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221 00 Lund
+46 46-222 00 00

Prevention of Hip Dislocation in Children with Cerebral Palsy

Maria Hermanson



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DOCTORAL DISSERTATION

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To be defended at Lecture Hall F1, Blocket, Getingevägen 4, Skåne University
Hospital, Lund. Friday June 16, 2017, 9.00 a.m.

Faculty opponent
Docent Piotr Michno

Organization: LUND UNIVERSITY Department of Clinical Sciences, Lund Section of Orthopaedics Lund University, Sweden Author: Maria Hermanson		Document name: DOCTORAL DISSERTATION Date of issue: 2017-06-16	
Title: Prevention of Hip Dislocation in Children with Cerebral Palsy			
<p>Background: Children with cerebral palsy (CP) have an increased risk of developing hip dislocation, a painful complication that makes lying, sitting and standing difficult. The CPUP is a national surveillance programme and quality registry with a standardized follow-up of the hips of children with CP. The purpose of this thesis was to provide further information about children with CP who are at risk for hip dislocation, to identify the parameters that contribute to the risk of hip dislocation and to determine how follow-up and treatment can be improved to prevent hip dislocation in children with CP.</p> <p>Methods: Total populations of children with CP within the CPUP served as study groups in this thesis. Migration percentage (MP) and head-shaft angle (HSA) were measured on radiographs, and age, Gross Motor Function Classification System (GMFCS) level and range of motion in the hip joint were recorded. All variables were analysed.</p> <p>Results: Of the 24 children with CP, 2 received an operation on the contralateral side after unilateral femoral osteotomy within a follow-up period of 5 years (Study I). The HSA was measured on radiographs of 145 children with CP, and the risk ratio for hip displacement (MP \geq40%) was 1.05 (95% confidence interval 1.02–1.08; $p < 0.001$) (Study II). The odds ratio for hip displacement (MP \geq40%) was calculated for age, GMFCS level, MP and HSA. All variables were significantly associated with an MP \geq40%. A risk score was constructed using multiple logistic regression analysis, which showed a discriminatory accuracy of area under the receiver operating characteristic curve of 0.87 (Study III). The inter- and intra-rater reliability of the HSA was calculated and produced intraclass correlation coefficients of 0.92 and 0.99, respectively (Study IV).</p> <p>Conclusions: A high HSA is a risk factor for hip dislocation in CP. The CPUP hip score is a risk score and has a high predictive ability to distinguish high- from low-risk individuals for hip displacement (MP \geq40%) within 5 years. The HSA has excellent inter- and intra-rater reliability. If hip displacement occurs and skeletal surgery is needed, unilateral varus femur osteotomy is recommended when only one side is affected.</p>			
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Prevention of Hip Dislocation in Children with Cerebral Palsy

Maria Hermanson



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Contact information

Maria Hermanson

Tel: +46 31 342 10 00

Mail: maria.hermanson@med.lu.se

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*Life isn't about waiting for the storm to pass.
It's about learning to dance in the rain.*
Vivian Greene

To Jesper and Valdemar

Prevention of Hip Dislocation in Children with Cerebral Palsy

Maria Hermanson

Department of Clinical Sciences, Section of Orthopaedics
Lund University, Lund, Sweden

Abstract

Background: Children with cerebral palsy (CP) have an increased risk of developing hip dislocation, a painful complication that makes lying, sitting and standing difficult. The CPUP is a national surveillance programme and quality registry with a standardized follow-up of the hips of children with CP. The purpose of this thesis was to provide further information about children with CP who are at risk for hip dislocation, to identify the parameters that contribute to the risk of hip dislocation and to determine how follow-up and treatment can be improved to prevent hip dislocation in children with CP.

Methods: Total populations of children with CP within the CPUP served as study groups in this thesis. Migration percentage (MP) and head-shaft angle (HSA) were measured on radiographs, and age, Gross Motor Function Classification System (GMFCS) level and range of motion in the hip joint were recorded. All variables were analysed.

Results: Of the 24 children with CP, 2 received an operation on the contralateral side after unilateral femoral osteotomy within a follow-up period of 5 years (Study I). The HSA was measured on radiographs of 145 children with CP, and the risk ratio for hip displacement (MP \geq 40%) was 1.05 (95% confidence interval 1.02–1.08; $p < 0.001$) (Study II). The odds ratio for hip displacement (MP \geq 40%) was calculated for age, GMFCS level, MP and HSA. All variables were significantly associated with an MP \geq 40%. A risk score was constructed using multiple logistic regression analysis, which showed a discriminatory accuracy of the area under the receiver operating characteristic curve of 0.87 (Study III). The inter- and intra-rater reliability of the HSA was calculated and produced intraclass correlation coefficients of 0.92 and 0.99, respectively (Study IV).

Conclusions: A high HSA is a risk factor for hip dislocation in children with CP. The CPUP hip score is a risk score and has a high predictive ability to distinguish high- from low-risk individuals for hip displacement (MP \geq 40%) within 5 years. The HSA has excellent inter- and intra-rater reliability. If hip displacement occurs and skeletal surgery is needed, unilateral varus femur osteotomy is recommended when only one side is affected.

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List of papers

The present thesis is based on the following original papers, which are referred to in this thesis by their Roman numerals:

- I Larsson M, Hägglund G, Wagner P. Unilateral varus osteotomy of the proximal femur in children with cerebral palsy: a five-year follow-up of the development of both hips. *J Child Orthop.* 2012;6(2):145–51
- II Hermanson M, Hägglund G, Riad J, Wagner P. Head-shaft angle is a risk factor for hip displacement in children with cerebral palsy. *Acta Orthop.* 2015;86(2):229-32
- III Hermanson M, Hägglund G, Riad J, Rodby-Bousquet E, Wagner P. Prediction of hip displacement in children with cerebral palsy: development of the CPUP hip score. *Bone Joint J.* 2015;97-B(10):1441-4
- IV Hermanson M, Hägglund G, Riad J, Rodby-Bousquet E. Inter- and intra-rater reliability of the head-shaft angle in children with cerebral palsy. *J Child Orthop.* 2017 (Accepted)

Abbreviations

AUC = area under the receiver operating characteristic curve

BTX-A = botulinum toxin type A

CI = confidence interval

CP = cerebral palsy

CPUP = Cerebral Palsy Follow-up Programme and National Quality Registry

GABA-B = metabotropic gamma-aminobutyric acid

GMFCS = Gross Motor Function Classification System

HEA = Hilgenreiner epiphyseal angle

HSA = head-shaft angle

ICC = intraclass correlation coefficient

ITB = intrathecal baclofen

MP = migration percentage

NSA = neck-shaft angle

OR = odds ratio

RCT = randomized clinical trial

ROM = range of motion

RR = risk ratio

RS = risk score

SCPE = Surveillance of Cerebral Palsy in Europe

SDR = selective dorsal rhizotomy

VOPF = varus osteotomy of the proximal femur

WS = windswept hip deformity

Definitions

Cerebral palsy	A group of permanent disorders affecting the development of movement and posture that limit activity and are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain. The motor disorders of CP are often accompanied by disturbances of sensation, perception, cognition, communication, behaviour, by epilepsy, and by secondary musculoskeletal problems (1, 2).
CPUP hip score	A risk score for the development of lateral hip displacement within 5 years that includes the parameters age, GMFCS level, MP, and HSA (3).
Hip displacement	Lateral displacement of the femoral head. The greater the MP, the more displaced is the hip. Throughout this thesis, hip displacement is defined as an MP $\geq 40\%$.
Hip dislocation	Localization of the femoral head outside the acetabular socket; MP = 100%.
Index hip	The hip measured at the baseline.
Scoliosis	Spinal deviation from the midline in the coronal plane.
Windswept hip deformity	A hip deformity involving adduction and internal rotation of one hip and abduction and external rotation of the contralateral hip.

Thesis at a glance

	Questions	Methods	Results	Conclusions
I	How is the development of the hips after unilateral varus osteotomy?	Retrospective longitudinal cohort study of all 24 children from the CPUP registry in Skåne and Blekinge, with unilateral varus osteotomy in 1994-2005.	After a follow-up of 5 years, 2 of the 24 children had a history of surgery with varus osteotomy in the contralateral hip.	There is a low risk of developing contralateral hip displacement after unilateral varus osteotomy.
II	Is a higher HSA a risk factor for hip displacement in children with CP?	Retrospective longitudinal cohort study involving radiographs from 145 children in the CPUP with MP <40% in both hips at the time of the first radiograph, and a follow-up period of 5 years or development of an MP >40% in either hip.	The risk ratio for hip displacement was calculated as 1.05 (95% CI 1.02–1.08; p<0.001).	A high HSA appears to be a risk factor for hip displacement in children with CP.
III	Can the follow-up and treatment of children with CP be made more efficient by including a risk score?	Prospective study of 145 children in the CPUP with MP <40% at the time of the first radiographic examination. HSA and MP were measured at the baseline and after 5 years or development of an MP >40% in either hip. GMFCS and age were registered.	Age, GMFCS level, MP and HSA were significantly associated with the risk of hip displacement (MP >40%) within 5 years. The predictive ability of the CPUP hip score was high with an AUC of 0.87.	We have developed the CPUP hip score; which is a risk score to identify children with CP who are at high or low risk for hip displacement.
IV	Is the HSA reliable?	Retrospective analysis of radiographs from 50 children examined in the CPUP in 2016. HSA was measured by 3 independent raters at the baseline and after 4 weeks.	The ICCs for inter- and intra-rater reliability of the HSA were 0.92 (95% CI 0.87–0.96) and 0.99 (95% CI 0.98–0.99), respectively.	The HSA showed excellent inter- and intra-rater reliability, which provides further evidence supporting the use of the HSA as a risk factor for further hip displacement.

Introduction

Cerebral palsy

William John Little of London (1810–1894) (Figure 1) was the first person to describe cerebral palsy (CP) in 1862 (4). During medical school, Little was treated for club foot caused by polio and underwent a successful tenotomy of the Achilles' tendon by Louis Stromeyer (1804–1876), a pioneer of tenotomy (5). Little was impressed by Stromeyer's work and started to practice tenotomies himself. In 1840, he opened the world's first hospital for orthopaedic disorders, and was one of the first to work in the fields of both neurology and orthopaedics. Little described the cause of the paralysis and spasticity of CP to be damage to the brain in infants, especially preterm birth or perinatal asphyxia. He wrote many books and papers, and, in 1863, his best-known work was published, in which he described spastic deformities (6) and grouped 47 cases of children with CP into hemiplegia (one side more affected than the other), paraplegia (both legs affected more than the arms), and generalized rigidity (7). What was for many years known as Little's disease in the literature is today known as CP (8).

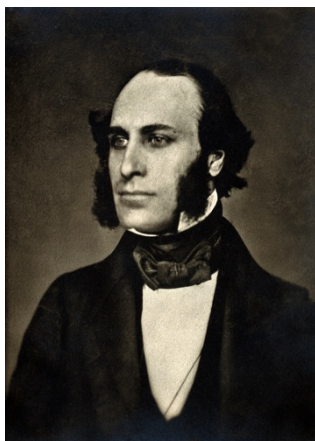


Figure 1. William John Little (1810–1894), the first man to describe cerebral palsy. Reprinted with permission from Wellcome Library, London.

CP is the most frequent cause of motor disability in children and has a prevalence of 2–3 per 1000 live births (9-12). The prevalence has decreased since 1980, but has remained stable over the last years (11). CP is an umbrella term covering a group of conditions caused by static encephalopathy affecting the immature brain. Although the malformation or lesion of the immature brain is static, the musculoskeletal manifestations are often changing (13). Associated impairments such as learning disability, epilepsy and visual impairment are common and related to the severity of CP (14, 15). The expected survival rate for individuals with CP is slightly shorter than that in the general population (16, 17). Most children with CP live to adulthood, and it is important to integrate the provision of educational, social and health services for children with CP.

