

Slipped Capital Femoral Epiphysis. Growth, Remodeling and Cartilage Quality after Unthreaded Fixation.

Örtegren, Jakob

2018

Document Version: Publisher's PDF, also known as Version of record

Link to publication

Citation for published version (APA): Örtegren, J. (2018). Slipped Capital Femoral Epiphysis. Growth, Remodeling and Cartilage Quality after Unthreaded Fixation. [Doctoral Thesis (compilation), Department of Clinical Sciences, Lund]. Lund University: Faculty of Medicine.

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Slipped Capital Femoral Epiphysis

Growth, Remodeling and Cartilage Quality after Unthreaded Fixation

Jakob Örtegren



DOCTORAL DISSERTATION

by due permission of the Faculty of Medicine, Lund University, Sweden. To be defended at the Clinical Research Center Aula, SUS Malmö.

June 2, 2018 at 9 am.

Faculty opponent
Professor Young-Jo Kim

Harvard University, Boston Children's Hospital, Boston, Massachusetts, USA

Organization	Document name		
LUND UNIVERSITY Department of Orthopedics	DOCTORAL DISSERTATION Date of issue		
Clinical Sciences, Lund	2018-06-02		
Author: Jakob Örtegren	Sponsoring organization		
Title and subtitle			
Slipped Capital Femoral Epiphysis—Growth,	Remodeling and Cartilage Qu	ality after Unthreaded Fixation	
Abstract Background: Slipped capital femoral epiphysi approximately 5 in 10 000 children. In this cond between the femoral head and neck. This slip Is Symptoms such as pain and limping are typics or screw is inserted with the intention of stab contrast to the global standard, the Swedish thansson hook pin) over the physis with the go	ition, a progressive slip occurs eads to an improper relationsh ally initially vague but graduall ilizing the physis to prevent for cradition is to perform in situ fi	due to weakening of the physis located ip between the femoral head and neck. y escalate. Treatment is surgical; a pinurther slippage (i.e., in situ fixation). In xation with an unthreaded pin (i.e. the	
Purpose: To increase knowledge about the old hook pin, and to investigate how various factor		ı fixation for SCFE using the Hansson	
Methods: Four studies were conducted on a cohort of 54 children treated for stable SCFE with in situ fixation using the Hansson hook pin, in Malmö, Lund and Kristianstad from 2001 to 2009. In papers I and II, physeal growth and remodeling of hip morphology were investigated using radiographic evaluation until skeletal maturity. In paper III, cartilage status in 22 individuals from the cohort was assessed an average of 11 years after slippage using delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC). Clinical investigation of hip status was performed, as well as patient related outcome. In paper IV, the duration between symptom onset and treatment was investigated by reviewing medical charts and with personal interviews.			
Results: Paper I established that continued physeal growth occurs in both the SCFE and the contralateral, prophylactically pinned, hips. Growth significantly increased femoral offset. Younger children grew more compared with older children. Significant remodeling of the hip deformity, particularly femoroacetabular impingement (FAI), was verified and correlated with growth. Eleven years after slippage, cartilage status in the SCFE hip was mildly but significantly impaired. Cartilage degeneration correlated with the prevalence of FAI but not with original slip severity. Impaired cartilage status was correlated with impaired self-reported clinical outcome. The duration between symptom onset and diagnosis was median six months. Patients' delay was significantly longer than doctors' delay. Boys and children with a predominance of knee pain were at increased risk for delay.			
Conclusion: Unthreaded in situ fixation for SCFE with the Hansson hook pin leads to continued physeal growth with preserved femoral offset in adulthood. The growth-related remodeling of the femoral neck deformity emphasizes the importance of continued growth to minimize the risk of residual FAI. Early cartilage degeneration is related to the prevalence of FAI in adulthood rather than the initial slip severity. Thus, findings suggest that future focus should be on how to diagnose and treat persisting FAI after physeal closure. Patients' delay is the primary contributor to late SCFE diagnosis. Therefore, educational efforts should be implemented to improve awareness of this condition among both health care providers and the general public.			
Key words: slipped capital femoral epiphysis, dGEMRIC, cartilage, Hansson hook pin	osteoarthritis, femoroacetabu	lar impingement, adolescent hip,	
Classification system and/or index terms (if a	ny)		
Supplementary bibliographical information Lund University, Faculty of Medicine, Doctoral Dissertation Series 2018:77 Language English			
ISSN and key title		ISBN 078 01 7610 643 4	

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Slipped Capital Femoral Epiphysis

Growth, Remodeling and Cartilage Quality after Unthreaded Fixation

Jakob Örtegren



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Lund University, Faculty of Medicine Doctoral Dissertation 2018:77 Department of Orthopedics

ISBN 978-91-7619-643-4 ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University Lund 2018



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I don't know where I'm going from here, but I promise it won't be boring.

