standardized assessment of manual activity capacity in children with CHD, we tested manual activity capacity using the Eliasson test. Eliasson et al developed this test for children based on the Sollerman test, evaluating 6 types of grip in 9 tasks (Table 2).[10] This test, which is less extensive than the Sollerman test and more suitable for children of our age group, consists of tasks that require grasping objects either transverse grasping or diagonal grasping and tasks that require pinch grip. All tasks are scored on a 5-level ordinal scale. The scores range from 0 if the child cannot grip the object to 4 if the child can grip the object and complete the task with a normal grip and motion. If relevant anatomical structures or body functions were absent, children could not score maximally on the task, but only a maximum of 2 out of 4 (see Table 2). All scores are added up and provide a sum score between 0 and 36. Based on this score

the limitation of manual activity capacity can be qualified as severe (score <13), moderate (score 14-21), and mild (score >22).

Table 1. Characteristics of Participating Children

Characteristics	Values
Age	11.8 ± 1.6 (10-14) yr
Gender	
Boys	55
Girls	45
Affected side	
Unilateral	69
Dominant affected	7
Non-dominant affected	62
Bilateral	31
Number of affected digits	
1	30
2	11
3	12
4	10
5	37
Surgical treatment	
None	36
1 or more	64
Diagnosis according to the IFSSH classification	
Failure of formation	25
Failure of differentiation or separation of parts	21
Duplication	21
Overgrowth	1
Undergrowth	29
Congenital constriction ring syndrome	3
Generalized skeletal abnormalities	0

NOTE: Values are mean ± SD or %

Table 2. Eliasson Test for Manual Activity Capacity ; Tasks and Scoring System

Grip	Task
Transverse grasp	Grasp a 2.5 cm diameter horizontal bar in mid-air and place it on the table
Transverse grasp	Move a 2.5 cm diameter vertical bar from one pegboard position to another
Transverse grasp	Lift a glass and pretend to drink
Diagonal grasp	Hold a knife and cut paste into pieces
Five-finger pinch	Pull a sleeve on and off the unaffected arm
Tripoid pinch	Unscrew a 2 cm diameter cap from a toothpaste tube
Tripoid pinch	Unscrew a 7 cm diameter lid from a jar
Lateral pinch	Grasp a vertically oriented plate (5 x 5 x 1 cm) in mid-air and place it on a table; requiring supination of the forearm
Pinch	Pick up a small cube and touch the chin with it
Score	**Judgement of grips**
0	Cannot grip the object
1	Grips object but cannot complete task
2	Grips object using an awkward grip and motion but completes task
3	Grips object using a slightly deviant grip and motion but completes task
4	Grips object using normal grip and motion and completes task

Body Function

The variables taken into account at the domain of body functions were the total active range-of-motion (TAROM), palmar abduction of the thumb, Kapandji thumb range-of-motion score, and grip-, tip-tip pinch-, tripod pinch-, lateral pinch- and opposition strength. We evaluated joint mobility using a finger goniometer to calculate TAROM per hand as the sum of the AROM of all present joints.[11] As a result, if joints or fingers were lacking, a lower TAROM was scored. Additionally, we evaluated thumb range of motion using Kapandji thumb range-of-motion,[12] and palmar abduction using the Pollexograph.[13] Muscle strength was evaluated by measuring grip- and pinch strength (tip-tip pinch, tripod pinch and lateral pinch) with the Lode handgrip and pinch grip dynamometer (Lode Medical Technology, Groningen, The Netherlands) and opposition strength was measured using the Rotterdam Intrinsic Hand Myometer (RIHM).[14-16] The mean force of 3 maximum voluntary contractions was recorded for all strength measurements. In addition, we used the reference values for grip and pinch strength for children reported by Surrey et al and Molenaar et al to express the forces as a percentage of the reference values.[15,17] To correct for severity of CHD, we added the number of affected digits per

hand and affected sides (unilateral involvement versus bilateral involvement) as possible covariates. In addition, hand dominance was taken into account as a covariate in the model. Hand dominance was established by taking the writing hand as the dominant hand. Both manual activity capacity examination and body functions measurements were evaluated for both hands.

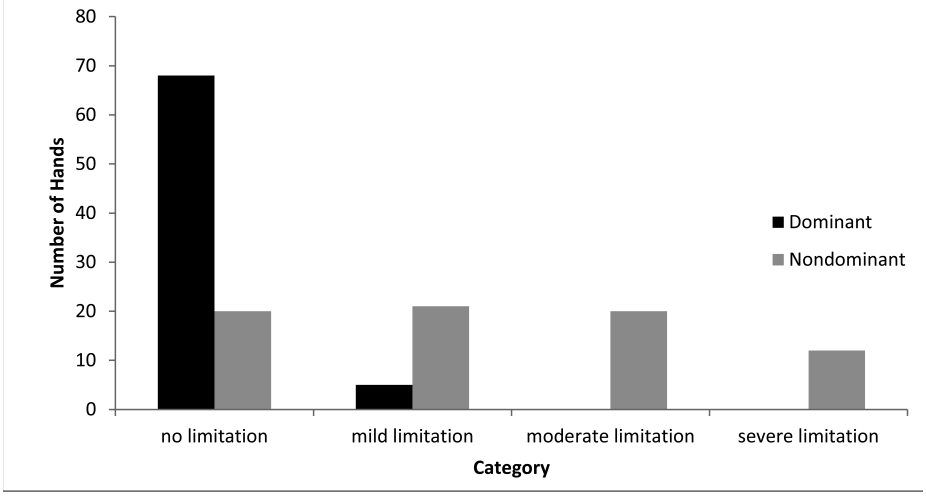
Table 3. Descriptive Results (Median, Inter Quartile Range (IQR), Mean and Standard Deviation (SD)) of Manual Activity Capacity and Body Functions for the Dominant (D) and Non-Dominant (ND) Hand; Absolute Values and Percentage of Norm Values

			Median (IQR)	Mean ± SD	% of norm Median (IQR)	% of norm Mean ± SD	P
Manual activity capacity		D	36 (35 to 36)	34 ± 4	100 (97 to 100)	94 ± 11	< .001
		ND	28 (17 to 36)	25 ± 11	78 (47 to 100)	78 ± 30	
Body functions							
Mobility	Thumb opposition	D	10 (9 to 10)	9 ± 3	NA	NA	< .001
		ND	6 (1 to 10)	6 ±4			
	TAROM	D	760 (661 to 1281)	911 ± 344	NA	NA	.143
		ND	693 (292 to 1295)	745 ± 508			
	Palm abd	D	48 (34 to 54)	42 ± 19	100 (71 to 113)	89 ± 39	.058
		ND	41 (18 to 53)	35 ± 23	85 (38 to 110)	71 ± 47	
Strength (Newton)	Grip	D	160 (120 to 210)	165 ± 84	89 (71 to 107)	87 ± 37	< .001
		ND	75 (38 to 140)	90 ± 71	47 (21 to 75)	49 ± 36	
	Tip-tip	D	30 (20 to 40)	31 ± 16	77 (59 to 91)	73 ± 33	< .001
		ND	20 (40 to 60)	20 ± 16	54 (0 to 77)	47 ± 36	
	Tripod	D	40 (30 to 50)	42 ± 20	79 (60 to 90)	75 ± 32	< .001
		ND	20 (0 to 40)	22 ± 22	43 (0 to 65)	40 ± 39	
	Key	D	50 (40 to 60)	51 ± 25	80 (67 to 99)	79 ± 33	< .001
		ND	30 (0 to 40)	31 ± 26	56 (0 to 76)	48 ± 39	
	Opposition	D	54 (46 to 63)	54 ± 19	86 (78 to 102)	85 ± 28	.001
		ND	47 (0 to 57)	36 ± 27	74 (0 to 91)	59 ± 43	

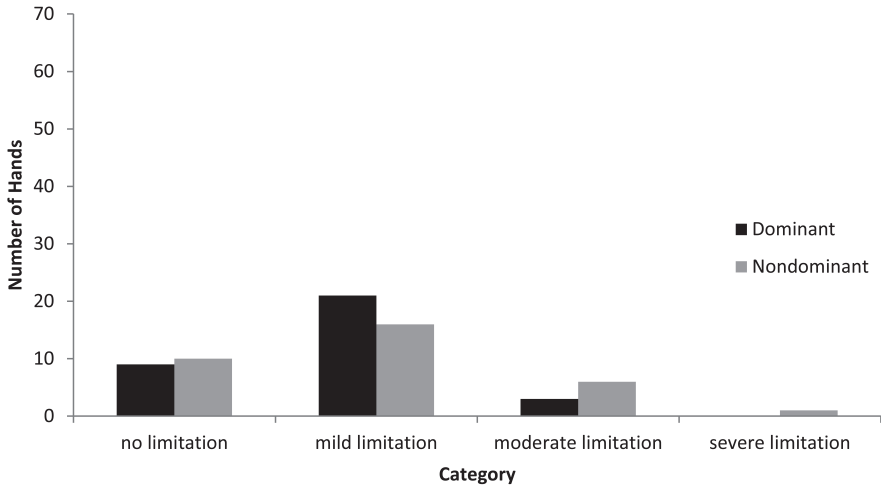
Statistical Analysis

Measures of centrality and spread on all outcome measures per hand are presented in Table 3. Differences between dominant hands and non-dominant hands were tested with the Friedman's test. A mixed model of 212 hands was constructed to determine whether the Eliasson score was related to the covariates. Intrapatient correlation in the Eliasson score was accounted for by taking all dominant and non-dominant hands (not only the affected hands) as random effect in the model. The initial model consisted of all the covariates as fixed effects together with the interaction terms between the covariates and the effect of hand dominance. From the full model non-significant fixed effects were removed stepwise using likelihood ratio test with p-values for removal >.1. The main fixed effects were kept in a final model if the interaction term was significant and are displayed in Table 4. The need for the random effect was tested using a mixture of chi-square distributions.