The definition of CP has been debated for over 150 years (7), and there have been a number descriptions of CP (2, 13, 18, 19). In 1992, Mutch et al. (13) defined CP as “an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development”. Study I in the current thesis is based on this definition. In 2006, Rosenbaum et al. (2) defined CP as “a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing foetal or infant brain. The motor disorders are often accompanied by disturbances of sensation, perception, cognition, communication and behaviour, by epilepsy, and by secondary musculoskeletal problems”. This definition of CP is used in Studies II–IV.

Tachdijan is said to be the first person to write that hip dislocation can be prevented. In 1956, he stated that if one is aware of and understands the pathomechanics of coxa valga and hip displacement, one would look at every spastic child as having a potential hip displacement or dislocation (20). He also said that one should evaluate the patient as a whole before deciding or outlining treatment. “Since many patients are poor operative risks, prophylaxis, early diagnosis and treatment are very important to forestall major surgical procedures” (20).

Classifications of cerebral palsy subtypes

Over the years, there have been several different classifications of CP (4, 10, 19, 21-24), based on topographical or neurological findings. The Swedish classification by Hagberg et al. (10) has been used from the 1950s until recently. The Surveillance of Cerebral Palsy in Europe (SCPE) network released a classification in 2000 (24) that is used worldwide at the time of writing this thesis, and was used in Study I.

According to the SCPE network, CP can be classified into unilateral spastic, bilateral spastic, dyskinetic, ataxic, and non-classifiable CP (Figure 2).

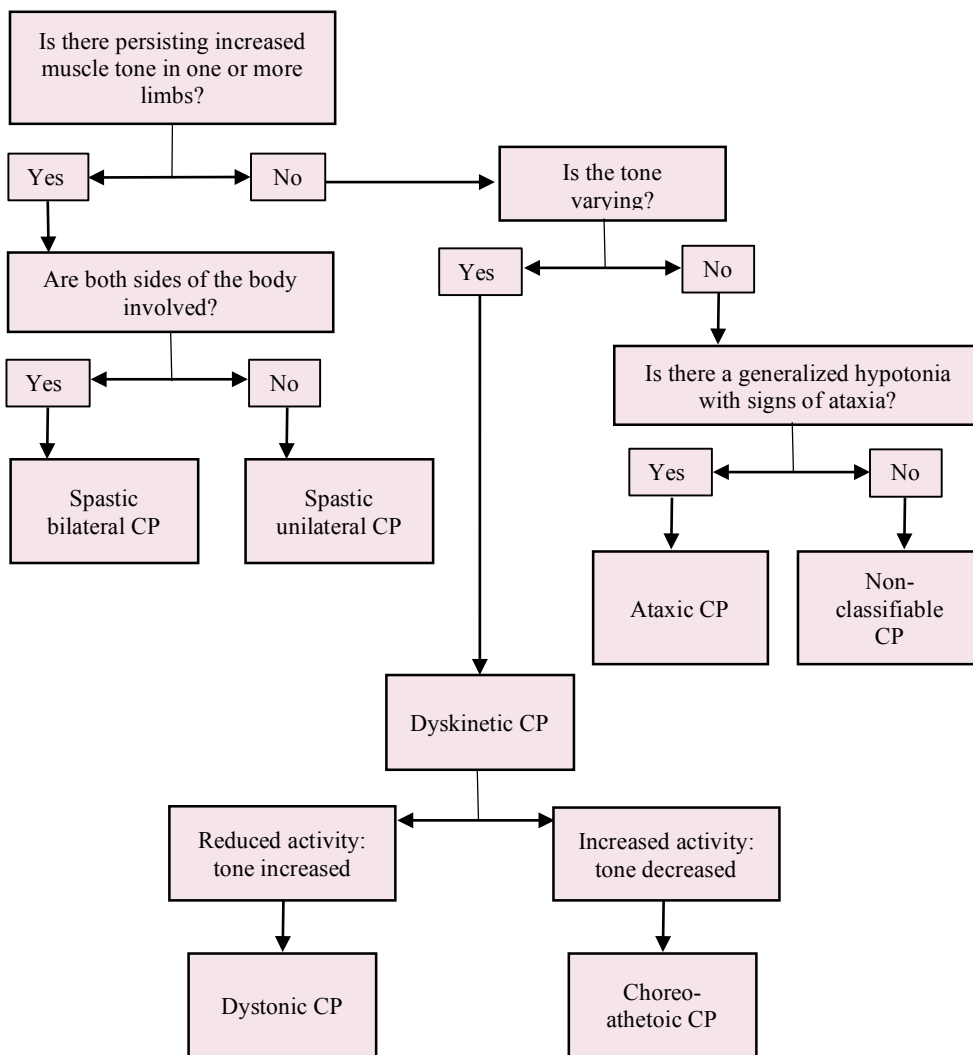
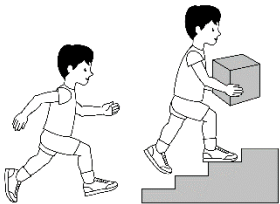
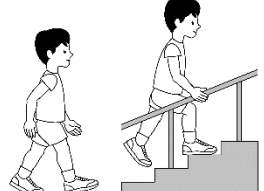
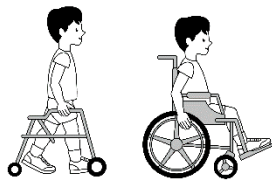
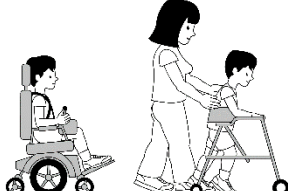
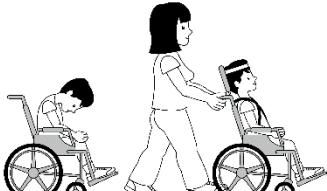


Figure 2. Classification of cerebral palsy (CP) subtypes according to Surveillance of Cerebral Palsy in Europe network (24).

Classification of gross motor function

The main symptom in children with CP is restricted motor function. Therefore, the classification of subtypes is combined with classification of the gross motor function. The Gross Motor Function Classification System (GMFCS) (25) is widely used to describe the severity of gross motor function in children with CP. It is based on 5 levels according to the children's self-initiated movement and focuses on sitting, transfers and mobility. The GMFCS has been revised (26) and now covers 5 age bands from ≤ 2 years to 18 years. This system was used for Studies I–IV in the present thesis (Figure 3).

GMFCS E & R between 6th and 12th birthday: Descriptors and illustrations

	<p>GMFCS Level I</p> <p>Children walk at home, school, outdoors and in the community. They can climb stairs without the use of a railing. Children perform gross motor skills such as running and jumping, but speed, balance and coordination are limited</p>
	<p>GMFCS Level II</p> <p>Children walk in most settings and climb stairs holding onto a railing. They may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Children may walk with physical assistance, a hand-held mobility device or used wheeled mobility over long distances. Children have only minimal ability to perform gross motor skills such as running and jumping.</p>
	<p>GMFCS Level III</p> <p>Children walk using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. Children use wheeled mobility when traveling long distances and may self-propel for shorter distances.</p>
	<p>GMFCS Level IV</p> <p>Children use methods of mobility that require physical assistance or powered mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community children are transported in a manual wheelchair or use powered mobility.</p>
	<p>GMFCS Level V</p> <p>Children are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements.</p>

GMFCS descriptors: Palisano et al. (1997) Dev Med Child Neurol 39:214-23
CanChild: www.canchild.ca

Illustrations copyright © Kerr Graham, Bill Reid and Adrienne Harvey,
The Royal Children's Hospital, Melbourne

Figure 3. The 5 levels of gross motor function (I–V), according to the Gross Motor Function Classification System (GMFCS). Reprinted with permission from Professor Kerr Graham.

The hip in cerebral palsy

Children with CP have an increased risk of hip dislocation, which is a painful and severe complication (27-29) that should be prevented. Hip displacement in CP is caused by an imbalance of forces acting on the hip; the spastic flexors and adductors are stronger and/or more spastic than the extensors and abductors (30). External forces caused by gravity might contribute to the imbalance related to the position of the spine, pelvis and leg. The natural history of the hips in children with CP usually begins with normal hips at birth (31) (Figure 4).

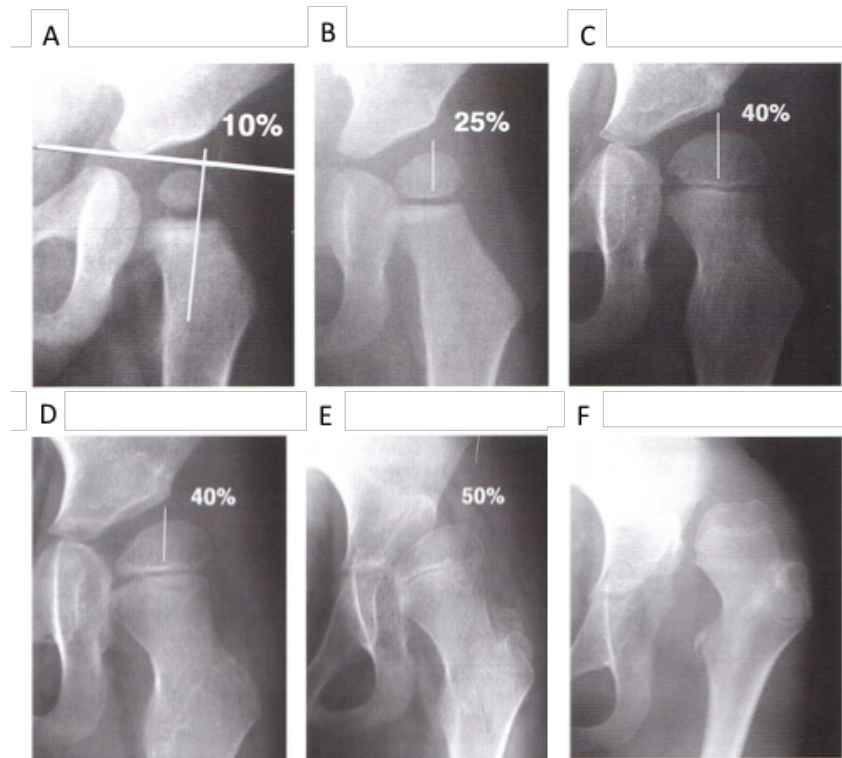


Figure 4. The natural history of hip dislocation in children with cerebral palsy. This child was not treated for hip displacement, and the radiographs show changes over time. (A) The first radiograph shows a normal hip in infancy at an age of 18 months. (B) At 2.5 years, there is a valgus development of the femoral neck combined with a valgus of the femoral head, and the migration percentage (MP) has increased. (C) At 5 years of age, the MP has increased further. (D) At 8 years of age, acetabular dysplasia has developed, and the femoral head has flattened medially. (E) At the age of 10 years, there is osteoporosis laterally of the femoral head with an MP of 50%, and the acetabular dysplasia has progressed. (F) By the age of 13 years, the hip is totally dislocated (MP = 100%) and the femoral head is deformed. Reprinted with permission from Freeman Miller (31).

Without preventive treatment, hip dislocation would affect 15–20% of all children with CP (32, 33). Hip dislocation often occurs at an early age (34) and is associated with contractures, pelvic obliquity, windswept hip deformity (WS), and scoliosis (35-37), which cause difficulty walking, standing, sitting and positioning (27-29). The side that is adducted and internally rotated is at higher risk of hip displacement, compared with the contralateral side. In very rare cases the hip dislocation is anterior (38), usually with an extended externally rotated hip. Anterior hip dislocation is detected by clinical examination and not by radiographic hip screening. No child in Studies I–IV had an anterior dislocation, and this subject will not be covered in the following.

Spasticity

The predominant motor disorder in CP is spasticity (39). Maintaining posture and facilitating movement are accomplished by regulating muscle tone (40). The neuromuscular system responds to muscle stretch by altering muscle tone through the stretch reflex, which is important for maintaining balance and controlling motion (41). In spasticity, the stretch reflex increases and intensifies with the velocity of movement (42-44). Spasticity can lead to postural deficits and motor dysfunction, which limit activity, cause discomfort, and may lead to contractures, skeletal torsion deformities and hip displacement (45). Symmetry of posture in normally developing infants is achieved at 3 months of age; if asymmetry persists beyond this age, long-term gross asymmetry is likely to occur (46). In children with CP, spasticity often starts developing in the second year of life (31), and increases with brain development.