David Bowie



To Dolores and Bodil

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Original papers

- I. Unthreaded Fixation of Slipped Capital Femoral Epiphysis Leads to Continued Growth of the Femoral Neck. Örtegren J, Björklund-Sand L, Engbom M, Siversson C, Tiderius CJ. J Pediatr Orthop. 2016 Jul-Aug;36(5):494-8.
- II. Continued Growth of the Femoral Neck Leads to Improved Remodeling After In Situ Fixation of Slipped Capital Femoral Epiphysis. Örtegren J, Björklund-Sand L, Engbom M, Tiderius CJ. J Pediatr Orthop. 2018 Mar;38(3):170–5.
- III. Persisting CAM Deformity is associated with Early Cartilage Degeneration after Slipped Capital Femoral Epiphysis: 11-year follow-up including dGEMRIC. Örtegren J, Peterson P, Svensson J, Tiderius CJ. Osteoarthritis and Cartilage. 2018 Apr;26(4):557-563.
- IV. Patients' Delay is the Major Cause of Late Diagnosis of Slipped Capital Femoral Epiphysis—a Review of 54 Cases in Southern Sweden. Örtegren J, Österman J, Tiderius CJ. Manuscript submitted 28 March 2018.

Abbreviations

AP anteroposterior

AVN avascular necrosis
BMI body mass index
CI confidence interval

COSMIN consensus-based standards for selection of measurement instruments

CV% coefficient of variation

dGEMRIC delayed gadolinium enhanced magnetic resonance imaging of cartilage

FAI femoroacetabular impingement

FCD fixed charge density
GAG glycosaminoglycan

Gd(DTPA)²⁻ gadolinium dietyhylene triamine pentaacetic acid

HAGOS (copenhagen) hip and groin outcome score

HSA head shaft angle

LLD leg length discrepency

MRI magnetic resonance imaging

OA osteoarthritis

PROM patient related outcome measure

ROI region of interest
ROM range of motion

SCFE slipped capital femoral epiphysis

THA total hip arthroplasty

Populärvetenskaplig sammanfattning

Fyseolys (Slipped capital femoral epiphysis - SCFE) är en höftsjukdom som drabbar barn i tonåren, oftast i åldrarna 9-15 år. Ungefär ett barn av 2000 drabbas, vilket motsvarar 50-60 barn per år i Sverige. Vid fyseolys sker en glidning i lårbenhuvudets tillväxtzon (fysen) under tillväxtspurten. Eftersom fysen är belägen i nedre delen av lårbenshuvudet orsakar glidningen en successivt tilltagande felställning mellan lårbenshuvudet och lårbenshalsen.

I de allra flesta fall ger glidningen till en början upphov till relativt lindriga symtom i form av hälta och smärta från benet. Det dröjer därför tyvärr ibland länge innan sjukdomen upptäcks. Eftersom glidningen successivt ökar om den inte behandlas är det viktigt att sjukdomen upptäcks tidigt.

Behandlingen av fyseolys är kirurgisk. Syftet med operationen är att förhindra fortsatt glidning vilket kan göras med en skruv eller spik som förs in i lårbenshalsen förbi fysen. Denna behandling är väletablerad och har små risker men kan göras på två principiellt skilda sätt: 1) Med en gängad skruv över fysen som har som syfte att stoppa tillväxten helt. Detta är den vanligaste tekniken som används i de flesta länder i världen. 2) Med en slät spik för att minska risken för att påverka fysen och dess tillväxt. I Sverige har man använt sådana spikar under de senaste 40 åren, med övertygelsen att fortsatt tillväxt är gynnsamt för höftens fortsatta utveckling.

Kunskapen om hur det går för barn som drabbats av fyseolys är begränsade. På längre sikt är det känt att de som drabbats i klart större omfattning utvecklar ledsvikt (artros) och är i behov av en höftledsprotes som vuxen. Kunskapen om sambandet mellan fyseolys och artros är begränsat vilket gör att det finns dåliga förutsättningar att förutsäga och förebygga risken för utveckling av artros.