Figure 1.



Distribution of Manual Activity Capacity of Unilaterally Affected Children.

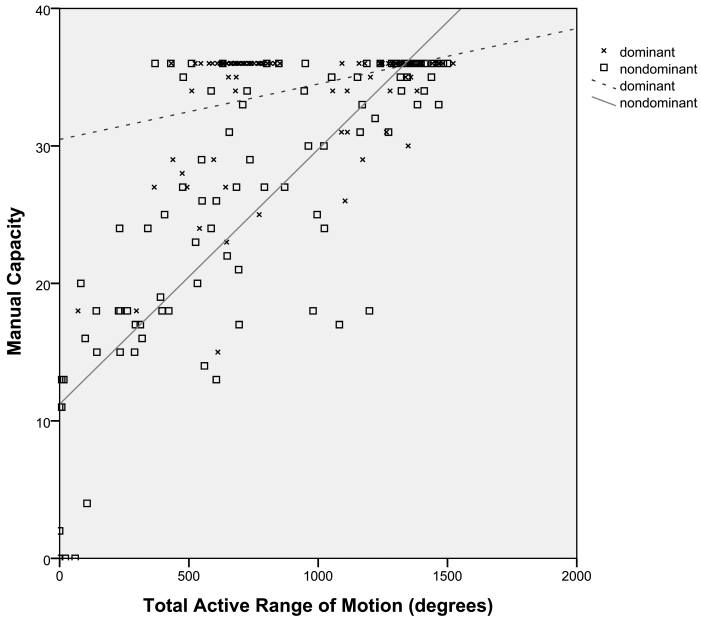


Distribution of Manual Activity Capacity of Bilaterally Affected Children.

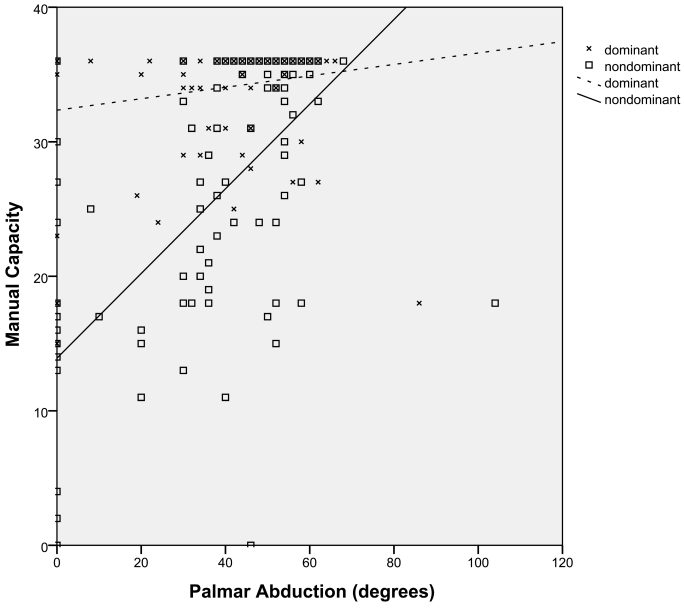
Results

The distribution of the scores on manual activity capacity is displayed in Figure 1. Only 8 unilaterally affected children were affected at the dominant hand with no or mild limitation of manual activity capacity. Limitation of manual activity capacity of the other unilaterally affected children's non-dominant hand was almost equally spread over all severity categories (Fig. 1a). In the bilaterally affected children, the non-dominant hand was more limited in manual activity capacity than the dominant hand (Fig. 1b). Table 3 represents measures of central tendency and statistical significance of all outcome measures. Despite of the large variance within both dominant and non-dominant hands on all outcome measures at body function level, dominant hands scored significantly better on all body functions than non-dominant hands (Table 3). On average, children with CHD showed reduced muscle strength on all strength measurements compared to reference values and differences were more evident in the non-dominant hand. Bilateral involvement lowered the score on manual activity capacity, as did the number of affected fingers.

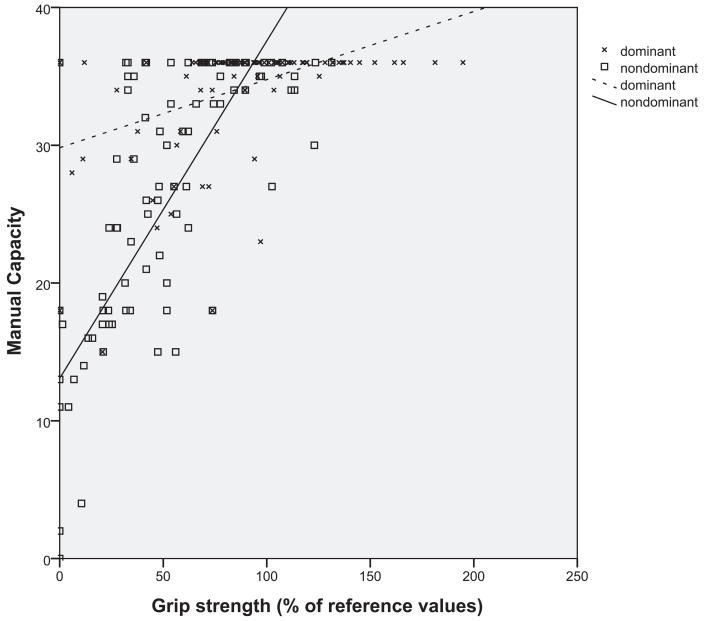
Figure 2.



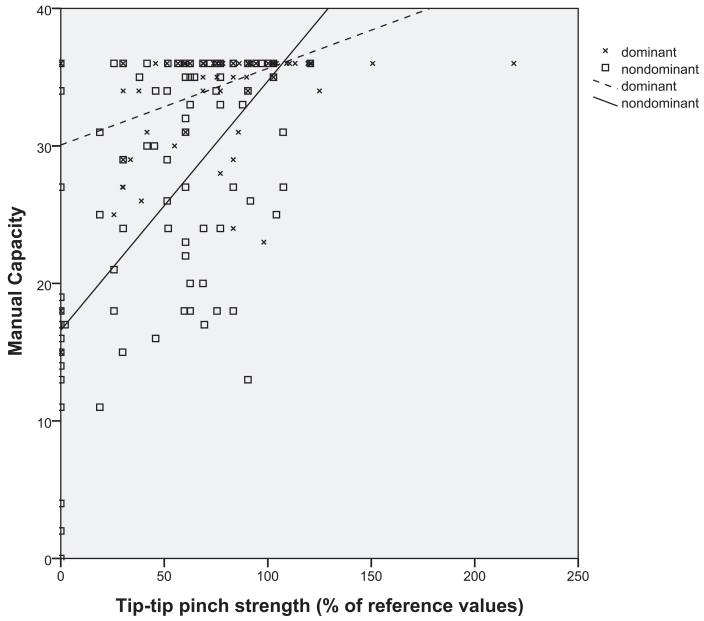
a) Scatterplot of Correlation between Total Active Range of Motion and Manual Activity Capacity Divided for Dominant Hands and Non-Dominant Hands.



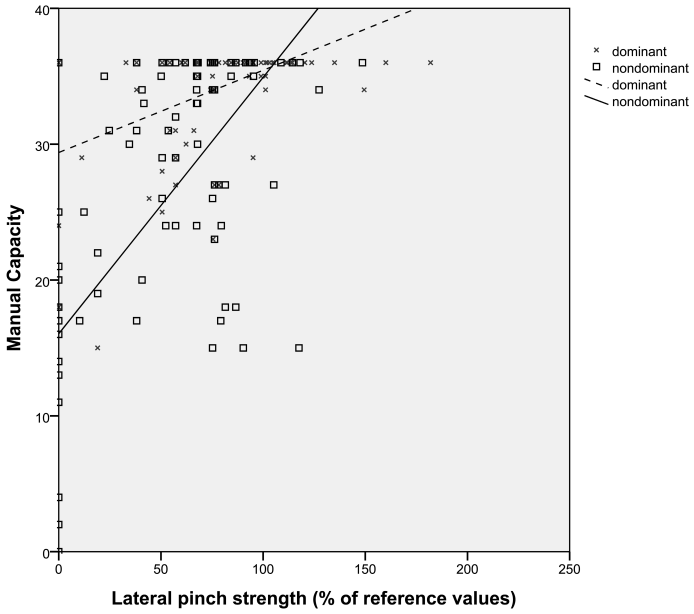
b) Scatterplot of Correlation between Palmar Abduction and Manual Activity Capacity Divided for Dominant Hands and Non-Dominant Hands.



c) Scatterplot of Correlation between Grip Strength and Manual Activity Capacity Divided for Dominant Hands and Non-Dominant Hands.



d) Scatterplot of Correlation between Tip-Tip Pinch Strength and Manual Activity Capacity Divided for Dominant Hands and Non-Dominant Hands.



e) Scatterplot of Correlation between Lateral Pinch Strength and Manual Activity Capacity Divided for Dominant Hands and Non-Dominant Hands.