The spasticity in a child with CP may cause the leg to be positioned in flexion, adduction, and, commonly, internal rotation. This causes the femoral head to displace laterally, superiorly, and posteriorly in the acetabulum (31). The acetabular rim becomes deformed and develops a posterosuperior channel (47). In younger children, the acetabulum comprises mainly cartilage, and the hips are at higher risk of instability and deformity than in older children.

Contractures

The growth of the skeleton and the resulting muscle excursion stimulates the growth of the muscle-tendon unit (48). Muscle excursion is reduced in spasticity, which reduces the ability to extend the muscles and causes sustained postures for long periods of time (49), which can lead to contractures and attenuated muscle growth (50). Contractures also occur as a result of muscle weakness, which in turn can reduce muscle excursion (51). An untreated contracture often causes contractures in adjacent joints. Skeletal growth is influenced by spasticity and contractures, and torsion deformities can develop (Figure 5) (51). The musculoskeletal situation

associated with spasticity, contractures and deformities can be complex to treat, which is why early treatment is essential.

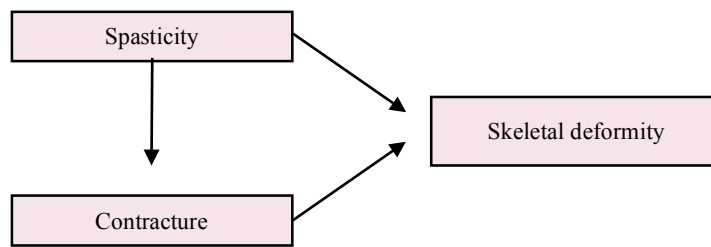


Figure 5. The relationships between spasticity, contracture, and skeletal deformity.

Windswept hip deformity

The pathology of WS places one hip in adduction and internal rotation, and the contralateral hip in abduction and external rotation (28, 35, 36, 52). Young et al. (52) showed an association between WS and asymmetric tone, in which the hip with the stronger adductors is more often adducted or dislocated than is the contralateral hip. Hip dislocation may be a direct cause of WS, and WS may contribute to the development of hip dislocation. WS affects about one-third of children with CP at GMFCS levels III–V (35). It develops most commonly in children younger than 10 years, but the risk is increased up to 20 years of age. WS is difficult to treat and the deviation from the midline is reinforced by gravity. WS impairs the child’s ability to stand and interferes with sitting and lying comfortably (28). The risk of developing WS can be reduced by early treatment of contractures and scoliosis, and early participation in a hip surveillance programme (35).

Scoliosis

Scoliosis is a lateral deviation of the spine in the coronal plane caused by muscle imbalance and weakness, and is reinforced by gravity. Scoliosis is associated with pain, pelvic obliquity, sitting problems, pressure ulcers, WS, hip dislocation, and impairments of cardiorespiratory and gastrointestinal functions (36, 37, 53-56). The risk of hip dislocation increases on the elevated side of the pelvis, when the pelvis is involved in the scoliosis (35, 36). Involvement of the pelvis in scoliosis might be a risk factor for hip dislocation, and vice versa, although the relationship is unclear (57, 58). Children with CP have an increased risk of scoliosis. The reported prevalence is 15-68% (37, 59), with the risk related to the child’s GMFCS level and age (37, 60). The range of prevalence reflects differences in the definition of scoliosis and selection of the study populations.

Risk factors for hip dislocation

Some parameters are well-known risk factors for hip displacement in children with CP; these include young age, high GMFCS level, high migration percentage (MP), and WS (3, 34-36). There is also believed to be a correlation between hip dislocation, pelvic obliquity and scoliosis, although the relationship remains unclear (58). A relationship between pelvic obliquity and the severity and presence of scoliosis has been reported by Pritchett et al. (57). However, Lonstein and Beck (33) did not find a correlation between hip displacement and pelvic obliquity. Senaran et al. (61) found a correlation between hip dislocation and progression of pelvic obliquity, but not with the progression of scoliosis. Hägglund et al. (34) showed that the risk of hip dislocation varied with the subtype of CP – from 0% in ataxic CP to 79% in spastic tetraplegic CP. It is not always possible to determine CP subtype before the age of 4 years, and the risk of hip displacement and dislocation is high in 2–3-year-olds with CP. GMFCS level can be classified before the age of 2 years (26), and has been shown to be a valid risk factor for hip dislocation with 0% risk for hip displacement at GMFCS level I to 64% risk for GMFCS level V (34). Recently a high head-shaft angle (HSA) has been found to be an additional risk factor (62-64), and together age, GMFCS level, MP and HSA form the CPUP hip score (Study III).

Prevention of hip dislocation

Regular clinical and radiographic examinations as part of a surveillance programme with early intervention have been shown to reduce the incidence of hip dislocation markedly (65, 66). When identifying children with hips at risk for displacement, preventive treatment aims to diminish the imbalance of forces to reduce the risk of lateral migration of the femoral head, and can be initiated at an early stage. Examples of preventive treatment include non-operative treatments such as physical therapy with good positioning and avoidance of immobility, botulinum toxin type A (BTX-A), braces and baclofen, and operative treatments such as soft-tissue release and skeletal surgery, in which the femoral head is replaced into the acetabulum. Only soft-tissue release, skeletal surgery and positioning have been shown to have positive effects in the treatment of hip displacement (31, 46).

Hägglund et al. (67) analysed radiographs from a total population of children with CP (n = 272) aged 6.5–13.5 years at the latest examination. Of these 272 children, 44 developed an MP $\geq 40\%$, and only 5 of these children had a decrease in the MP without operative treatment. The authors recommended intense observation and treatment when the MP is $\geq 33\%$, and concluded that surgical intervention is

preferable when the MP is $\geq 40\%$, because the risk for further hip displacement is high in this group.

Positioning

Over time, an asymmetric posture increases the risk for tissue adaption, which may lead to contractures and the risk of hip displacement (68-71). About 30–40% of children with CP use assistive devices to sit or stand (72). The development of a contracture is affected by the amount of time spent in a posture, and the risk for contracture increases with the time spent in an abnormal and asymmetrical posture (49). Rodby-Bousquet et al. (73) performed a cross-sectional study of 102 young adults with CP. The GMFCS level correlated with postural asymmetries in standing, sitting and supine. At GMFCS levels IV–V, all of the participants used a postural sitting support, and a higher proportion of the young adults at GMFCS level V had postural asymmetries while sitting and lying supine, whereas participants at GMFCS levels I–III showed more asymmetries in standing.

In a retrospective study, Pountney et al. (46) investigated postural management and its role in prevention of hip dislocation in 59 children with CP. The MP was analysed in relation to different types of postural approaches. Given that the amount of time in an abnormal posture is related to the development of contractures (49), Poutney et al. (46) suggested that intensive treatment with postural management can be successful in preventing hip dislocation.

Supported standing

A weight-bearing stander is a supported standing device to help children who cannot stand on their own to practice weight bearing (74). Martinsson et al. (74) studied the effect of daily weight bearing on the MP in 14 children with CP, GMFCS levels III–V and a history of bilateral soft-tissue release who stood upright in maximum hip abduction and extension for 0.5–1.5 hours per day for 1 year. They concluded that the MP after adductor-psoas-tenotomy may be reduced in children with CP who stand in a weight-bearing standing brace for 1 hour per day. However, the study group was small and the evidence supporting the effects of weight bearing is still limited.

Graham et al. (75) did not recommend treatment with a hip abduction brace in combination with BTX-A (see section *Botulinum toxin type A* below).

Spasticity treatment

Selective dorsal rhizotomy (SDR), intrathecal baclofen treatment (ITB) and BTX-A, were introduced in the south of Sweden in the 1990s (51). In 2005, Hägglund et al. (51) studied a total population of children with CP (n = 209) and analysed the

range of motion (ROM) and outcomes of orthopaedic surgery. The study population was born in 1990–1991, 1992–1993 and 1994–1995, and comparisons were made at 8 years of age. Passive ROM in non-ambulatory children improved significantly in the later age groups, which had received early inclusion into the CPUP, early non-operative treatment of contractures and the new techniques to treat spasticity. Orthopaedic surgery to treat contractures or deformity of the skeletal torsion decreased from 40% to 15%. This study showed that early treatment of spasticity and contractures with non-operative treatment, and thus prevention of hip dislocation, decreases the need for later orthopaedic surgery.

Botulinum toxin type A

Injection of BTX-A blocks acetylcholine release at the motor end plate (76), which results in chemical denervation that leads to reduced muscular activity (77). The affected muscles usually recover within 3–4 months (76, 78), after re-innervation or restoration has occurred. However, the long-term outcome of BTX-A injection has not been investigated fully, and there are concerns that the affected muscles will experience altered muscle growth and function, although the function may be improved in the short term (79).

Graham et al. (75) conducted a randomized clinical trial (RCT) that included 47 children with bilateral spastic CP and hips at risk for displacement, which was defined as an MP 10–40%. The children received BTX-A every 6 months for 3 years with additional use of hip abduction braces for 6 hours per day. The control group received standard treatment without BTX-A or braces. Serial measurement of the MP was used to analyse the development of the MP. There was no significant treatment benefit (95% CI -0.6–3.4, $p = 0.16$).

Intrathecal baclofen treatment

Baclofen is a metabotropic gamma-aminobutyric acid (GABA-B) receptor agonist that blocks excitatory neurotransmitters in the spinal cord, inhibits presynaptic pathways and decreases muscle tone (80). ITB has been shown to decrease spasticity in CP (81–86). Several authors have reported benefits such as functional improvements and improved quality of life (82, 87–89). The role of ITB in ambulatory children with CP is not clear, and further studies are needed.

A multicentre study was conducted by Krach et al. (90), in which 33 participants, aged 12.1 (4.0–31.4) years, received ITB, and the changes in MP were measured. One third of the study group had an increase in MP of 5% or more, and 12% showed a decrease in MP of 5% or more during the 1-year follow-up. The authors found no associations between the change in the MP and the severity of CP or age. Studies of the prevention of hip dislocation with ITB are limited (31), and more research is needed.

Oral medications such as dantrolene, tizanidine, benzodiazepines and baclofen are sometimes used as a systemic treatment of spasticity. The side-effects (sedation, somnolence) are frequent, the effect of the drugs varies, and ITB is an option for treatment of spasticity in CP.

Selective dorsal rhizotomy

SDR involves cutting the dorsal sensory nerve rootlets (31), to reduce spasticity in a set of muscle groups (91). SDR is most commonly performed in ambulant children with CP to gain motor function. However, at higher GMFCS levels, the focus of intervention is more often to reduce spasticity and improve the ease of care.

Tedroff et al. (92) studied 19 children with spastic CP with a mean age of 4.6 years at the time of SDR and followed them for 10 years. In another study, Tedroff et al. (93) included the same 18 patients (1 dropped out), 15–20 years after the SDR. Normalized muscle tone in the lower extremities was sustained for 17 years after SDR. A decline in gross motor function was seen after 3 years of follow-up. The authors concluded that SDR did not improve function in the long term and did not prevent contractures.

Some studies have suggested that SDR increases the risk of hip displacement (94–96). A comparative analysis of 3 RCTs confirmed the reduction in spasticity and found small positive effects on gross motor function after SDR combined with physiotherapy, compared with physiotherapy alone (97). Miller (31) stated that SDR is not sufficiently focused and that the operative procedure is too complex compared with the effective and fairly small procedure performed for soft-tissue release. The effects of SDR on the hips remain unclear, and further studies are needed.

Orthopaedic surgery

Soft-tissue release

When contractures and spasticity of the adductor muscles cause hip displacement, adductor and iliopsoas muscle lengthening can improve the positioning and symmetry of forces. There is a consensus in the literature that soft-tissue release should be performed bilaterally, to avoid muscle imbalance involving the risk of pelvic obliquity or pelvic tilt with hip displacement of the contralateral hip (29, 98, 99).