LIH-spiken (Hansson hook pin) som utvecklades av den svenske ortopedläkaren Lars Ingvar Hansson i Lund på 1970-talet är en slät spik som används rutinmässigt i Sverige för att operera fyseolys med syfte att inte stoppa tillväxten i höften. Denna avhandling studerar hur det gått för 54 barn som opererats med LIH-spiken i Skåne mellan 2001-2009

I studie 1 och 2 har vi genom att granska röntgenbilder, studerat om lårbenshalsen verkligen fortsätter att växa efter operation med LIH-spiken och vilken betydelse detta har för höftens ombyggnad (remodellering) till en mer normal form. Studierna visar att lårbenshalsen fortsätter växa i medel ungefär en centimeter vilket ger

upphov till förbättrade förutsättningar för höftledens muskelkrafter. Längdtillväxten ger också upphov till förbättrad remodellering. Framförallt minskar risken för att höftleden skall få en kvarstående formförändring som gör att lårbenshalsen slår mot höftskålens kant (höftimpingement).

I studie 3 har vi studerat ledbroskets kvalitet (med kontrastförstärkt magnetkameraundersökning - dGEMRIC) i höftleden hos unga vuxna som drabbats av fyseolys i barndomen. Vi har också undersökt om dessa individer har några aktuella höftbesvär. Resultaten visar att höfter som drabbats av fyseolys har större risk att få försämrad broskkvalitet redan i 25-års åldern. Risken för utveckling av artros är störst om man har kvarvarande höftimpingement. Försämrad broskkvalitet kunde också kopplas till ökat missnöje med höftfunktionen.

I studie 4 har vi studerat sjukhusjournaler och genomfört intervjuer med patienter för att förstå hur lång tid som går mellan att de som drabbas av fyseolys börjar få symtom till man söker hjälp hos sjukvården och slutligen blir opererade. Vi har också försökt förstå vilka faktorer som orsakar fördröjningar. Studien visar att tiden från första symtom till operation i medel var ett halvår och att den största delen av fördröjningen berodde på att patienterna väntade med att söka vård. Pojkar sökte senare än flickor. Barn med ovanligare symtom (mer knä än höftsmärta) blev fördröjda längre av sjukvården. Långa fördröjningar orsakade större felställningar i höftleden med ökad risk för framtida men.

Sammanfattningsvis visar avhandlingen att det finns stora fördelar med att använda en slät spik för att operera fyseolys. Det leder till att höftleden fortsätter växa vilket är avgörande för den positiva ombyggnaden av skelettet till en mer normal form. Detta ger i sin tur upphov till minskad risk för framtida men. Fördelarna talar för att man i andra länder borde byta operationsteknik och inte längre stoppa höftens tillväxt när man opererar barn med fyseolys.

Vidare talar resultaten för att man bör fokusera på att minska risken att få kvarstående höftimpingement efter fyseolys. Kvarvarande höftimpingement ger upphov till ökad risk för artros i framtiden. Eftersom LIH-spiken leder till minskad risk för impingment stärker detta ytterligare dess fördelar.

Slutligen är det av största vikt att öka kunskapen om fyseolys, både inom sjukvården och i samhället i övrigt. Det idealiska vore att föräldrar, lärare och idrottssledare reagerar tidigt, och söker hjälp, när barn haltar och klagar över icke snabbt övergående höft, lår eller knäsmärta. Om de barn som drabbas i framtiden får rätt diagnos tidigare ökar chanserna att kunna leva ett normalt liv utan smärtor och behov av ytterligare operationer.