Relations between Manual Activity Capacity and Hand Dominance

The scatterplots of the explaining variables versus manual activity capacity are shown in Figures 2a to e. The non-dominant hand scored lower on manual activity capacity than the dominant hand, with the difference being larger on the left side of the scatterplots, i.e. when the scores on the body functions variables are lower. However, when adjusting for the effects of other covariates in the model (Table 4), the largest effect was found for hand dominance ($p < .001$). More specifically, in children with low scores on body functions, the difference between the dominant and non-dominant hands can add up to 20 points (i.e. the estimate of the intercept of the dominant hand minus the intercept of the non-dominant hand, Table 4). The interaction effect between "non-dominant" and "bilateral involvement" indicates that the effect of bilateral involvement on the manual activity capacity was different for dominant and non-dominant hands. In comparison with unilaterally affected children, the dominant hand of bilaterally affected children scored 3.8 points lower on manual activity capacity and the non-dominant hand of bilaterally affected children scores 1 point (4.8 to 3.8) better than the non-dominant hand of unilaterally affected children (Table 4).

Relations between Manual Activity Capacity and Range of Motion

Smaller effects were found for TAROM, palmar abduction, grip-, tip-tip- and lateral pinch strength and number of affected digits. While hand dominance and TAROM interact on estimating manual activity capacity, the effect of TAROM on manual activity capacity was different for the dominant and non-dominant hand. Namely, for the non-dominant hand the increase is larger by .008 per degree increase in TAROM. Since the scoring range on TAROM is about 1400 degrees, the difference of TAROM on the manual activity capacity score between the lowest and the highest TAROM score for the dominant hand is 2.8 points and for the non-dominant hand 14 points on manual activity capacity. This interaction effect was also found with palmar abduction. The increase in manual activity capacity score per degree increase in palmar abduction for the non-dominant hand is larger by .07. Since the scoring range on palmar abduction is 0°-60° the difference in manual activity capacity between the lowest and the highest score on palmar abduction is for the dominant hand 3 points and for the non-dominant hand 7.2 points.

Table 4. Results from the Bivariate Mixed Model, Including the Measurement Units of the Variables, the Estimates[1], the Standard Error of the Estimates, the 95% Confidence Interval and the Significance.

Outcome variable	Fixed effects	Units	Estimate[1]	Std. Error	95% Confidence Interval	P
Manual activity capacity	Intercept dominant hand		28.9	1.49	26.0 to 31.8	<.001
	Intercept non-dominant hand	NA	8.9	1.57	5.8 to 12.0	<.001
	Bilateral involvement vs unilateral involvement	NA	-3.8	.67	-5.1 to -2.5	<.001
	Nr[2] of affected fingers		-.6	.17	-.9 to -.3	.001
	TAROM	degrees	.002	.0009	.0002 to .0038	.029
	Palmar abduction	degrees	.05	.02	.01 to .09	.001
	Grip strength	% of norm	.005	.01	-.01 to .03	.616
	Tip Pinch	% of norm	.03	.01	.01 to .05	.026
	Lateral pinch	% of norm	.02	.01	.0004 to .04	.034
	Non-dominant * TAROM	NA	.008	.001	.0006 to .0010	<.001
	Non-dominant *palmar abduction	NA	.07	.03	.01 to .13	.005
	Non-dominant *bilateral involvement	NA	4.8	1.1	2.6 to 7.0	<.001
	Non-dominant * gripstrength	NA	.07	.02	.03 to .11	<.001

NOTE: 1: All estimates refer to the both hands, unless there is an interaction effect with "non-dominant hand" and that effect should be added to the equation, stating differences between dominant and non-dominant hands.
2: number

Relations between Manual Activity Capacity and Muscle Strength

For grip strength,1% increase in strength enlarges the score with .075 points in the non-dominant hand group on manual activity capacity (Table 4). With a range of 0-100% grip strength, this means a maximum difference of 7.5 points on the Eliasson test. For tip-tip pinch strength, the score increases with .03 points on manual activity capacity with a 1% increase in relative strength for both dominant and non-dominant hands. This means a 100% strength is associated with a 3-point increase in manual activity capacity. The effect of lateral pinch is also the same for dominant and non-dominant hands, namely .02 per 1 percent increase in relative strength. This means that the largest difference between the worst and the best scoring child on pinch strength is 2 points. An increasing number of affected digits have a negative effect on the manual activity capacity score. Each additionally affected digit decreases the score by .6 points for both the dominant and non-dominant hand.

Discussion

In this study, we investigated limitation of manual activity capacity and its relation with body functions in 106 children with diverse forms of CHD. Manual activity capacity, measured with the Eliasson functional handgrip test, showed mild to moderate limitation. We found that manual activity capacity in these children is to great extent determined by hand dominance. Hand dominance also interacts with TAROM, palmar abduction of the thumb and grip strength in estimating manual activity capacity. Therefore, the effect of these body functions on manual activity capacity is different for the dominant hand than for the non-dominant hand. While "bilateral involvement" interacts with hand dominance, the effect of hand dominance is different for unilaterally than bilaterally involved children. Due to the positive relation between grip-, tip- tip pinch-, and lateral pinch strength and manual activity capacity, higher strength scores result in better manual activity capacity. More affected digits per hand have a negative effect on the manual activity capacity scores.

Measuring body functions in children with CHD is generally accepted for diagnostic purposes and for evaluating interventions. Although interest in manual activity capacity is growing, this is a less frequently-used outcome measure than measures regarding body functions. Manual activity capacity of children with a CHD of different severity, as measured in our study, is to our knowledge not previously reported. Since there is no well-defined score or classification to express disease severity in CHD and its subgroups, in the regression model, we have taken into account objective measures of severity, such as unilateral or bilateral involvement and number of affected digits, but also TAROM and muscle strength are indicators for severity. Correcting for these measures of severity, the

regression analysis then allowed us the study the individual contributions of these body functions on manual activity capacity.

In this study, we included a relatively heterogeneous population of children with CHD, with differences that varied from a simple syndactyly that will have little impact on body functions, to severe forms of radial deficiency that lead to very severe impairments in body functions. Consequently, based on the present findings, we cannot make statements for specific diagnosis groups. On the other hand, however, the large and diverse study population enabled us to study body functions, manual activity capacity and their interrelationships and determinants regardless of the diagnosis.

These interactions otherwise could not be studied due to the small group sizes per diagnosis and even within these groups all subforms of CHD and its different comorbidities.

Hand dominance was the strongest predictor in our model, which means that if all other variables in the model are kept constant, hand dominance predicted most strongly the variance in manual activity capacity (i.e., when impairments are similar in both hands, dominant hands have a better manual activity capacity than non-dominant hands). It should be noted, however, that hand dominance is largely debated[18-20] and a difficult concept to describe, especially in case of CHD. Although hand dominance has been described as the tendency to perform the majority of tasks with one hand rather than the other, this does not necessarily mean that the chosen hand is more efficient. The distinction between hand dominance and hand performance has been extensively studied and conflicting theories are used to describe the development of the dominant hand.[21,22] Some researchers describe that children choose their best performing hand to be their preferred or dominant hand,[22] whereas others conclude that preference precedes performance.[21] In the first model, the preferred hand in children with unilateral CHD will generally be the unaffected hand and in children with bilateral CHD the less-affected hand. In the second model, the child's preferred hand could be either hand, regardless of the impairment. In this study, since we did not expect hand dominance to be a major factor in determining the relation between manual activity capacity and body functions and for the time burden of the children, we choose to define the dominant hand by asking the children about their writing hand instead of a questionnaire. Now that we found that dominance played a major role in relation between the two levels, in retrospect we better might have chosen a questionnaire, enabling us to make firmer statements on hand dominance.

In our institution, surgeons often choose in bilaterally affected children to operate on the dominant hand first. The idea is that this makes the dominant hand stronger and better in manual activity capacity to perform daily activities. Sometimes children and their parents do not opt for a second operation due to experiences with the first operation.

Therefore, it is crucial to choose the best option the first time. This depends also on the goal of the intervention. Based on our findings we would suggest that there is more to gain in manual activity capacity from body functions in the non-dominant hand.

In this study, we found that when we compare children with similar scores on all body functions, the non-dominant hand of bilaterally affected children scored better on manual activity capacity. This difference may be explained by the alternate use of both hands in bilaterally affected children in unimanual daily tasks while unilaterally involved children may only use the non-affected hand. As a result, the non-dominant hand of bilaterally affected children may be more trained than that of unilaterally affected children. This phenomenon is referred to as developmental disregard in children with cerebral palsy and as learned non-use in other groups of unilaterally affected children and in adult stroke patients.[23,24] If this is the case, forced use techniques or bimanual training could be an option for treatment in these children and needs to be further investigated since these therapy options have already proven to be effective in children with cerebral palsy and brachial plexus lesions.[25,26]

Although their contribution was less explicit than hand dominance and severity of the CHD, several body functions also influenced manual activity capacity: TAROM, palmar abduction of the thumb, grip-, tip-tip pinch-, and lateral pinch strength. The effect of the body functions on manual activity capacity was larger for the non-dominant hand than for the dominant hand. The univariate relations of all body functions with manual activity capacity seem to have a large effect in the non-dominant hand (Fig. 2a-e), but when they are entered in the multivariate regression their effect is significant, but smaller.