Varus osteotomy of the proximal femur

When non-operative treatment and soft-tissue release are not sufficient to maintain or decrease the MP, skeletal surgery with varus osteotomy of the proximal femur (VOPF) is often the next step for preventing further migration of the hip. A VOPF

can correct deformity in 3 planes (rotation, varus/valgus, flexion/extension). The aim of this surgery is to realign the femoral head with the acetabulum (Figure 6).

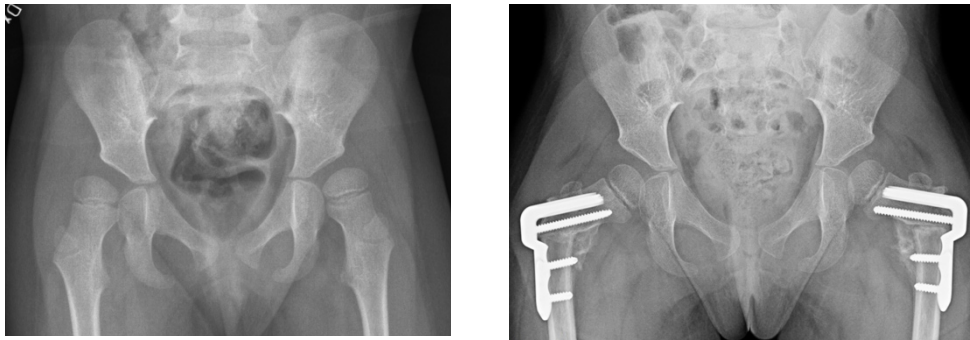


Figure 6. The left radiograph shows bilateral displaced hips, and the right radiograph shows the reduced hips after a bilateral varus osteotomy of the proximal femur.

Pelvic osteotomy

If a reconstruction of the acetabulum is needed, a peri-ilial acetabular osteotomy is the standard procedure (31). The Dega osteotomy (100) is a peri-acetabular osteotomy directed towards the posterior triradiate cartilage (101), which provides an opening of the osteotomy that is more posterior and inferior (31). There are several other types of pelvic osteotomies described, such as the Chiari (102), Pemberton (103, 104), and San Diego acetabuloplasties (101), which are not described further in this thesis.

Salvage surgery for the dislocated hip

A long-standing hip dislocation is commonly associated with deformity of the femoral head and articular cartilage erosion (105). The femoral head comes into painful contact with the lateral iliac wing, and the cartilage erosion is thought to be a major reason for pain in dislocated hips. Salvage surgery, in the form of femoral head resection (Castle procedure) or subtrochanteric valgus osteotomy (Schanz procedure) is sometimes performed in these cases (106, 107).

Radiographic measurements

Neck-shaft angle - NSA

Coxa valga of the proximal femur is a common deformity in spastic hips (63) and can be measured as the neck-shaft angle (NSA) (108) (Figure 7). The NSA of an infant in a normally developed hip is about 150° (31) and decreases to around 130° at 2 years. In a non-ambulatory child with CP, the NSA in a 2-year-old is about 170° (31).

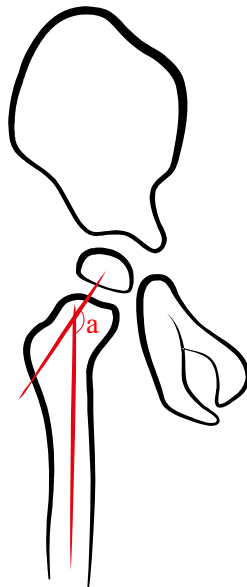


Figure 7. Measurement of the neck-shaft angle (NSA). A line is drawn through the middle of the femoral shaft. A second line is drawn to intersect the femoral head centre with the line drawn through the middle of the femoral shaft. Angle a is the NSA.

Head-shaft angle - HSA

Besides the increased NSA, the femoral head is also commonly in valgus in relation to the femoral neck, and these deformities are measured as the HSA (109) (Figure 8). There are no published reference values for the HSA. van der List et al. (110) reported in a study that the HSA of a normally developed hip decreased by 2° per year. In children with CP, the HSA decreased with 0.6° per year at GMFCS level II, and by 0.9° per year at GMFCS level III. At GMFCS levels IV and V, the HSA did not decrease.

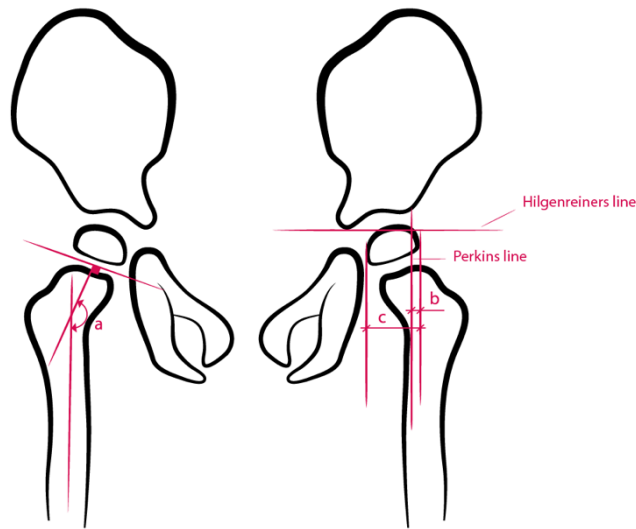


Figure 8. Measurement of the head-shaft angle (HSA) is shown in the right hip. A line is drawn to connect the superior and inferior margins of the epiphysis. A second line is drawn perpendicular to the epiphyseal line, and a third line is drawn through the midshaft femur. The angle formed between the second and third line (a) is known as the HSA. The left hip shows the measurement of the migration percentage (MP). Marks are set at the lateral and medial margins of the acetabulum and the femoral head. A horizontal line is drawn through the medial marks of the acetabulum; the Hilgenreiner line. Perkin's line is drawn perpendicular to Hilgenreiner's line, intersecting the lateral acetabular roof. The distances b and c are then measured. $MP = b/c \times 100$.

Migration percentage - MP

The MP was introduced by the Danish orthopaedic surgeon Jørgen Reimers in 1980 (98) and has become one of the most meaningful and used methods to assess hip displacement. The MP describes the degree of lateral displacement of the femoral head (98) (Figure 8). It is important that the legs be in a neutral position and the pelvis in a horizontal view when performing radiographic examination. If the femur is in adduction, the MP will be falsely high, and if the femur is in abduction, the MP will be falsely low (98). External or internal rotation does not have the same effect on measurement of the MP (98). Eklöf et al. (111) studied 507 children with typical development of the hips, and reported an MP of 5.9 (0–29.5)%. An MP of 33–40% is an indication for intense follow up, regarding of the child's age, GMFCS level, and clinical status. A hip with an $MP \geq 40\%$ is at high risk for further displacement and eventually dislocation, and surgical intervention is often indicated (67).

CPUP – the follow-up programme for cerebral palsy

The CPUP is a national surveillance programme for children and adults with CP. It was initiated in southern Sweden in 1994 as a co-operative effort between paediatric orthopaedics and child habilitation centres and, since 2005, the CPUP is also certified as a national health care quality registry. The CPUP surveillance programme is also used in Norway (CPOP), Denmark (CPOP), Scotland (CPIPS) and parts of Iceland (CPEF) and Australia (Cerebral Palsy Alliance). The CPUP was initiated with the aim of controlling the many hip dislocations and contractures seen among children with CP. The aims of the CPUP are early identification and prevention of hip dislocation and contractures through standardized follow-up, to increase and spread knowledge about CP and to improve the co-operation between professions working with children and adults with CP and their families. In Sweden, children are offered inclusion in the CPUP at the time of the suspected CP diagnosis, as hip dislocation and contractures can occur at an early age.

According to the SCPE network, the diagnosis is determined by a neuropaediatrician when the child is aged 4 years (24) (Figure 9). Over 95% of children with CP are included in the CPUP in Sweden. The children are followed up with standardized radiological examinations of the hip according to their GMFCS level (Figure 10), with annual radiographs until 8 years of age at GMFCS levels III–V, and thereafter on an individual basis. Occupational therapists and physiotherapists examine the children according to another standardized schedule (Figure 11), in which children at GMFCS levels II–V are examined twice a year until 6 years of age and thereafter annually. The prevalence of hip dislocation in children with CP has been reduced from 10% to 0.4% in Sweden since the introduction of the CPUP (65).

When the CPUP was initiated, GMFCS had not been introduced, and the standardized schedule for radiographic examination was based on CP subtype (34). Since 2007, the GMFCS level is used in the standardized examinations. Most children with ataxic CP and spastic hemiplegic CP are at GMFCS level I, and all children with spastic tetraplegic CP are at GMFCS level V. This change in the standardized follow-up in the CPUP has resulted in 35% fewer radiographic examinations in children with CP aged less than 8 years (34).

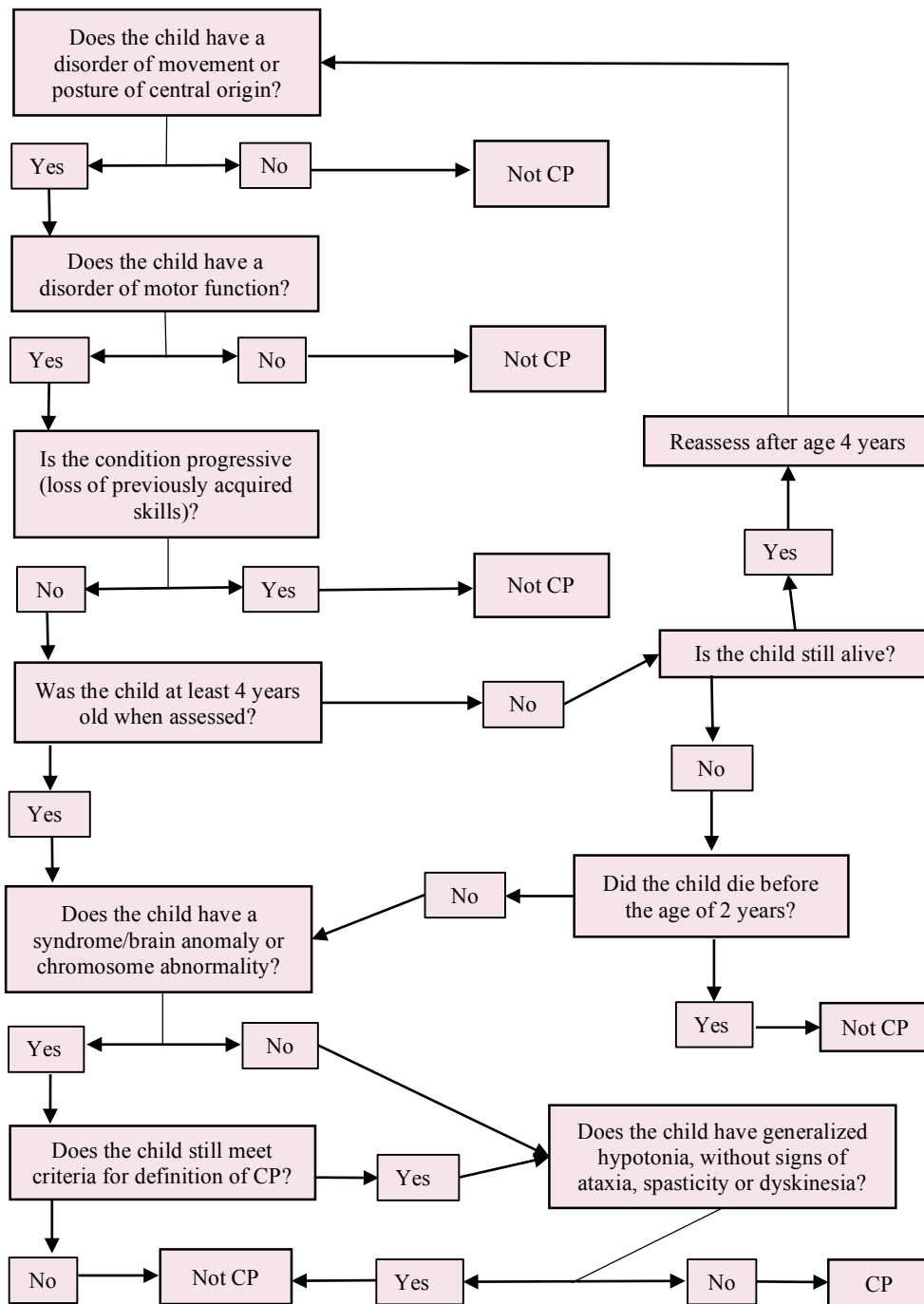


Figure 9. Diagnostic flow chart for cerebral palsy (CP). Modified from the Surveillance of Cerebral Palsy in Europe.

Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
GMFCS I	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
GMFCS II	Green	Orange	Green	Green	Green	Orange	Green	Green	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS III	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS IV	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS V	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue

Figure 10. Schedule for radiographic hip examination within the CPUP: Green = radiographic examination is considered if the clinical examination and migration percentage indicate a risk for hip displacement. Orange = radiographic examination should be performed at this age and GMFCS level. Blue = radiographic examination is performed individually, depending on earlier radiographic findings and clinical examination. Age = age in years, GMFCS = Gross Motor Function Classification System.

Age	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
GMFCS I	Blue	Blue	Blue	Blue	Blue	Blue	White	Blue	White	Blue	White	Blue	White	Blue	White	Blue
GMFCS II	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS III	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS IV	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue
GMFCS V	Orange	Orange	Orange	Orange	Orange	Orange	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue	Blue

Figure 11. Schedule for examination by physiotherapist and occupational therapist within the CPUP. Blue = examination once a year. Orange = examination twice a year. White = no examination performed. Age = age in years, GMFCS = Gross Motor Function Classification System.

The purposes of this thesis

The aims of this thesis were to provide further information about children with CP who are at risk for hip dislocation, to identify the parameters that contribute to hip dislocation and to find ways to improve follow-up and treatment to prevent hip dislocation.

- Paper I: To analyse the development of both hips during 5 years after unilateral VOPF.
- Paper II: To analyse the development of MP in relation to HSA.
- Paper III: To develop a risk score for hip displacement including the parameters age, GMFCS, MP and HSA.
- Paper IV: To analyse the reliability of the HSA using the agreement over time for the same rater (intra-rater reliability) and between raters (inter-rater reliability).

Materials and methods

Design

Studies I and II were retrospective longitudinal studies, Study III was a prospective study and Study IV was a reliability study. Studies I–IV were based on total populations of children from selected regions of Sweden (Skåne, Blekinge, Skaraborg and Gothenburg) and described the development of both hips after unilateral VOPF (Study I), the development of the MP in relation to HSA (Study II), the development of the CPUP hip score – a risk score (RS) for hip displacement (Study III), and the inter- and intra-rater reliability of the HSA (Study IV).

Patients and methods

Study I

Between 1994 and 2005, 24 children (19 boys) with CP at GMFCS levels III–V, followed by the CPUP, were treated with unilateral VOPF and had been followed for at least 5 years in southern Sweden (Skåne and Blekinge). This total population of children was included in the study (Table 1). The number of VOPFs after the index operation, the MP preoperatively and at 5 years postoperatively, and the ROM for abduction, internal and external rotation were recorded in both hips. Two of the children had moved into the area after their index VOPF, and their information on preoperative ROM was therefore missing. The results for ROM are consequently based on 22 children.

Study II

We identified 161 children, who were followed by the CPUP in the southern and western Sweden (Skåne, Blekinge, Skaraborg and Gothenburg) at GMFCS levels III–V. Their first radiographic examination showed an MP <40% for both hips. They were followed up for at least 5 years, or with development of hip displacement during time of follow-up. Sixteen children were excluded for various reasons (Figure 12) (Table 1). There was no exclusion due to poor quality of the radiographs. In total, 145 children were included: 51 developed a hip displacement during the 5-

year follow-up, and 94 children continued to have an MP <40% for both hips for at least 5 years. Radiographs from these 145 children were collected and analysed, and the MP and HSA of the most affected hip at the time of follow-up, according to the MP, were measured and analysed at the baseline and the follow-up. The GMFCS level and age were registered at the time of the first radiograph, and age was also registered at time of follow-up.

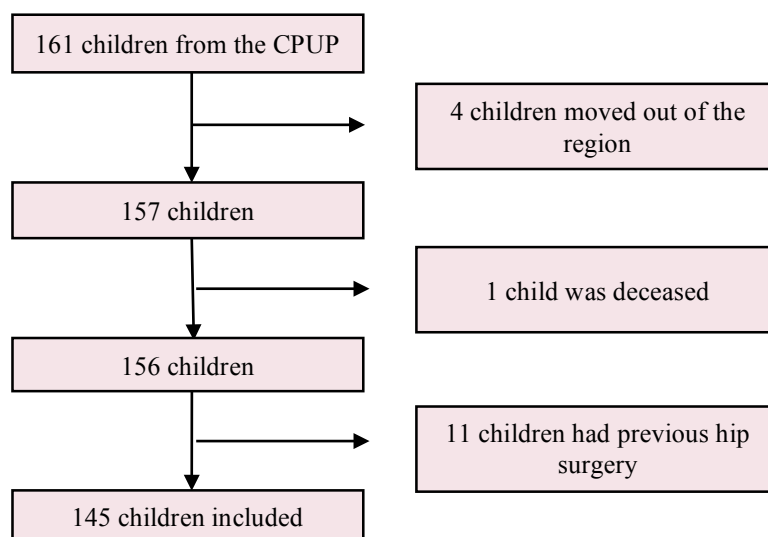


Figure 12. Flow chart for inclusion and dropouts in Studies II and III.

Study III

The participants in this study were the same as those in Study II (Figure 12) (Table 1). The MP and HSA were measured at the first radiographic examination, and the MP was then measured prospectively once a year until hip displacement, or for the follow-up time of 5 years. The GMFCS level was registered at the baseline, and the age was registered at each data collection point.

Study IV

Radiographs of children from southern Sweden (Skåne and Blekinge), who were followed up by the CPUP and who received anteroposterior pelvic radiographs during the first half of 2016 were included. Radiographs of 107 children were identified. Radiographs were excluded if <3 cm of the femoral shaft was visible, as measured from the distal part of the lesser trochanter (n = 34). Radiographs showing that the physis had closed (n = 4) or previous hip surgery (n = 6) were excluded. One radiograph could not be obtained because the child had moved out of the region (n = 1). A total of 50 children, all at GMFCS levels II–V (Table 1), were included

(Figure 13). One hip was randomly designated for measurement using the Bernoulli distribution. The HSA was measured by 3 raters, independently and blinded to each other, at the baseline and after 4 weeks.

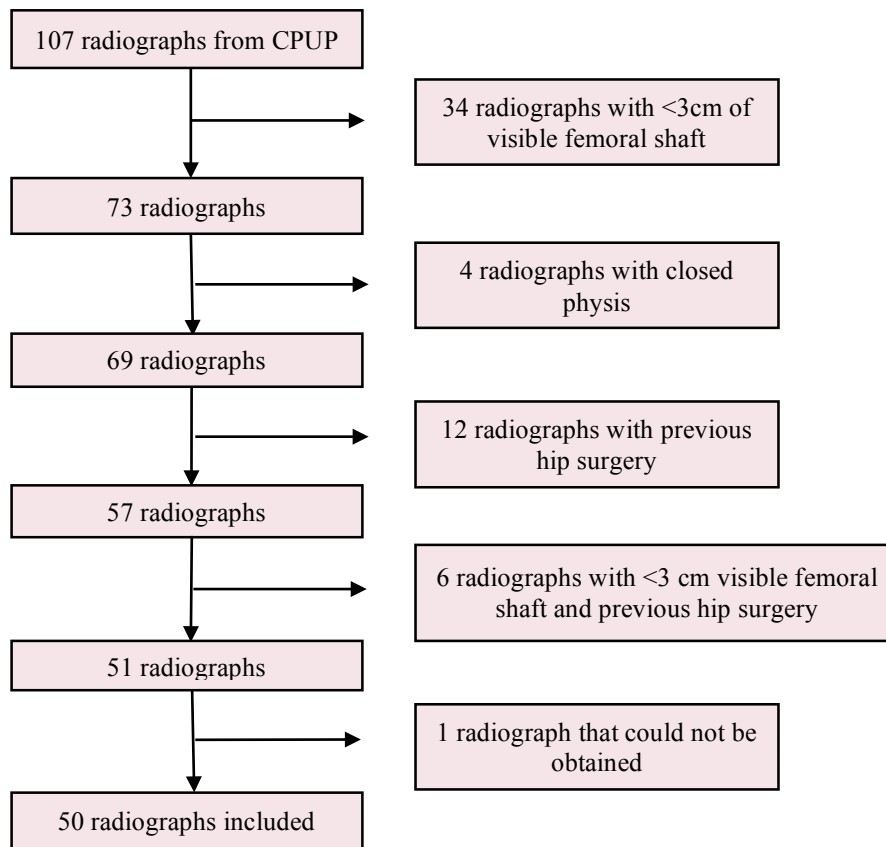


Figure 13. Flow chart for Study IV.

Table 1 – Participants in Studies I–IV.

Participants	Study I	Studies II and III	Study IV
Number of patients	24	145	50
Mean age in years (range)	7.6 (2.8–13.2)	3.5 (0.6–9.7)	6.6 (1.3–14.3)
Boys n (%)	19 (79)	73 (50)	25 (50)
GMFCS I n (%)	-	-	-
GMFCS II n (%)	-	-	10 (20)
GMFCS III n (%)	1 (4)	29 (20)	12 (24)
GMFCS IV n (%)	4 (17)	62 (43)	15 (30)
GMFCS V n (%)	19 (79)	54 (37)	13 (26)
Time of follow-up in years	5	5 or until MP \geq 40%	-

n = number of patients, GMFCS = Gross Motor Function Classification System.

Statistics

P-values of less than 0.05 were considered significant for all analyses in this thesis. The statistical analyses were performed using STATA 12 and 13 software (Studies I–III) and IBM SPSS Statistics version 24.0 (Study IV).

Study I

The average change in differences in ROM between the index hip and the contralateral hip before the index VOPF until the time of follow-up was analysed using a paired *t* test. 95% confidence intervals (CIs) were calculated for the mean differences for each ROM.

Study II

The risk ratios (RRs) between children differing in HSA by 1° were calculated with corresponding 95% CIs. Correction was made for potential confounders (MP and age at the first examination and GMFCS level) using Poisson regression with robust error variance, according to Zou (112). The Wald test was used to test the null hypothesis of no effect of HSA on the risk of hip displacement.

Study III

The odds ratio (OR) with 95% CI for hip displacement was calculated for age, GMFCS level, MP and HSA. Multiple logistic regression analysis was used to construct a RS with these variables. The discriminatory accuracy of the RS was evaluated using the area under the receiver operating characteristic curve (AUC). Potential effects of overfitting on the AUC were evaluated using 10-fold cross validation.

Study IV

Bernoulli distribution was used to select randomly which hip to be measured (left or right). Inter- and intra-rater reliability for the HSA was evaluated using the intraclass correlation coefficient (ICC) and 95% CI with two-way random and absolute agreement for single measures (113). Intra-rater reliability was analysed for each rater and was based on the mean HSA for the 3 raters.

Ethical considerations

Ethical approval was obtained by the Medical Research Ethics Committee at Lund University for Studies I-IV (LU-443-99).

Results

Development after unilateral VOPF (Study I)

Bilateral adductor-psoas tenotomy was performed in all 24 children, either on a previous occasion (n = 16), or at the time of VOPF (n = 8). Dega osteotomy was performed simultaneously with the index operation in 7 patients. During the time of follow-up, 2 children received VOPF of the contralateral hip, and 5 repeat VOPF of the index hip. The mean age at time of the index VOPF was 7.6 (2.8–13.2) years.

The mean MP was 65 (38–100)% in the index hip preoperatively, and 29 (7–52)% in the contralateral hip. At the time of follow-up the mean MP was 34 (8–75)% in the index hip, and 26 (0–86)% in the contralateral hip.