Thesis at a glance

Paper	Questions	Methods	Results	Conclusions
I	Is there continued growth of the femoral neck after in situ fixation of SCFE with the Hansson hook pin?	Retrospective radiographic evaluation of 54 children with SCFE.	SCFE hips and unaffected hips grew a mean 7 mm and 10 mm, respectively. Children younger than 11 years grew a mean of 12 mm. Offset increased by a mean of 16%.	Use of the Hansson hook pin leads to continued growth and a secondary increase in femoral neck offset.
п	Is there any remodeling of the femoral neck deformity after in situ fixation of SCFE with the Hansson hook pin?	Retrospective radiographic evaluation of remodeling of head–shaft angle, alpha angle and Klein's line in 54 children with SCFE.	Significant remodeling was measured in all parameters. A decrease in alpha angle was correlated with longitudinal growth.	Use of the Hansson hook pin leads to significant remodeling of the femoral neck. Remodeling is growth dependent.
111	What are the cartilage status and clinical function in young adults treated for SCFE with the Hansson hook pin? What factors affect cartilage status?	Contrast MRI of cartilage (dGEMRIC) and PROMS in 22 adults (mean age 24 years) treated with the Hansson hook pin for SCFE in childhood.	Cartilage quality was mildly impaired in SCFE hips. Cartilage quality was lower in hips with signs of FAI. Cartilage status was correlated with symptoms.	SCFE causes clinically relevant cartilage degeneration that is primarily correlated with the prevalence of persisting FAI in adulthood.
IV	What is the duration between symptom onset and treatment in SCFE in Sweden? What factors cause a delay?	Medical chart reviews and personal interviews with 54 children treated for SCFE.	Median delay was six months, primarily caused by patients' delays. Late diagnosis was correlated with more severe physeal slippage.	Late diagnosis of SCFE is common and causes impaired treatment conditions. Increased awareness is essential.

An introduction to slipped capital femoral epiphysis

Briefly – What is SCFE?

Slipped capital femoral epiphysis (SCFE) is a disorder affecting the immature hip, typically at puberty. In this condition, a progressive slip occurs due to a weakening of the physis (growth plate) located between the femoral head and neck. This slip leads to an improper relationship between the femoral head and neck (Figure 1). Symptoms such as pain and limping are typically initially vague but gradually escalate. The diagnosis is confirmed by plain radiographic examination. Surgical treatment is normally conducted, with the intention to stabilize the physis to prevent further slippage. Subsequently, during adulthood, SCFE patients are at increased risk of degenerative hip disease.

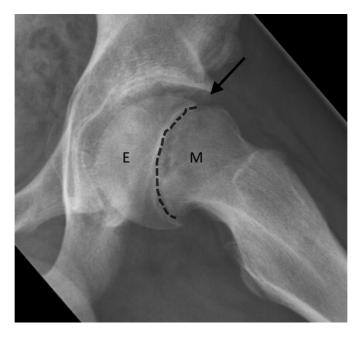


Figure 1
Slipped capital femoral epiphysis. The epiphysis (E) is slipped in relation to the metaphysis (M). The physis is marked with a dotted line.

Background

A glimpse of history

Separation of the proximal femoral epiphysis was first described in 1572 by the French barber-surgeon Ambroise Paré (1510–1590). Paré is considered a father of surgery and modern forensic pathology and was a pioneer in surgical techniques and battlefield medicine. He is quoted, "... l'épiphyse de la tëte de cet os quelquefois se separe et non disjonction de l'épiphyse dudit os," which is the first known description of a slip in the proximal femoral physis. During the 1800s, a few reports introduced the theory of nontraumatic slippage caused by overload, leading to a bend in the femoral head–neck junction (coxa vara adolescentium).



Figure 2
Ambroise Paré (1510-1590) was first to describe SCFE in the litterature. Reprint with permission from Musée Virtuel.

At the Department of Orthopedics in Lund, a great deal of interest has been paid to SCFE. In 1926, Frising presented his thesis: The Relation between Epiphyseolysis Capitis Femoris and Coxa Vara, in which he concluded that proximal physeal separation may be both spontaneous and trauma-initiated. Further, in his thesis 1950, Jerre evaluated 166 cases from 1917 to 1945 and reported patients treated with closed reduction did not have an inferior outcome compared with nontreated cases. During the 50s and 60s, Wiberg presented several studies showing superior outcomes after in situ pinning compared with femoral neck osteotomy. In the mid-70s, Lars Ingvar Hansson invented the Hansson hook pin, which was popularized during the 80s and is today one of the most common devices for the treatment of SCFE in Sweden. Hansson mentored both Gunnar Hägglund and Gunnar Ordeberg, who presented their theses on SCFE in 1986. Their foci of interest included epidemiology, natural history, etiology and outcome after closed treatment during the 20th century. Their work may be considered the culmination of scientific interest in SCFE in Sweden.