Surgeons improve body functions aiming at an increase in manual activity capacity, but, based on our findings, this improvement in body functions may result in only small improvements in manual activity capacity. Children showed an average of 15-27% impairment in the dominant hand compared to typically developing children, but 0-3% limitation of manual activity capacity. For the non-dominant hand, an average difference of 29-60% in body functions was found compared to reference values but only a decrease in manual activity capacity of 22% as measured with the test of Eliasson et al. Since the Eliasson test has a limited scale, it may have restricted finding stronger relations between manual activity capacity and body functions. On the other hand, this phenomenon is also found in other diagnosis groups.[27,28] Even when all body functions that enhance manual activity capacity score 0 preoperatively and maximum postoperatively, the maximum increase in manual activity capacity for the dominant hand may be 11 points. On the other hand, for the non-dominant hand this all may add up to 33 points on a scale from 0 to 36. Manual activity capacity may be higher in our study group compared to all children with CHD, because we also included children that underwent surgery in the past. This may influence the generalizability of the outcome on manual activity capacity

for all children with CHD, but does not hinder the analysis of the relation between manual activity capacity and body functions.

In clinical practice, opposition strength is often mentioned as a key variable and several surgical techniques are practiced to enhance thumb opposition strength. However, in this study, we found that this variable did not significantly influence manual activity capacity in a multi-variate analysis. This means that it does not significantly contribute to manual activity capacity, when corrected for other variables. However, this does not mean that opposition is not important in functioning of the hand. For instance, for tip-tip pinch besides a stable thumb a child needs good opposition strength. This should be further investigated whether there is a difference in manual activity capacity pre- and postoperatively in children that underwent opposition strengthening.

Conclusion

In conclusion, the present study shows that in children with CHD the dominant hand scores better on manual activity capacity, even after correcting for differences in hand functions (e.g., strength and mobility) and that there is a stronger relationship between body function and manual activity capacity in non-dominant hands of bilaterally affected children.

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Chapter 7

General Discussion

Counting fingers and toes is, besides asking for the gender, one of the first things parents of new born babies do. When they discover that there are less or more than ten of each, parents start to worry.[1] Parents of a child diagnosed to have a congenital hand difference (CHD) ask many questions, such as "How did this happen?", "What is going to become of my child?", "Will there be any problems in future functioning?", "What are the chances that something like this will happen when we would have another baby?"[2] The congenital hand team, consisting of a hand surgeon, rehabilitation physician, clinical geneticist and hand therapist, is confronted weekly with these questions. Parents deserve a high level of competence from their physician and want reliable, well-informed answers and an appropriate management plan.[1]

In this thesis, we aimed to establish insight in HRQoL and levels of functioning of children with CHD and to study associations with child characteristics such as gender, severity of the CHD, and comorbidity. Furthermore, we studied whether the ICF-CY levels of body function and activities were related with each other and with HRQoL. Since congenital differences may be part of a syndrome that also affects other body parts, we tried to evaluate what the role is of these upper extremity problems in determining daily functioning and HRQoL. Therefore, we additionally studied outcome on function, activity, participation and HRQoL in patients with Apert Syndrome.

We strived to find answers on some of the questions that parents ask who are confronted with a new born child with a CHD. We mainly focussed on how the children experience their life and if there are domains that need special attention.

The cohort of patients studied in chapters 2, 3, 5 and 6 of this thesis consists of 10-14 year old children visiting the congenital hand team of our hospital with different kinds of CHD. While some of them underwent surgery, others were treated conservatively or just followed prospectively. The cohort of patients used in chapter 4, included children and adults with Apert Syndrome treated in our hospital.

Main Findings

The impact of a CHD on HRQoL and functioning is apparent on different levels. Successively, we studied HRQoL, participation, activity (actual performance and capacity) and body functions of the hand, referred to as hand function.

Health-Related Quality of Life

In our first study, we found that all children with CHD report similar HRQoL as healthy peers, except for social functioning, which was lower in children aged 13-14 years (**chapter 2**).[3] However, while on group level they scored similar to their healthy peers, we found a larger variation within the CHD group than in the Dutch child population.[3] When looking at predictors of HRQoL, we found that when activities were performed more easily, children experienced a higher HRQoL, while presence of comorbidity was related to lower scores on all HRQoL subdomains except for school functioning. Additionally, scores on some subdomains were improved by the number of affected digits, but were reduced by age, ethnicity, bilateral involvement and surgery.

If children are too young or incapable to rate their own HRQoL, parent proxy are asked about their child's HRQoL.[4-7] We found that, on group level, children did not score different from their parents (**Chapter 3)**. On individual level, however, agreement in scoring was subject to high variation, with children reporting both higher and lower scores than their parent proxy. On social functioning and emotional functioning these scores can vary up to 30 points on the 0-100 scale. There were no major determinants for agreement. We only found that agreement was higher on emotional functioning in children with more affected fingers and on social functioning in bilaterally involved children. Therefore, care should be taken in choosing the parents' score as a representative substitute for the child's score.

HRQoL of children and adults with Apert Syndrome was studied in **Chapter 4.** On generic HRQoL, we found that, children's summary scores on psychosocial functioning and family activities were comparable with healthy peers, but on some subdomains differences between children with different types of hands were seen.

Children with Apert Syndrome seemed to score lower on self-esteem and general health and in contrast, family cohesion is higher in all children compared with healthy peers.[8] All adults in our study sample experienced more limitations on physical functioning, but experienced less pain and felt less limited in roles due to physical problems, or due to emotional problems than the Dutch norm group.[9] Although both children and adults perceive problems with dexterity, children score less than adults.

Participation

As defined by the World Health Organization, participation is the involvement in a life situation.[10] Participation has a positive influence on health and well-being and is therefore vital for all humans. Decreased physical functioning has been found to lead to restricted participation. When participation is restricted it is mostly less in diversity, located more in the home, involving fewer social relationships, and including less active recreation. However, in children and adults with Apert Disease, that not only comprises functioning of the upper limb, but also the lower limb and brain, we found in regard to participation that the affected children scored similar to their healthy peers, regardless of the type of hand. Similar to the children, the adult group did not perceive large restrictions in participation either.(**Chapter 4**)

Activity (Actual Performance and Capacity)

A child's activity, which the ICF-CY defines as the execution of a task or action by an individual, can be described by the two qualifiers of capacity and performance.[10]

Studying the bimanual performance of children with a CHD (**Chapter 5**), we found that the median score on ease of performance was high and that, on average, children used their affected hand actively in 97% of all activities. Manual capacity, i.e. the activity capacity of the hands, and opposition strength of the non-dominant hand as well as lateral pinch strength of the dominant hand was associated with bimanual performance. Further, we wanted to reduce the number of items in the PUFI to minimize the time burden in evaluating bimanual performance, but we still wanted to discriminate between children with different levels of bimanual performance. We determined that the number of items on the PUFI could be reduced from 38 to 6 items in children with CHD.[11]

In addition to bimanual performance, we investigated the separate capacity of both hands in daily activities: manual capacity (**Chapter 6**). Manual capacity was strongly influenced by hand dominance. Severity of the CHD, expressed as the presence of bilateral involvement and the number of affected digits, and hand function (i.e. mobility and muscle strength measures) had only small effects on manual capacity. Dominant hands scored higher on manual capacity than non-dominant hands that were similarly impaired at hand function level. This means that in non-dominant hands an improvement in hand function more strongly improves manual capacity than in dominant hands. This may suggest that, in contrast with common practice, first surgical or therapeutic interventions offered to children with CHD involving either or both hands should be done to the non-dominant hand first, since this hand's manual capacity would benefit the most from an increase in, for example, strength or mobility of the hand.

For children with Apert Syndrome, activity scores were comparable with scores of children with cerebral palsy. Since no reference values of healthy peers are available,

comparison with healthy peers is not possible, but our group scored 60% of the maximal scores. For the adults, activity scores were worse than that of patients with radial dysplasia after centralization of the wrist and worse than that of healthy peers.**(Chapter 4)**

Hand Function

The third domain described in the ICF-CY is that of anatomical structures and body functions.[10] In this thesis, we refer to the body functions of the upper limb, especially those of the hand, as hand function (**Chapter 6**). Nowadays, emphasis of overall treatment is more shifted from hand function to enhancement of daily activity performance. Still, to alter this, hand surgeons and in many situations hand therapists use hand function level as the starting point. They frequently stabilize or reposition joints or enhance muscle power by performing tendon transfers, all with the ultimate goal to enhance performance.

Methodological Considerations

Considerations of the Study Population and Design

To study the impact of a CHD on daily functioning of children and teenagers with a CHD, we decided to select a heterogeneous group of children. However, due to the heterogeneity of our study group, some restrictions on generalizability arise. First, we selected the age range from 10-14 years old, because in this range both the transition from child to teenager and the transition from primary school to secondary school take place. Since we expected to measure an effect of both transitions on the impact of the CHD, we selected children in this age group, which may restrict generalizability.