ROM was compared between the preoperative examination and examination at the time of follow-up (Table 2). The mean range of hip abduction decreased by 6° in the index hip and 7° in the contralateral hip. The difference in range of abduction between the hips was 12 (0–40)° before the index VOPF, and 11 (0–28)° at the follow-up. The mean range of hip internal and external rotation decreased by 11° and 6°, respectively, in the index hip and by 9° and 3°, respectively, in the contralateral hip. The mean difference in ROM between the hips increased from 13 (0–55)° to 22 (0–60)° for internal rotation and from 13 (0–45)° to 17 (0–80)° for external rotation. The changes in difference in ROM were not significant (Table 3).

Table 2. Hip range of motion in degrees (range), preoperatively and 5 years postoperatively.

	Preoperatively (°)	5 years postoperatively (°)
ROM index hip		
Abduction	25 (10–50)	19 (0–45)
Internal rotation	59 (40–80)	48 (20–80)
External rotation	45 (10–80)	39 (10–90)
ROM contralateral hip		
Abduction	37 (20–60)	30 (5–50)
Internal rotation	50 (20–80)	41 (10–90)
External rotation	52 (15–80)	49 (15–90)

ROM = Range of motion.

Table 3. Difference in hip range of motion, and 95% confidence intervals between the index hip and the contralateral hip preoperatively and 5 years postoperatively.

ROM	Difference (°)	95% Confidence interval
Abduction	-1.0	-6.2 – 4.4
Internal rotation	1.2	-11.1 – 13.5
External rotation	-1.3	-11.0 – 8.4

ROM = Range of motion.

The HSA and the CPUP hip score (Studies II and III)

The mean HSA of all 145 included children was 166 (140–189)°. The mean age of the 51 children who developed hip displacement was 2.6 (0.7–7.0) years at the time of the first radiographic examination. The initial mean MP was 23 (0–39)% and the mean HSA was 171 (154–189)°. The GMFCS levels were III (n = 4), IV (n = 14) and V (n = 33). At the time of hip displacement, the mean age was 5.1 (1.9–10.8) years, and the mean HSA was 172 (150–183)°.

The 94 children who were followed up for at least 5 years without hip displacement had a mean age of 3.8 (0.6–9.7) years, at the time of the first radiographic examination. The initial mean MP was 16 (0–39)% and the mean HSA was 166 (146–182)°. The GMFCS levels were III (n = 25), IV (n = 48) and V (n = 21). At the time of the follow-up, the mean MP was 23 (0–39)% and the mean HSA was 159 (140–183)°.

HSA was analysed as a risk factor for developing hip displacement independently of age, GMFCS, and MP (Study II). There was no significant interaction between the MP and HSA (Wald test, $p = 0.3$). The RR for hip displacement was 1.05 (95% CI 1.02–1.08, $p < 0.001$) in the corrected analysis.

The analysed variables age, GMFCS level, MP and HSA, all had a significant effect on the risk of hip displacement within 5 years (Study III) (Table 4). The risk of hip displacement increased with a higher level of GMFCS, higher MP and greater HSA, but decreased with age. These relationships are shown by the formula for calculating the RS:

$$RS = -14.1 + 0.71 \cdot GMFCS_{IV} + 2.48 \cdot GMFCS_V + 0.07 \cdot HSA + 0.09 \cdot MP_{max} - 0.5 \cdot age$$

GMFCS_{IV} and GMFCS_V are dichotomous variables that assume the value of 1 when a child has the corresponding GMFCS level, and otherwise assumes the value of 0. When measuring both hips, the HSA is the degree of HSA in the hip with the maximum MP, and MP_{max} is the maximum MP. Age is measured in years. The RS can be translated into the risk of hip displacement within 5 years using Table 5. For example, a child at GMFCS level V, HSA 165°, MP_{max} 30% and an age of 3 years will have a RS of 1.13 and a risk of developing hip displacement within 5 years of 70–80%. Figure 14 shows the sensitivity and specificity of the RS. The predictive ability of the CPUP hip score was calculated at AUC = 0.87. The 10-fold cross validation AUC was 0.85, which lessens concerns of overfitting and confirms the predictive ability of the CPUP hip score.

Table 4. Odds ratio for potentially influential factors in predicting hip displacement with migration percentage ≥40% within 5 years.

Factors	Odds ratio	95% CI	p-value
GMFCS IV vs III	2.04	0.51–8.16	0.316
GMFCS V vs III	12.0	2.96–48.2	<0.001
HSA (comparing levels by 1°)	1.07	1.01–1.14	0.028
Max MP (comparing levels by 1%)	1.09	1.04–1.14	<0.001
Age at examination (comparing levels by 1 year)	0.61	0.45–0.82	0.001

CI = confidence interval, GMFCS = Gross Motor Function Classification System, HSA = head-shaft angle, MP = migration percentage.

Table 5. Risk of hip displacement with migration percentage $\geq 40\%$ corresponding to specific risk score levels.

Risk score	Risk of hip displacement (%)
<(-2.20)	0–10
(-2.20)–(-1.39)	10–20
(-1.39)–(-0.85)	20–30
(-0.85)–(-0.41)	30–40
(-0.41)–0	40–50
0–0.41	50–60
0.41–0.85	60–70
0.85–1.39	70–80
1.39–2.20	80–90
>2.20	90–100

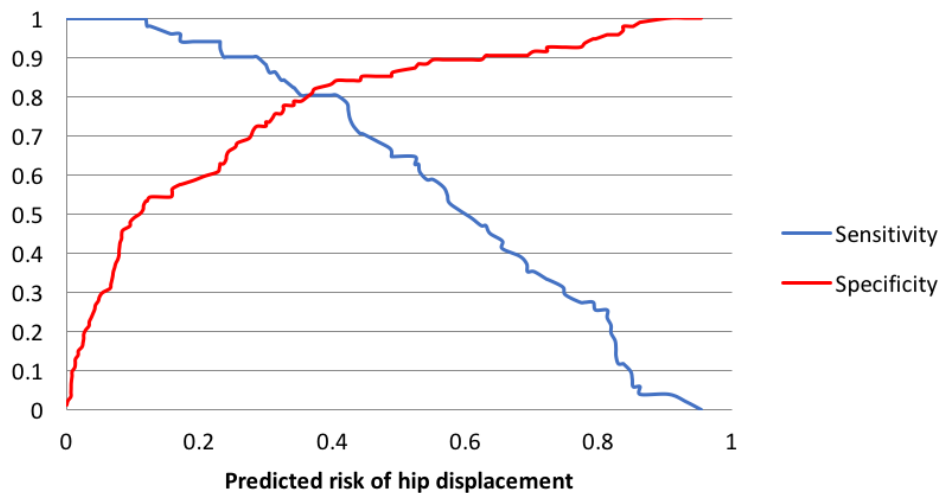


Figure 14. The sensitivity and specificity for predicting the risk of hip displacement.

Reliability of the HSA (Study IV)

A total of 50 children were included, their mean age was 6.6 (1.3–14.3) years. Inter-rater reliability was high, as shown by an ICC of 0.92 (95% CI 0.87–0.95). Intra-rater reliability was also high, as shown by ICCs of 0.98, 0.94 and 0.98 for each rater, and an average ICC of 0.99 (95% CI 0.98–0.99) for the 3 raters. These ICC values were excellent and significant ($p < 0.001$) (Table 6).

Table 6. Inter- and intra-rater reliability for the 3 raters measuring the head-shaft angle.

	ICC	95% Confidence Interval	p-value
Inter-rater reliability	0.92	0.87–0.96	<0.001
Intra-rater reliability	0.99	0.98–0.99	<0.001
Rater A	0.98	0.94–0.99	<0.001
Rater B	0.94	0.88–0.96	<0.001
Rater C	0.98	0.97–0.99	<0.001

ICC = intraclass correlation coefficient.

Discussion

This thesis shows that hip dislocation in children with CP can be prevented by identifying high- and low-risk individuals for hip dislocation and apply early participation in a hip surveillance programme with early intervention. This thesis has studied the risk factors for hip displacement in order to optimize the hip surveillance. The parameters shown to contribute to hip displacement identified in this thesis were age, GMFCS level, MP and HSA (Study II), which combined form the CPUP hip score (Study III), a risk score for hip displacement. The HSA has been shown to have excellent inter- and intra-rater reliability (Study IV). This thesis also showed that, when hip displacement is present, it is recommended that skeletal surgery with VOPF should be performed unilaterally, since the risk of hip displacement of the contralateral hip is low (Study I).

One limitation is the small study population in Study I. However, the 24 children are representative of a subgroup of a total population of children with CP. There were no dropouts during the follow-up. The radiographic examinations in Studies I–IV were performed with the femur positioned in the frontal plane and with no adjustments for degrees of anteversion, which is preferable when measuring the NSA. The NSA has been shown to be sensitive to rotation, and the HSA has a measurement error of only 5° up to a rotation of 45° (62), which makes the HSA a more reliable clinical measurement than the NSA in a hip surveillance programme. Lee et al. (63) studied 384 radiographs from children with CP and reported a mean NSA of 144° and mean HSA of 157°, at GMFCS levels III–V. The effect of rotation should be less when the angle is closer to 180°, which may explain why the HSA is less sensitive to rotation than the NSA. Also, if the HSA is sensitive to rotation, the statistical precision in the relative risk estimate in Study II would have been reduced, leading to wider CIs and reduced power.

The radiographs in Studies I–IV were not adjusted according to how much of the femoral shaft distal to the lesser trochanter that was visible. This might be of importance when measuring the HSA (Figure 8), since one of the lines is drawn through the midshaft femur. In Study IV, we included radiographs where ≥ 3 cm of the femoral shaft was visible, and the reliability of the HSA was shown to be excellent. A recommendation of performing every radiographic examination so that ≥ 3 cm of the femoral shaft is visible is therefore in place. In Study IV, there are

relatively many radiographs from children at GMFCS level II. This is probably because of the exclusion of children with previous skeletal surgery of the hip, which is more common at higher GMFCS levels.

One strength with the studies in this thesis (Studies I–IV) is that all of them were based on total populations of children with CP, which indicates that the results can be generalized to other, similar, populations. The radiographic examinations in Study IV were performed in 11 different radiology departments, with the one instruction that the radiographs should be anteroposterior. Despite this, the inter- and intra-rater reliability of the HSA was excellent, and this outcome provides further evidence for use of the HSA in hip surveillance programmes.

The children in Studies I–III were all at GMFCS levels III–V. A higher level of GMFCS increases the risk of hip dislocation (Study III). A younger age is associated with a higher risk of hip displacement, which is why it is important to identify hips at risk early, to be able to provide appropriate interventions before displacement/dislocation occurs. If hip dislocation occurs, the epiphysis deforms eventually and it becomes more difficult to perform skeletal surgery with a good result (105). In Study I, the development of the hips was followed for 5 years after treatment with unilateral VOPF. There is a consensus in the literature that soft-tissue release should be performed bilaterally, to avoid muscle imbalance, which has a high risk of hip displacement in the contralateral hip (Figure 15) (29, 98, 99). However, earlier studies of the prognosis of hip displacement in the contralateral hip after unilateral VOPF were inconclusive, some authors recommend unilateral VOPF involving only the affected hip (114-116), whereas others recommend bilateral osteotomy in all cases (117-119).