The second consideration we should address is that in children with CHD, the differences can vary from a simple syndactyly that will have little impact on hand function if the syndactyly is released adequately, to severe forms of radial deficiency that lead to very severe hand function problems.[12] Consequently, we cannot make statements for specific diagnosis groups. On the other hand, however, the large and diverse study population enabled us to study HRQoL, daily functioning and their interrelationships and determinants regardless of the diagnosis. The interactions between the levels of functioning and HRQoL otherwise could not be studied due to the small group sizes per diagnosis and even within these groups all subforms of CHD and its different comorbidities.

Third, since we also included children that underwent surgery in the past, function and daily activities may be higher in our study group compared to all children with CHD, which also includes conservatively treated or untreated children. Although this may influence the generalizability of the outcome on these measures for all children with CHD, it does not hinder the analysis of the interrelations between all measures.

We need to take into account the cross-sectional design of both the CHD and the Apert Syndrome studies. Although cross-sectional study design is an efficient way to evaluate a relatively large sample of children with CHD and to generate hypotheses regarding future intervention studies and treatment, it also has some limitations. We cannot infer causality in the relations that we studied, but the relations rather show associations at a particular moment in time and give suggestions for future research.

Considerations of the Outcome Measures

To study the HRQoL in children with CHD we choose a generic HRQoL measure since disease-specific instruments were not available.[13] Generic HRQoL is an important health outcome and enables comparison across diseases. Even so, generic HRQoL outcome measures are helpful in measuring rehabilitation or psychosocial goals and interventions. However, it may not be sensitive to reveal specific problems that children with CHD encounter in daily life or to detect changes over time or changes following treatment in children with CHD. The unavailability of disease-specific instruments may have caused underestimation of the impact of a CHD on HRQoL. For instance, generic questionnaires assess whole body functioning and upper extremity functioning is just a small portion of the whole list of items.

Since the present diagnoses schemes or classification schemes for CHD do not predict function, to our knowledge, there is no technique available to quantify disease severity. In this thesis, we used bilateral involvement, number of affected digits and comorbidity as proxies for disease severity. However, a more sensitive measure of severity might have provided more insight into how CHD influence HRQoL and functioning.

Functioning on different ICF-CY levels was determined using different outcome measures. At the domain of hand functions, we choose Total Active Range-of-Motion (TAROM), palmar abduction of the thumb[14], Kapandji thumb range-of-motion score[15], and grip-, tip-tip pinch-, tripod pinch-, lateral pinch- and opposition strength. Additionally, we used the reference values for grip and pinch strength for children reported by Surrey et al. and Molenaar et al. to express the forces as a percentage of the reference values.[16,17] All measurements are reliable and valid measures of hand function.[14,18] Similarly, the original version of the Prosthetic Upper extremity Functional Index (PUFI) was slightly adapted and was proven to be reliable in children with CHD.[19,20] In contrast, the manual capacity test according to Eliasson et al. was originally developed for children with cerebral palsy and not specifically adapted for CHD.[21] Even so, the psychometric properties for the Abilhand –kids[22] were tested only for CP-children. Despite of this, since disease-specific measures were lacking, we considered these measures to be the best options for evaluating activities, since these instruments are age-specific and both measure bimanual activities of the upper-extremity.

Hand dominance in children with a CHD is a complex issue. Although hand preference has been described as the tendency to perform the majority of tasks with one hand rather than the other, this does not necessarily mean that the chosen hand is more efficient. The distinction between hand preference and hand performance has been extensively studied and conflicting theories are used to describe the development of the dominant hand.[23,24] Some researchers describe that children choose their best performing hand to be their preferred or dominant hand[24], whereas others conclude that preference precedes performance.[23] In the first explanation model, the preferred hand in children with unilateral CHD will generally be the unaffected hand and in children with bilateral CHD the less-affected hand. Although we were aware of the conflicting theories, we did not expect hand dominance to be a major factor in determining the relation between manual capacity and hand function. For this reason and for the time burden of the children, we choose to define the dominant hand by asking the children about their writing hand. Since we found that dominance played a major role in the relation between the two levels, in retrospect we could have better chosen a "dominance questionnaire" to be able to make firmer statements on hand dominance. Moreover, it is an interesting topic to study in a longitudinal cohort in future research in children with CHD.

To our knowledge, this was the first study to evaluate daily functioning and HRQoL in children with diverse forms of CHD. Consequently, we needed to assess all ICF-levels of functioning and HRQoL. This meant that the time burden for the children and their parents was high. On forehand, we knew that we had to make decisions on the maximal amount of questionnaires and variables. For time burden, we needed as less as possible, but without lacking vital information. Taking into account the pre's and con's we decided not to systematically measure, for instance information on parental stress or socioeconomic status, although it is considered to be associated with agreement on HRQoL.[25,26] In our group this might have explained some individual differences between child-parent scoring.

Statistical Considerations

To investigate hand function, activity and participation in children with CHD and children with Apert Syndrome, we decided to measure the most commonly-used outcome measures on these aspects. Subsequently, we measured a selection of factors we considered to be potential determinants of activity and participation. However, in our sample 120 children with CHD, we were limited in the amount of factors that could be studied and we had to make decisions on what to measure. It would not have been statistically acceptable to investigate many characteristics in one model. Similarly, in the sample of patients with Apert Syndrome, due to the small group size, we were only able to

describe these determinants. Consequently, we might have missed factors that influence the level of daily functioning or HRQoL.

We choose to measure manual capacity with the handgrip test of Eliasson et al, since it is a test scoring daily tasks according to the handgrip needed to fulfil the task. Secondly, in comparison with the Sollerman test, which also could be considered appropriate to measure manual capacity, the Eliasson test takes less time and is a more qualitative test. In contrast with the Sollerman test, our manual capacity scores were on a 5-level ordinal scale. Since all scores are added up to provide a sumscore[21], this may be a threat for the validity of the results and they should be interpreted with care.

Clinical Implications and Recommendations for Future Research

In this thesis, on children with CHD and patients with Apert Syndrome, we combine information on HRQoL with human functioning on all ICF-CY-levels. To our knowledge, this is the first study to assess all of these levels in children with CHD, regardless of the diagnosis. Therefore, we were able to investigate both areas and their determinants in a relatively large sample size for CHD population studies. The results enable physicians consulting children with a CHD and their parents to provide them with evidence based information.

Based on our findings, we can reassure parents that their child with CHD will probably rate their own HRQoL as high as that of healthy peers. Furthermore, we found that, if clinicians want to gain insight in the effect of an intervention on HRQoL, generic HRQoL outcome measures may not be sensitive enough to detect changes and additional information on HRQoL should be obtained by disease-specific measures. When children are too young or otherwise incapable to validly rate their own HRQoL, clinicians should be careful interpreting the parents' opinion. Since children and their parents on an individual level do not always agree on the child's HRQoL, this should be noted as the parents' opinion rather than a substitute for the child's score.

While children with diverse forms of CHD reported near normal values of HRQoL, patients with Apert Syndrome scored from 33% - 100% within the normal range, depending on the domain that was measured. Consequently, in patients with Apert Syndrome, HRQoL depends on the outcome measure used and the domain that is measured. They mostly report problems in the domains of vision, hearing, speech and dexterity.

Regarding daily activities, we found that bimanual performance is associated with manual capacity and muscle strength (e.g. opposition strength of the non-dominant hand and lateral pinch strength of the dominant hand). Therefore, improvement of bimanual performance would be most beneficial when intervening at these items.

Although we stated that children with CHD generally have good bimanual performance and, on average, activities are performed with active use of the affected hand, bimanual performance can still be enhanced.

For clinicians to get a good impression of bimanual activity performance, we found that addressing only six items of the PUFI questionnaire should suffice. This is convenient considering the time burden for both the children and the physicians or surgeons. In order to improve the clinical applicability and interpretation of the results on the PUFI, a future Rasch analysis of the items using a larger group of children would be beneficial.

In this thesis, we focussed on bimanual performance in performing activities with both hands simultaneously. In general, we found children with CHD do not experience very large problems in bimanual performance. This may be caused by children with CHD having developed alternate strategies and being able to choose the acting and stabilizing hand depending on the activity. In multitasking, however, when both hands are supposed to be occupied with two different tasks, e.g. holding a mobile telephone with one hand and opening the door with the other hand, both hands need to be acting hands. Hypothesizing that in some situations children with CHD are in disadvantage, simultaneous task performance may be a more sensitive measure of function that could be addressed in future studies.

We demonstrated that the relation between manual capacity and hand function in dominant hands is different from non-dominant hands. Therefore, we suggest that the first surgery offered to children with CHD involving both hands, should be done to the non-dominant hand since that is the hand were surgery would most strongly improve manual capacity. Moreover, later, when the dominant hand is also operated consecutively, the non-dominant hand will be extensively trained in its new function due to the post-operative immobilisation of the dominant hand.

Our results showed that bilaterally-affected children scored better on manual capacity with their non-dominant hand than the affected hand of unilaterally-affected children, even if all other hand function scores were similar. We hypothesized that this difference may occur because of the alternate use of both hands in bilaterally affected children in unimanual daily tasks while unilaterally involved children may only use the non-affected hand. This may be related to the concept of developmental disregard as known in children with cerebral palsy and as learned non-use in other groups of unilaterally affected children and in adult stroke patients. To explore if this is the case, intervention studies need to be executed. Even so, due to the cross-sectional design of our study, statements on causality between, for instance, opposition strength and bimanual performance, cannot be made and should be confirmed in longitudinal studies or randomized clinical trials.

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Summary

Summary

Hand function is of extreme importance in interacting with our environment. From the moment we rise until the moment we go to bed our hands perform numerous daily activities. Normal daily activities may become challenges if hand function is compromised. For instance, only a cutting wound at the top of the index finger may force you to use the hand differently for a couple of days. What if hand function is compromised since you were born? Will you encounter problems in feeding, bathing, or leisure activities? Will you be able to manage household activities? How will you experience your quality of life? Exactly these questions arise in the minds of parents who are faced with a child with a congenital hand difference (CHD). In this thesis, we try to find answers on these questions. For this purpose, we conducted two cross-sectional studies. This thesis presents these studies on HRQoL and daily functioning in 10-14 year old children with a CHD and in children and adults with Apert Syndrome.

The introductory **Chapter 1** describes congenital hand differences (CHD) and its possible consequences. These consequences are described using the international classification of functioning, disability and health, the child and youth version (ICF-CY). This model shows how the different domains and child's characteristics may interact. Although health-related quality of life (HRQoL) officially stands outside the ICF-CY framework, it has close relations with the domains of activities and participation.

After discussing HRQoL of our patient group, we follow the top-down approach that we practise in our institution in older children with CHD. We start with the "complex comprehensive " level of functioning, social participation, and end with the "basic" level, functions of the hand, i.e. mobility and muscle strength.

In **Chapter 2**, we compared HRQoL, as measured with the PedsQL generic core scales, in children with CHD with healthy peers. Additionally, we examined the associations between HRQoL, severity of the CHD and ease of activity performance at the activity level. Except for a lower score on social functioning in children aged 13-14 years, children with CHD did not score lower than their healthy peers. When looking at predictors of HRQoL, we found that if activities were performed more easily, this lead to higher HRQoL scores. On the other hand, the presence of comorbidity lowered the scores on all HRQoL subdomains, except for school functioning. Additionally, we described the positive effect of more affected digits and the negative effect of age, bilateral involvement and ethnicity on some subdomains. We concluded that we can reassure parents that their child with CHD will probably rate their own HRQoL as high as that of healthy peers.

Knowledge on the child's HRQoL can be of major importance to the child's physician. In some cases, however, it is not possible to obtain the child's opinion. In those cases, a parent's or caregiver's opinion is often taken as a representative substitute. In **Chapter 3**,

we investigated whether results on HRQoL obtained by measuring the parents' opinion are indeed a representative substitute for the child's opinion. We found that, on group level, the children scores did not differ from their parents; both children and their parents scored high on a scale of 0-100: physical health: 89.1 (SD:14.1) versus 88.0 (SD:15.6), psychosocial health: 80.6 (SD:13.4) versus 79.0 (SD:14.5) and total HRQoL: 83.5 (SD:12.3) versus 82.0 (SD:13.6). In contrast, on individual level, scores showed high variation, with children reporting both higher and lower scores than their parent proxy. The limits of agreement are large and on social functioning and emotional functioning even as large as 30 points on the 0 -100 scale. Despite of this variation, we were not able to detect major determinants for agreement; we only found that children with more affected fingers agreed more with their parents on emotional functioning. This was also true for the agreement on social functioning in bilaterally involved children. Therefore, we suggest that care should be taken in choosing the parents' score as a representative substitute for the child's score and they should not be used interchangeably. For clinical use, we advise to make decisions based on one report, when possible the child's self-report.

To get an impression of the functioning of patients with CHD in the presence of a syndrome, we conducted a cross-sectional study in children and adults with Apert Syndrome **(Chapter 4)**. We found that upper-extremity activity scores were comparable with scores of children with cerebral palsy. Since reference values of healthy peers are lacking, comparison with those children was not possible, but children in our sample scored 60% of the maximal scores. For the adults, upper-extremity activity scores are worse than healthy peers or patients with radial dysplasia after centralization of the wrist, but comparable to a large group of patients with injuries or clinical conditions of the upper limb. For lower limb activity, the scores on the LEFS showed large variance within the group. The adults in our sample scored better than patients with hip or knee osteoarthrosis. Social participation in children with Apert Syndrome score was similar to their healthy peers, regardless of the type of hand. Even so, the adult group did not perceive large restrictions in participation. For HRQoL, all children experience more limitations on self-esteem, emotional parental impact, general health and impact on parental time than healthy peers, but family cohesion is higher in all children with Apert Syndrome. Some subgroups score lower on different domains. All adults in our study sample experienced more limitations on physical functioning, but experienced less pain and felt less limited in roles due to physical problems, or due to emotional problems than the Dutch norm group.

Children with CHD may perceive several problems in performing daily activities. While their surrounding world is designed for two-handed use, they sometimes need to perform activities with one hand. **Chapter 5** examines the bimanual performance of children with CHD using the Prosthetic Upper extremity Functional Index (PUFI) questionnaire and

explored relations with hand function. In this chapter, we demonstrated that 96% of all activities could be performed independently and therefore concluded that children with a CHD generally perform their bimanual activities well. We also found that, although hand function of the affected hand is compromised and numerous alternative strategies can be used to perform bimanual tasks, they are mostly performed with active use of the affected hand. Main predictors of bimanual performance were the manual capacity of the non-dominant hand together with muscle strength (e.g. opposition strength of the non-dominant hand and lateral pinch strength) of the dominant hand**.** Therefore, we suggest that surgical interventions at function level with the ultimate goal to improve bimanual performance should specifically aim at enhancing manual capacity and muscle strength.

Additionally, we determined that spread on the PUFI scores is mainly explained by only 6 of the 38 items. Consequently, we propose that the number of items of the presently very extensive PUFI questionnaire potentially could be reduced when evaluating children with CHD.

Chapter 6 outlines the ICF-CY domains of manual capacity to perform daily activities, hand functions (e.g., strength and mobility) and their interrelations. In this chapter, we present the results on manual capacity and hand function of both hands. Since we found that hand dominance strongly influenced manual capacity, we reported outcome measures for both hands separately. We found that manual capacity of the dominant of the CHD children was only mildly limited, while the non-dominant hand score was more strongly limited. Even when the dominant hand and the non-dominant hand were similarly impaired at hand function level, dominant hands scored higher on manual capacity than non-dominant hands. Although we found small effects of separate hand function measures on manual capacity, we did find that the relation between these outcome measures was stronger in non-dominant hands than dominant hands. We speculated that in bilaterally affected children, interventions, both surgical and conservative, should primarily focus at the non-dominant hand since improving functions such as strength and mobility of this hand may lead to a larger gain in this hand's manual capacity in comparison with the effects of the intervention at dominant hand. In addition, we found that severity of the CHD (bilateral involvement, number of affected digits) and hand function had only small effects on manual capacity.

Finally, **Chapter 7** describes the main findings of this thesis and discusses the methodological considerations, both strengths and limitations. In this chapter we also addressed clinical implications and made recommendations for future research.

Samenvatting (Summary in Dutch)

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Een goede hand functie is van belang voor interactie met onze omgeving. Vanaf het moment dat we opstaan, tot we 's avonds weer naar bed gaan, voeren onze handen ontelbare dagelijkse activiteiten uit. Op het moment dat de handfunctie verminderd is, kunnen normale dagelijkse activiteiten uitdagingen worden. Alleen al een snijwond op de top van de vinger kan er bijvoorbeeld voor zorgen dat de hand een aantal dagen op een andere manier moet worden gebruikt. Maar wat als je handfunctie beperkt is sinds je geboorte? Ervaar je dan problemen met het eten, douchen of je vrijetijdsbesteding? Kun je je huishoudelijke taken wel uitvoeren? Hoe ervaar je dan je kwaliteit van leven? Juist deze vragen komen op bij ouders die te maken krijgen met een aangeboren handaandoening bij hun kind. In dit proefschrift proberen we antwoord te krijgen op deze vragen. Hiervoor hebben we twee cross-sectionele studies uitgevoerd, waarvan dit proefschrift de uitkomsten beschrijft. In de eerste studie onderzochten we de ervaren kwaliteit van leven en het dagelijks functioneren van 10-14 jarige kinderen met een aangeboren handaandoening, in de tweede werden dezelfde onderwerpen onderzocht, maar in deze studie bestond de onderzochte groep uit kinderen en (jong)volwassenen met het Syndroom van Apert.

Het inleidende **Hoofdstuk 1** beschrijft de verschillende aangeboren hand-aandoeningen en de gevolgen die deze kunnen hebben voor het algehele functioneren. Deze gevolgen worden beschreven aan de hand van de "international classification of functioning, disability and health, the child and youth version (ICF-CY)". Dit model laat zien hoe de verschillende domeinen en de karakteristieken van het kind op elkaar inwerken. In dit hoofdstuk wordt tevens de gezondheidsgerelateerde kwaliteit van leven van onze patiëntengroep besproken. Hoewel gezondheidsgerelateerde kwaliteit van leven officieel niet in het ICF-CY model opgenomen is, heeft het nauwe relaties met de domeinen van activiteiten en participatie. In de hierop volgende hoofdstukken wordt het functioneren van de kinderen besproken, waarbij de top-down benadering wordt gehanteerd, zoals ons kinderhandenteam deze gebruikt bij het behandelen van de oudere kinderen met aangeboren aandoeningen. We beginnen bij het "complex en veelomvattend " niveau van functioneren, sociale participatie en eindigen bij het "basale" niveau van functies van de hand, zoals beweeglijkheid en spierkracht.