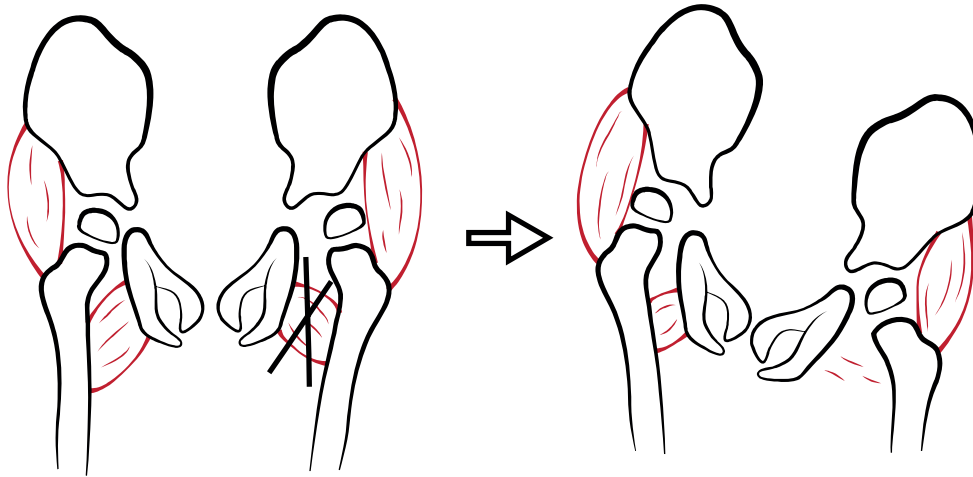


Figure 15. Soft-tissue release with adductor tenotomy of the left hip, which results in a pelvic tilt with the contralateral side higher, and leads to increased adduction and decreased femoral head coverage.

Carr and Gage (114) studied 36 children who had been operated on with unilateral VOPF or unilateral soft-tissue release, with an average follow-up period of 4.8 years. The increase in the MP in the contralateral hip was 0.9% after unilateral VOPF and 12.8% after unilateral soft-tissue release. Gordon et al. (115) suggested that skeletal surgery in one hip should not be an indication for surgery in the contralateral hip. The authors examined 48 children, 5 (2–9) years after unilateral VOPF and found that the condition of the contralateral hip did not deteriorate regardless of the child’s age or ability to walk. Settecerrri et al. (116) studied 48 patients who underwent unilateral skeletal surgery with VOPF and found that only 2 required contralateral VOPF for progressive displacement after the index surgery within 5 (2–15) years.

Noonan et al. (117) described 35 children, of whom 34 underwent unilateral soft-tissue release and 19 unilateral VOPF. The authors found that unilateral hip surgery in children with CP is a relative contraindication, since 15 of the children later underwent surgery of the contralateral hip. Canavese et al. (118) studied 27 children who went through unilateral VOPF and concluded that bilateral surgery should be considered when the dislocation is unilateral. Twelve of these children underwent contralateral VOPF after the index surgery. However, the study group included children who had undergone unilateral soft-tissue release. Owers et al. (119) studied 30 children who all underwent bilateral soft-tissue release and VOPF. The authors found improvement in ROM, radiological containment and pain relief, and concluded that skeletal surgery in children with CP should be performed bilaterally.

The different opinions in the literature about uni- or bilateral skeletal surgery might be explained by the fact that the studies reporting a higher risk for contralateral hip displacement after unilateral surgery (117, 118) included patients who underwent unilateral soft-tissue release. In Study I, all children who underwent surgery received bilateral adductor-psoas release in addition to the unilateral VOPF.

Uni- or bilateral soft-tissue release and VOPF might affect pelvic balance and symmetry. When performing unilateral soft-tissue release, the adductor-abductor balance will shift towards abduction, which produces pelvic tilt with increased contralateral adduction and therefore increases the risk of hip displacement (Figure 15). When performing VOPF, the femur becomes shorter, and the greater trochanter is proximalized, which results in abductor insufficiency, but no increased contralateral adduction (Figure 16). Instead, pelvic tilt may occur if the operated hip is elevated, which reduces the risk of contralateral hip displacement after unilateral VOPF (Figure 17), and presumably increases the risk of redisplacement of the ipsilateral hip. Children with CP who develop hip displacement are commonly at GMFCS levels III–V and non-walkers. It is important for the sitting comfort to have a neutral pelvis and symmetric ROM. However, the muscle imbalance that gives the unilateral hip displacement is not convinced rebalanced by bilateral surgery. In the study by Owers et al. (119) in which bilateral soft-tissue release and VOPF were performed in 30 children, 44% had a WS after 3 years, compared with 50% preoperatively.

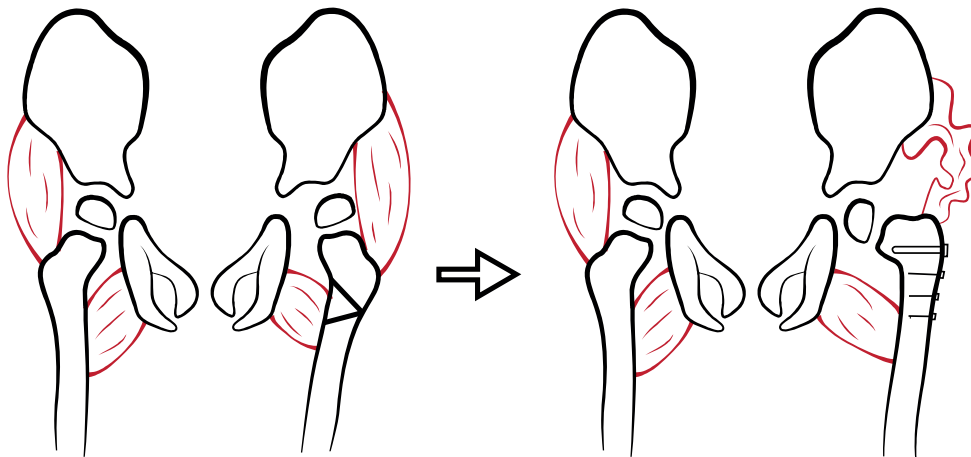


Figure 16. Varus osteotomy of the proximal femur of the left hip, which causes weakness in the abductors of the ipsilateral hip, without increasing adduction of the contralateral hip.

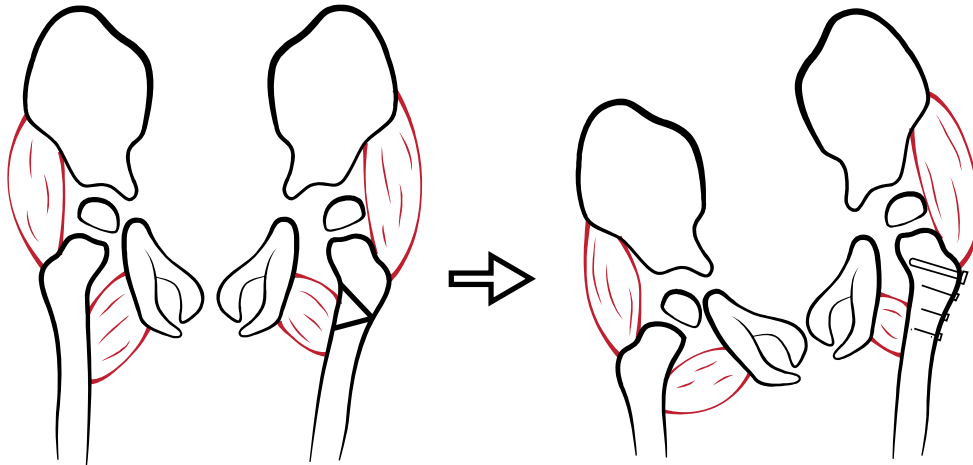


Figure 17. Varus osteotomy of the proximal femur of the left hip, which results in pelvic tilt, and causes the ipsilateral hip to move superiorly, and leads to adduction and decreased femoral head coverage.

To prevent hip dislocation, we need to understand the risk factors. There are several known risk factors, such as age, level of GMFCS and MP (34). HSA has been shown to be increased in children with CP (62) and also to be of prognostic value for hip dislocation (64). Recently, Chougule et al. (120) has been studying 100 children with CP, at GMFCS levels III–V, with a minimum follow-up of 5 years, and measurements of HSA and MP. The authors addressed that there was no significant effect of HSA on MP after adjusting for age. However, the statistical analysis was performed with random effect analysis, which is a linear analysis, when the data seem to be non-linear. They also randomized between right and left hip. In Studies II–III we analysed the hip with the highest MP, since we regard this hip as driver for hip displacement. According to the discussion above, this hip might in some cases cause a pelvic tilt, reducing the risk for hip displacement of the contralateral hip.

Van der List et al. (110) showed that the HSA in a normal hip decreased by 2° per year between the ages of 2–7 years. The HSA decreased by 0.6° and 0.9° per year in children at GMFCS levels II and III, respectively, but did not change significantly in children at GMFCS levels IV and V. Lee et al. (63) reported that the HSA tended to increase with higher GMFCS level. Foroohar et al. (62) reported a mean HSA of 161° in 15 children and concluded that the HSA is increased in children with CP. In children with hip displacement that required surgery, the mean HSA was 170° in 10 included children. The NSA decreases with age (121), which suggests that the HSA also normally decreases with age. The Hilgenreiner epiphyseal angle (HEA), the angle between the Hilgenreiner's line and the proximal femoral physis, is

significantly decreased in displaced hips (122), why the HEA was considered to be analysed in Study II–III. The HEA is the complimentary angle to the HSA in hips in neutral position. Since the HEA is sensitive to adduction and abduction, the HSA was considered more reliable for these analyses.

The orientation of the proximal femoral growth plate reflects the direction of growth. The Hueter-Volkman Law (123) states that growth is highly influenced by mechanical stresses, and in hips with a higher HSA the growth direction is unfavorable and increases the risk of hip displacement (31). The muscle imbalance in children with CP, in particularly at higher GMFCS levels, who have strong adductor and iliopsoas muscles in relation to abductor muscles (38), results in a more horizontally oriented physis when vertical forces are acting on the femoral head (31, 124, 125). Muscle imbalance is believed to cause anteversion, a horizontally oriented growth plate with an increased HSA, and contractures, which together may lead to further displacement of the hip (110). Varus osteotomy will lead to recentralization of the femoral head, and a decreased HSA which will allow the femoral head to have a more favourable growth. Foroohar et al. (62) and Lee et al. (63) have discussed the clinical importance of establishing a normal HSA when performing a VOPF.

The sensitivity and specificity of the CPUP hip score are shown in Figure 14. The cut-off for a high-risk individual for hip displacement has not been defined, and this decision is up to the orthopaedic surgeon. If a lower limit is chosen, the sensitivity will increase and the specificity decrease, which will predict hip displacement in a greater number of children. If a higher limit is chosen, fewer children will be predicted to develop hip displacement. The recommendation is to base the decision on the risk limit relevant to the treatment option being considered. When an extensive treatment such as skeletal surgery is being considered, a high predicted risk is advisable. A predicted risk of 0.80 will yield a sensitivity of 0.25 and a specificity of 0.95. In less extensive treatment such as intense radiographic examination, a lower risk limit may be chosen. A predicted risk of 0.50 will yield a sensitivity of 0.65 and a specificity of 0.86.

The reliability of the HSA was excellent in Study IV, and this finding agrees with that of Foroohar et al. (62), who reported an ICC of 0.94 (95% CI 0.86–0.98) for the inter-rater reliability of the HSA. A somewhat lower reliability was shown by Lee et al. (63) with ICC = 0.79 (95% CI 0.59–0.90). Chougule et al. (120) recently estimated Lin's concordance correlation coefficient as 0.88 (95% CI 0.79–0.93) for intra-observer reliability for the HSA. Both Lee et al. and Chougule et al. included older children, up to age 17 and 18 years, respectively (compared with 14 years in Study IV), and it is possible that the growth-plate was not well-demarcated on their

radiographs. Lee et al. and Chougule et al. did not specify how much of the femoral shaft was visible on the radiographs, which might explain the lower reliability.

Sometimes it can be difficult to know where to draw the epiphyseal line when measuring the HSA. Figure 18 shows 4 examples of the decision to draw lines by the authors of Study IV.