In **Hoofdstuk 2**, hebben we de gezondheidsgerelateerde kwaliteit van leven van kinderen met een aangeboren handaandoening, gemeten met de PedsQL generic core scales, vergeleken met die van gezonde leeftijdsgenoten. Daarnaast onderzochten we de relaties tussen gezondheidsgerelateerde kwaliteit van leven, ernst van de aangeboren handaandoening en het gemak van het uitvoeren van dagelijkse activiteiten. Kinderen met een aangeboren handaandoening scoorden niet verschillend van hun leeftijdsgenoten

met uitzondering van een lagere score op het gebied van sociaal functioneren bij de groep 13-14 jarigen. Uit het onderzoek naar predictoren van gezondheidsgerelateerde kwaliteit van leven, konden we concluderen dat wanneer activiteiten gemakkelijker werden uitgevoerd, dit leidde tot een hogere score op gezondheidsgerelateerde kwaliteit van leven. De kinderen scoorden lager wanneer ze een comorbiditeit hadden op alle subdomeinen van gezondheidsgerelateerde kwaliteit van leven, behalve op het functioneren op school. De score op sommige subdomeinen bleek positief te worden beïnvloed door een groter aantal aangedane vingers, maar er bestond een negatief effect van leeftijd, het tweezijdig aangedaan zijn en etnische achtergrond . We concludeerden dat we ouders gerust kunnen stellen dat hun kind waarschijnlijk zijn eigen gezondheidsgerelateerde kwaliteit van leven even hoog waardeert als dat van leeftijdgenoten.

Kennis op het gebied van gezondheidsgerelateerde kwaliteit van leven kan van groot belang zijn voor de behandelend arts. Echter, in sommige gevallen is het niet mogelijk om de mening van het kind te verkrijgen. In die gevallen wordt de ouder of verzorger gevraagd als representatieve vervanging. In **Hoofdstuk 3** onderzochten we of de resultaten van die waren verkregen op het gebied van gezondheidsgerelateerde kwaliteit van leven, die waren verkregen door de mening van de ouders te vragen, inderdaad een representatieve vervanging zouden kunnen zijn van de mening van het kind. Uit de resultaten bleek dat op groepsniveau de scores van de kinderen niet verschilden van die van hun ouders; zowel ouders als kinderen scoorden hoog op de schaal van 0-100: fysieke gezondheid: 89.1 (SD:14.1) versus 88.0 (SD:15.6), psychosociale gezondheid: 80.6 (SD:13.4) versus 79.0 (SD:14.5) en totale gezondheidsgerelateerde kwaliteit van leven: 83.5 (SD:12.3) versus 82.0 (SD:13.6).

In tegenstelling tot de vergelijkbare gegevens op groepsniveau lieten de resultaten op individueel niveau een hoge variatie zien, waarbij de kinderen soms hoger maar soms ook lager scoorden dan hun ouders of verzorgers. De "limits of agreement" waren breed en op de gebieden van sociaal functioneren en emotioneel functioneren konden de verschillen zelfs oplopen tot 30 punten op de schaal van 0-100. Ondanks deze variatie, waren er geen duidelijke determinanten voor de mate van overeenstemming; we vonden alleen dat kinderen met meer aangedane vingers het meer eens waren met hun ouders over hun emotioneel functioneren. Dit gold ook voor bilateraal aangedane kinderen en hun ouders op het gebied van sociaal functioneren. Voorzichtigheid is geboden om de score van de ouder als representatieve vervanging te gebruiken voor de score die het kind zelf zou hebben gegeven en beide scores zijn niet uitwisselbaar. Voor het gebruik in de klinische praktijk raden we aan besluiten te nemen op basis van één van beide scores, indien mogelijk die van het kind.

Om een indruk te krijgen hoe personen met een aangeboren handaandoening functioneren wanneer deze aandoening deel uitmaakt van een syndroom, voerden we een cross-sectioneel onderzoek uit bij kinderen en volwassenen met het syndroom van Apert **(Hoofdstuk 4).** Uit de resultaten bleek dat de scores voor de bovenste extremiteiten vergelijkbaar waren met kinderen met cerebral palsy. De vergelijking met gezonde leeftijdsgenoten was niet mogelijk door het ontbreken van normwaarden. Echter, de kinderen in onze onderzoeksgroep scoorden 60% van de maximaal scores. De groep volwassenen scoorde slechter dan gezonde leeftijdgenoten en dan personen met radiusdysplasie, die een centralisatie van de pols hadden ondergaan, maar de scores waren vergelijkbaar met een grote groep personen met diverse aandoeningen aan de bovenste extremiteit.

Op het gebied van activiteiten van de onderste extremiteit vertoonden de scores van de LEFS grote variatie. De volwassenen in onze groep scoorden hoger dan personen met artrose van de heup of knie.

Sociale participatie van kinderen met het syndroom van Apert was gelijk aan dat van gezonde leeftijdsgenoten, ongeacht het type Apert hand dat deze kinderen hadden. Ook de volwassenen beleefden geen grote beperkingen in participatie.

Op het gebied van gezondheidsgerelateerde kwaliteit van leven, werden in relatie tot gezonde leeftijdsgenoten het gevoel van eigenwaarde en de algemene gezondheid lager gescoord. Ouders scoorden een grotere emotionele impact en een grotere impact op de tijd van de ouders dan die van gezonde leeftijdsgenoten. Daar tegenover stond een hogere waardering van de saamhorigheid van de familie bij de kinderen met het Syndroom van Apert in vergelijking met dat van leeftijdsgenoten.

Alle volwassenen binnen onze onderzoeksgroep beleefden meer beperkingen op het gebied van lichamelijk functioneren, maar gaven aan minder pijn te hebben en zich minder beperkt te voelen in hun rolfunctie als gevolg van lichamelijk of emotionele problemen in vergelijking met de Nederlandse normpopulatie.

Kinderen met een aangeboren handaandoening kunnen hinder ondervinden bij het uitvoeren van hun dagelijkse activiteiten. De wereld om hen heen is ingericht op tweehandig gebruik, terwijl zij deze activiteiten soms maar met één hand kunnen uitvoeren. **Hoofdstuk 5** onderzoekt de bimanuele performance van kinderen met een aangeboren handaandoening door het gebruik van een vragenlijst: PUFI (Prosthetic Upper extremity Functional Index) en de relaties tussen bimanuele performance en hand functie. In dit hoofdstuk toonden we aan dat 96% van alle activiteiten zelfstandig door de kinderen kon worden uitgevoerd en concludeerden we dat kinderen met een aangeboren handaandoening over het algemeen hun tweehandige activiteiten goed kunnen uitvoeren. Vervolgens lieten we zien dat, ondanks dat de hand functie van de aangedane hand verminderd was en de kinderen een groot aantal alternatieve

strategieën gebruikten om een taak uit te voeren, ze veelal werden uitgevoerd met actief gebruik van de aangedane hand. Voorspellers voor bimanuele performance waren de manuele capaciteit van de non-dominante hand in combinatie met de spierkracht (de spierkracht van de oppositie van de non-dominante hand en de laterale pinch kracht) van de dominante hand**.** Vandaar dat we de suggestie deden dat chirurgische interventies die bedoeld zijn om de bimanuele performance te verbeteren, het best gericht kunnen zijn op het verbeteren van de manuele capaciteit en spierkracht. Aansluitend stelden we vast dat de spreiding van de PUFI scores grotendeels werd verklaard door slechts 6 van de 38 items en stelden we voor dat het aantal items van de huidige, uitgebreide PUFI mogelijk gereduceerd zou kunnen worden voor het evalueren van kinderen met een aangeboren handaandoening.

Hoofdstuk 6 schetst de ICF-CY domeinen van manuele capaciteit om dagelijkse activiteiten uit te voeren, hand functies (spierkracht en mobiliteit) en hun onderlinge relaties. In dit hoofdstuk presenteren we de resultaten van manuele capaciteit en hand functies van beide handen. Uit de resultaten bleek dat dominantie van de hand de manuele capaciteit sterk beïnvloedde en we besloten de uitkomstmaten voor beide handen afzonderlijk te presenteren. De manuele capaciteit van de dominante hand van de kinderen met een aangeboren handaandoening was slechts gering aangedaan in manuele capaciteit, echter de score van de non-dominante hand bleek meer beperkt. Zelfs wanneer de dominante hand en de non-dominante hand vergelijkbaar waren aangedaan op hand functie niveau, scoorden dominante handen hoger op manuele capaciteit dan non-dominante handen. Ondanks dat we slechts kleine effecten van uitkomstmaten van handfuncties op manuele capaciteit konden vaststellen, bleek de relatie tussen deze uitkomstmaten sterker te zijn in non-dominante handen dan in dominante handen. We speculeerden dat in bilateraal aangedane kinderen interventies, zowel chirurgisch als conservatief, primair zouden moeten focussen op de non-dominante hand, omdat het verbeteren van handfuncties zoals kracht en mobiliteit van deze hand kan resulteren in een grotere winst in de manuele capaciteit van deze hand in vergelijking tot het effect van deze interventie op de dominante hand. Aanvullend werd vastgesteld dat de ernst van de aangeboren handaandoening (bilaterale aandoening, het aantal aangedane vingers) en handfuncties slechts kleine effecten hadden op manuele capaciteit.

Afsluitend beschrijft **Hoofdstuk 7** de belangrijkste bevindingen van dit proefschrift en bespreken we de methodologische aspecten, zowel de sterke kanten als de beperkingen van de studies die zijn beschreven in dit proefschrift. In dit hoofdstuk bespreken we tevens de klinische implicaties en aanbevelingen voor toekomstig onderzoek bij kinderen met aangeboren handaandoeningen.

Dankwoord

Dankwoord

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Collega's van het Erasmus MC, afdeling Revalidatiegeneeskunde Onderzoek en Onderwijs ofwel de 16e en "beneden". In de loop van de jaren zijn er heel wat collega's gekomen en gegaan en ben ik zelf menigmaal van kamer moeten verwisselen, dus velen hebben mij als kamergenoot gehad. Agnes, Bionka, Carla, Channah, Diana, Fabiënne, Gerard, Hans, Hedwig, Henri, Ingrid, Janneke, Jan-Wiebe, Javad, Jetty, Jorrit, Karin, Laurien A, Laurien B, Lyan, Maaike, Majanka, Marian, Mark, Mireille, Myrna, Nienke, Rita, Robert, Tessa, Wilma en Wouter, dank voor de persoonlijke gesprekken, de vele leermomenten op alle vlakken tijdens de refereerbijeenkomsten, maar ook de lekkere stukken taart, al dan niet zelf gemaakt.

Anneke, Ellen, Hans, Lisette, Vera en Willie ik vind het prettig om weer "directe" collega's te zijn en hoop dat we nog jaren mogen genieten van een vruchtbare samenwerking.

Stagiaire, "jonge" Steven wat hebben wij samen een groot aantal uren doorgebracht met het verzamelen van de gegevens. Bedankt voor je medewerking en gezelligheid. Feroz, bedankt voor je inzet en analyse van de subgroepen. Het was niet altijd een gemakkelijke opdracht, maar je hebt het goed volbracht.

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Mijn mannen, lieve Cees, Joris en Rik, jullie hebben het niet altijd makkelijk gehad met mij, maar wat hebben jullie het goed gedaan. Jullie zijn zowel figuurlijk als letterlijk mijn steun en toeverlaat, ik houd van jullie! Op naar de volgende, deze keer gezamenlijke uitdaging.

About the Author

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Monique Saskia Ardon was born in Zevenbergen on the 6th of December 1974. After finishing her Atheneum at Thomas Moore College in Oudenbosch in 1993 she started her bachelor in Physical Therapy at Hogeschool West-Brabant. She graduated in 1997 and had to focus on her personal rehabilitation after an accident in that same period. In 1998 she started studying Health Sciences with a major in Human Movement Sciences at Maastricht University. During this study she worked as a teacher at Avans Hogeschool. She completed her master study with a thesis on reliability and validity of a new goniometer: the Compangle, developed at the department of Rehabilitation Medicine of the University Hospital Rotterdam. While finishing her thesis, she started working as a hand therapist at the rehabilitation department of the same hospital. After obtaining her MSc degree in 2002 she continued working as a hand therapist and, together with Ruud Selles, wrote a grant for a PhD study on functioning of children with congenital hand differences. After receiving the grant she started her research in May 2007, which resulted in the present thesis. At present, she is working at Rijndam Rehabilitation Centre, RVE Erasmus MC, as a pediatric hand therapist and is continuously involved in research projects.

List of Publications

List of Publications

1 Stam HJ, Ardon MS, den Ouden AC, Schreuders TA, Roebroeck ME.
The compangle: a new goniometer for joint angle measurements of the hand. A technical note. *Eura Medicophys*. 2006 Mar;42(1):37-40.

2 Anneke Hoekstra, Drs. Monique S. den Hollander-Ardon.
Kinderhandtherapie bij camptodactylie, meer bekendheid waard! *Ned. Tijdschrift voor Handtherapie.* 2008 April; 17 (1)

3 Ardon MS, Janssen WG, Hovius SE, Stam HJ, Selles RW.
Low impact of congenital hand differences on health-related quality of life. *Arch Phys Med Rehabil* 2012;93:351-7.

4 Ardon MS, Selles RW, Roebroeck ME, Hovius SE, Stam HJ, Janssen WG.
Poor agreement on health-related quality of life between children with congenital hand differences and their parents. *Arch Phys Med Rehabil*. 2012;93(4):641-6.

5 Hoekstra A, Ardon MS. Handtherapie bij kinderen in Kinderfysiotherapie. 2013

6 Ardon MS, Lopez Vilamil-Hoekstra A. Hand Function in Children with Congenital Disorders in Hand function: A practical Guide to Assessment. 2014

7 Ardon MS, Selles RW, Hovius SE, Stam HJ, Murawska M, Roebroeck ME, Janssen WG. Stronger relation between impairment and manual capacity in the non-dominant hand than the dominant hand in congenital hand differences; implications for surgical and therapeutic interventions. *J Hand Ther*. 2013 Dec 4. [Epub ahead of print]

PhD Portfolio

PhD Portfolio

Summary of PhD training and teaching activities

Name PhD student: M.S. Ardon	PhD period: 2007-2014
Erasmus MC Department: Rehabilitation Medicine & Plastic and Reconstructive Surgery	Promotoren: Prof. Dr. H.J.Stam Prof. Dr. S.E.R. Hovius
Research School: none	Supervisor: Dr. R.W. Selles

1. PhD training		
	Year	Workload (ECTS)
General academic skills		
Biomedical English Writing and Communication	2010	4.0
GCP	2012	2.0
Research skills		
Biostatistics for Clinicians	2009	1.0
Regression Analysis	2010	1.9
In-depth courses (e.g. Research school, Medical Training)		
Splinting the pediatric hand (Milano)	2011	0.1
Presentations		
Congenital Hand Deformities: Determinants of functioning and Evaluation of splinting therapy (Rotterdam)	2009	0.6
Quality of life in children with congenital hand anomalies (Rotterdam)	2009	0.5
Quality of life in children with congenital hand anomalies (Hamburg)	2009	1.0
Low impact of CHD on HRQoL (Rotterdam)	2010	0.6
Low impact of CHD on HRQoL (Milano)	2011	1.0
Low impact of CHD on HRQoL (Oslo)	2011	1.0
Health-related quality of life in children with congenital hand differences: parent-child agreement (Oslo)	2011	1.0
Manual activity performance in children with CHD (Dallas)	2012	1.0
Manual capacity in children with CHD (Rotterdam)	2012	0.2
International conferences		
8th World Symposium on Congenital Malformations of the Hand and Upper Limb	2009	1
2nd European Symposium on Pediatric Hand Surgery and Rehabilitation	2011	1
XVIth FESSH and Xth EFSHT congress 2011	2011	1
9th World Symposium on Congenital Malformations of the Hand and Upper Limb	2012	1
Hand Therapy Symposium and 19th Esser Course: "To the base of the thumb; the CMC Joint"	2013	1
3d European Symposium on Pediatric Hand Surgery and Rehabilitation	2014	1

	Year	Workload (ECTS)
Seminars and workshops		
MUSC - PhD day in Rotterdam	2007	0.3
PhD day of Erasmus University in Rotterdam	2010	0.2
CPO minisymposium	2012	0.3
PhD day of Erasmus University in Rotterdam	2012	0.3
Didactic skills		
Other		
Research meetings Dpt Rehabilitation Medicine	2007-2013	7.0
Research meetings Dpt Plastic and Reconstructive Surgery	2011	1.0
2. Teaching activities		
Lecturing		
"Handfunctietesten, betrouwbaarheid en validiteit", Praktijkopleiding Handtherapie, Rotterdam	2007 2008 2009	0.2 0.2 0.2
Minorenonderwijs Plastische en Reconstructieve Chirurgie	2009 2010 2011 2012	0.2 0.2 0.2 0.2
Supervising practicals and excursions		
Minorenonderwijs - practicum handfunctietesten	2009	0.2
Reviewopdracht tweedejaars	2012	0.4
Supervising Master's theses		
Steven van der Knaap - Introducing a new functional classification of hand function and a view at determining its reliability in a diverse group of congenital hand deformities.	2007-2009	2.9
Feroz Nizami - Performance of activities of daily living and participation of children with congenital hand differences, the impact of a thumb deformity.	2010	2.9
Renske Spierings - Latissimus dorsi transfer in AMC	2012	0.7
Other		
Keuze-onderzoek Medical student - 1- Apert handen	2010-2011	1.8
Keuze-onderzoek Medical student - 2 - Polydactylie	2010-2011	0.4
Artikel Ned Tijdschrift voor Handtherapie: Camptodactylie	2008	1.4
Hoofdauteur hoofdstuk "Handfunction in pediatric conditions" in Hand Function: A Practical Guide to Assessment	2010	3.6
Organisatie PHD-day voor Human Movement Sciences Rotterdam	2011	0.7
Peer review for Archives of Physical and Rehabilitation Medicine	2012	0.7
Peer review and rereview for BMC Musculoskeletal Disorders	2012	0.4
Expert in HandART Delphi	2012/2013	0.4
Tweede auteur Kinderhandtherapie in handboek Kinderfysiotherapie	2012	1.4
Total		**50.3**