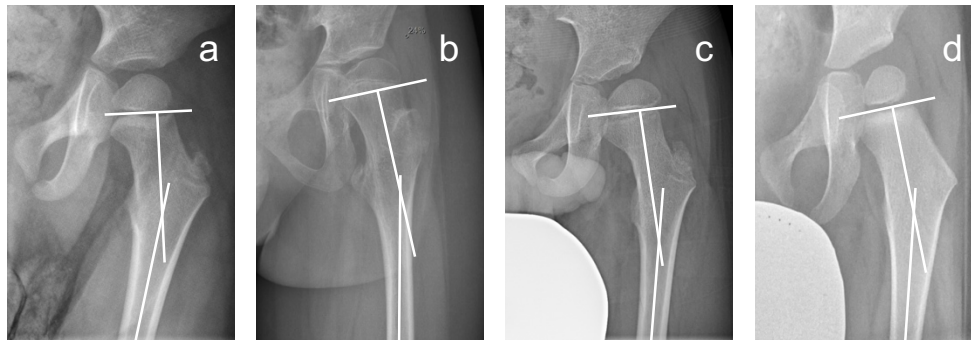


Figure 18. Radiographs showing examples of difficulties encountered when measuring the head-shaft angle. The authors of Study IV decided to draw the lines as follows. a) Undulating physis: a line is drawn parallel to the epiphysis, since the epiphysis is rounded without distinct inferior and superior margins. b) A line is drawn to connect the inferior and superior margins of the epiphysis. c) Oval physis: a line is drawn through the midline of the physis. d) Straight physis: a line is drawn parallel to the proximal end of the metaphysis, since the epiphysis is not yet fully ossified.

A hip surveillance clinic for children with CP was established in Australia in 1997, by Graham et al. (66). Clinical and radiographic examinations are performed to improve the outcome of spastic hips, by applying early identification and intervention (66). Radiographic examinations are performed at all GMFCS levels (I–V), and every 6 to 12 months in children at GMFCS levels III–V in Australia (126). By contrast, the CPUP Swedish hip surveillance programme includes radiographic examination of the hip in children at GMFCS levels II–V, but less frequently (Figure 10).

Pain has been reported in 30–75% of children with CP (127-133). Recurrent musculoskeletal pain with higher levels of mental health problems and decreased quality of life have been described by Ramstad et al. (134) and Findlay et al. (135). In a recent Swedish study by Alriksson-Schmidt et al. (132), 32.4% out of 2777 included children with CP reported pain. Penner et al. (133) noted that physicians reported pain in 38.7% of the 252 included children with CP, and that the most common cause of pain was identified as hip displacement/dislocation (16%). One could speculate that the lower prevalence of pain in the study by Alriksson-Schmidt et al. could be due to the CPUP hip surveillance programme, which has very few hip displacements/dislocations, and fewer severe contractures, WS and scoliosis.

To facilitate the use of the CPUP hip score, an application (Figure 19), that can be downloaded free of charge, has been constructed. At the time of writing this thesis, there have been 2100 downloads. The decision about whether surgery should be recommended for an individual child or whether radiographic and clinical examination should be performed at closer intervals is made by the orthopaedic surgeon together with the patient and his/her family. The CPUP hip score may be a valuable tool in these decisions. For example, when comparing 2 children with the same level of GMFCS, MP and age, a 10° higher HSA will give a $1.05^{10} = 1.6$ times higher risk for hip displacement within 5 years (Figure 20). There are probably adjustments and potential risk factors that could be added to the RS in the future, such as the degree of spasticity, range of hip motion, and CP subtype. However, the AUC has been calculated as 0.87, which shows that the CPUP hip score is highly accurate in distinguishing a high- from a low- risk individual for hip displacement.

Of the 91 children with hip displacement in a 20-year follow-up of the CPUP hip surveillance programme, 31 were treated successfully with adductor-psoas release. The other 60 children were treated with VOPF, which was combined with pelvic osteotomy in 2 children (65). Early identification of hips at risk for dislocation is crucial in hip surveillance. The CPUP hip score will improve the prediction of hips at risk for displacement, which will lead to treatment with less extensive surgery in children with CP.



Figure 19. Smartphone using the application CPUP hip score.

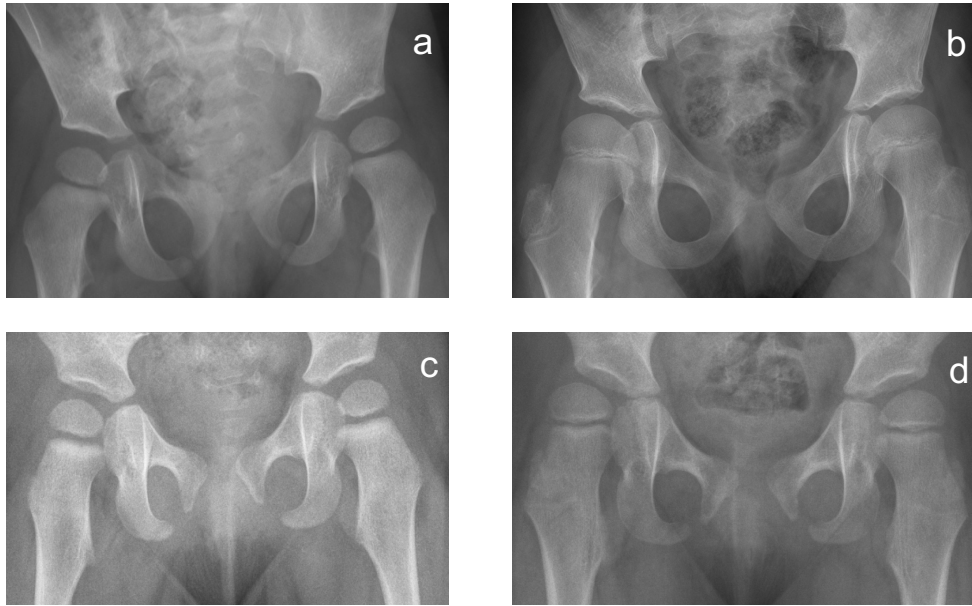


Figure 20. Radiographs of 2 children of similar ages, Gross Motor Function Classification System (GMFCS) levels and migration percentages (MP), but with difference in the head-shaft angle (HSA). a) Radiograph of a girl aged 1.8 years, GMFCS level IV. Right hip: MP 20%, HSA 165°. Left hip: MP 25%, HSA 159°. b) The same girl as in (a) at 7.2 years, without hip displacement. Right hip: MP 26%, HSA 167°. Left hip: MP 24%, HSA 164°. c) Radiograph of a girl aged 1.3 years, GMFCS level IV. Right hip: MP 21%, HSA 177°. Left hip: MP 25%, HSA 170°. d) The same girl as in (c) at age 3.3 years, with hip displacement. Right hip: MP 48%, HSA 179°. Left hip: MP 35%, HSA 171°. A higher HSA gives a higher risk for hip displacement, regardless of age, GMFCS level and MP (Study II).

Since William John Little first described CP in 1843, knowledge and management have improved steadily. It took more than 100 years until Tachdjian in 1956 first stated that hip dislocation is preventable. The development during the past decades has progressed from reactive to preventive management of hip displacement. The start of surveillance programmes for children with CP, such as the CPUP, has provided unique opportunities to standardize the active surveillance, to prevent hip dislocations and to continue the research on ways to provide even better care for children with CP.

Since the start of the CPUP in 1994, the prevalence of hip dislocation in children with CP has decreased markedly, from 10% to 0.4% (65). The results of this thesis may improve the ability to predict which children are at high- or low risk of hip displacement and, therefore, to improve the prevention of hip dislocation in children with CP.

Conclusions

- It is recommended that VOPF for prevention of hip dislocation is performed unilaterally when only one hip is displaced.
- A high HSA is a risk factor for hip displacement in children with CP.
- The CPUP hip score provides a risk score that can be used to differentiate high-risk from low-risk individuals for hip displacement within 5 years.
- The HSA has an excellent inter- and intra-rater reliability.
- The studies in this thesis are based on total populations of children with CP, within the CPUP, which makes the results generalizable to other hip surveillance programmes for children with CP.

Further research

Questions that should be addressed in the future are:

- Are there parameters besides age, GMFCS level, MP and HSA that could further improve the risk calculation for hip displacement in children with CP?
- Does it matter if ROM is asymmetric; that is, is it worse to have an abduction of 40° on one side and 20° on the other than to have 20° bilaterally?
- Are there prognostic factors for preventive surgery? When should soft-tissue release be performed, and when is VOPF preferable?
- Is there further evidence for the use of non-operative treatments, such as positioning and standing, to prevent hip dislocation?

Sammanfattning, summary in Swedish

Cerebral pares (CP) är den vanligaste orsaken till motorisk funktionsnedsättning hos barn, med en förekomst på 2–3 per 1000 barn. Personer med CP har en betydligt ökad risk för att höften ska växa ur led (höftluxation), en komplikation som orsakar smärta och svårigheter att sitta, ligga och stå. Höftluxation ökar också risken för snedställt bäcken, skolios och muskelförkortningar (kontrakturer). Det finns kända riskfaktorer för höftluxation, såsom låg ålder, nedsatt grovmotorisk förmåga, förskjutning av lårbenshuvudet (mäts som ökad migrationsprocent – MP, ett mått som beskriver andelen av lårbenshuvudet som ligger utanför leddskålen), samt en ökad vinkel mellan lårbenshuvudet och lårbenet, Head-Shaft angle (HSA).

CPUP är ett kvalitetsregister och uppföljningsprogram för barn med CP som startades 1994 i södra Sverige, och som är ett nationellt kvalitetsregister sedan 2005, och har internationell spridning. Över 95% av barn med CP i Sverige är med i CPUP, och följs där med en standardiserad uppföljning med bland annat klinisk- och röntgenologisk undersökning av höfterna.

Denna avhandling har syftat till att undersöka vilka barn med CP som har störst risk att drabbas av höftluxation, för att kunna förhindra denna komplikation. Studie I–IV har omfattat totala populationer av barn med CP, som följs i CPUP.

I Studie I undersöktes 24 barn som hade opererats med ensidig skelettkirurgi (femurosteotomi) på grund av hotande höftluxation. Endast 2 av 24 barn hade opererats med femurosteotomi i motsatta höften vid uppföljning efter 5 år, och risken för höftluxation i den motsatta höften bedöms därför vara låg.

I Studie II följdes höftutvecklingen på röntgenbilder i CPUP hos 145 barn. En grupp (n = 94) hade fortsatt normal MP efter en uppföljningstid på 5 år, medan den andra gruppen (n = 51) utvecklade förskjutning av lårbenshuvudet med MP $\geq 40\%$. Hög HSA visade sig vara en riskfaktor för förskjutning av lårbenshuvudet hos barn med CP, oberoende av ålder, grovmotorisk funktion och MP.

Med samma material som i Studie II utfördes Studie III. Ålder, nivå av grovmotorisk förmåga, MP och HSA sammanvägdes för att konstruera CPUP Hip Score, som är en riskvärdering för att utveckla höftluxation inom 5 år hos barn med CP. CPUP Hip Score hade stor förmåga att förutse vilka höfter som riskerar att utveckla höftluxation (AUC = 0,87).

I Studie IV undersöktes överensstämmelsen vid mätning av HSA. Tre personer mätte, oberoende av varandra, HSA på 50 röntgenbilder vid 2 tillfällen med 4

veckors mellanrum. Överensstämmelsen mellan de 3 personerna vid samma tillfälle och mellan personerna vid upprepad mätning var mycket hög (intraclass correlation coefficient (ICC) beräknades till respektive 0,92 och 0,99).

Då Studie I-IV inkluderar totala populationer av barn med CP kan resultaten generaliseras till liknande populationer och således andra uppföljningsprogram.

Sammanfattningsvis har avhandlingen visat att:

- Ensidig femurosteotomi rekommenderas vid skelettkirurgi när enbart en sida är drabbad av hotande höftluxation, då risken är låg för den motsatta höften att drabbas av höftluxation i ett senare skede.
- En hög HSA är en riskfaktor för att utveckla höftluxation hos barn med CP.
- CPUP hip score är ett riskvärderingsinstrument, med hög förmåga att bedöma vilka barn med CP som har hög respektive låg risk för höftlateralisering inom 5 år.
- HSA uppvisar mycket god överensstämmelse mellan bedömare, och är ett värdefullt mått när förskjutning av lårbenshuvudet bedöms hos barn med CP.

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She thought she could, so she did.

R.S. Grey

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