The immature hip

At birth, the proximal femoral epiphysis (chondroepiphysis) consists of cartilage only, not visible on plain radiographs. At 2–4 months of age, a secondary center of ossification forms and gradually enlarges until the cartilaginous area has been completely replaced by bone at skeletal maturity. When the hyaline cartilage of the chondroepiphysis first forms, there are no histological differences between the cells at the joint surface and the rest of the epiphyseal cartilage. At some point, physiologically different populations of cartilage cells form. The chondro–osseous transformation is highly vascular-dependent and at skeletal maturity, only articular cartilage remains. As the ossification center expands, the region adjacent to the physis forms a distinct subchondral plate perpendicular to the metaphysis, creating the characteristic radiographic physeal line.







Figure 3
Radiographs of the right hip in a 5 month old boy, 6 year old girl and 13 year old girl.

The physis

The primary function of the physis is integrated longitudinal and latitudinal skeletal growth. Histologically, the physis consists of an arrangement of chondrocytes surrounded by a matrix of proteoglycan aggregates [1]. The chondrocytes of the physis are divided into a system of zones based on different stages of maturation in the endochondral sequence of ossification and their functions (Figure 4):

- 1. The germinal cell layer (resting zone), adjacent to the epiphysis, has low differentiated cells with low rates of proliferation. Injury to this layer results in a high risk of growth disturbance.
- 2. In the proliferative zone, chondrocytes are flattened and stacked in well-defined columns. These cells produce a necessary matrix and are responsible for longitudinal growth of the bone via active cell division.

3. In the hypertrophic zone, adjacent to the metaphysis, cells increase in size and deteriorate. This finally results in cell death, which releases intracellular calcium, which is necessary for invasion of metaphyseal blood vessels and ingrowth of osteoblasts. No longitudinal growth occurs in this layer. It is the weakest portion of the physis and is commonly the site of fractures or other alterations, such as widening due to Rickets. This is also where the slippage occurs in SCFE.

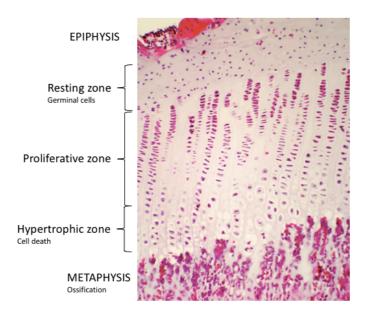


Figure 4
The cellular layers of the physis. Photo: Anders Bergström.

Blood supply

The physis blocks the blood supply between the epiphysis and metaphysis during childhood, after the age of one year. There is no intramedullary blood supply to the epiphysis, as opposed to the metaphysis, from the medullary artery in the femoral shaft. The vessels from the ligamentum teres contribute little to the vascularization of the femoral head after the age of eight years. The epiphysis and the physis are mainly supplied by the retinacular vessels, which originate from the anastomose between the medial circumflex artery and the posterosuperior branch of the lateral circumflex artery, that enter the capsule at the intertrochanteric groove and ascend along the femoral neck, mainly posteriorly (Figure 5). Multiple small vessels present in the young child join to form a limited number of larger vessels later in childhood; as a result, damage to a single vessel during adolescence may lead to avascular

necrosis. If the femoral epiphysis is gradually displaced in relation to the metaphysis, the joint capsule with the vessels may shrink posteriorly. If open or closed surgical reduction is performed to restore this anatomy, vessels may be strained and there is a risk of damaged blood supply to the epiphysis. At physeal closure, the epiphyseal and metaphyseal vessels join to supply the femoral head and neck.



Figure 5The posterioriosuperior branch of the lateral circumflex artery and one of the retinacular vessels that ascend along the posterior part of the femoral neck to the epiphysis. Reprint with permission from Elsevier.

Epidemiology

The estimated incidence of SCFE is 5 in 10 000 children. In a systematic review by Loder that included the populations of North America, South America, Europe and Asia, the incidence among children between 8 and 15 years of age varied from 0.5 to 11 per 10 000 [2]. The majority of the studies included in that review reported the incidence as 3–9 per 10 000. In Sweden, Hägglund et al. estimated the incidence to be 3 per 10 000 in females and 6.1 per 10 000 in males based on a review of 532 cases from 1910 to 1982 [3]. In a study based on the national Swedish Pediatric Orthopedic Quality Register (SPOQ) from 2007 to 2013, Herngren reported an incidence of 4.4 and 6.1 per 10 000 in females and males, respectively.

Boys are more often affected than girls, with values of approximately 60 vs 40% [3-7]. Because of basic differences in skeletal maturity between the genders, girls are affected by SCFE at younger ages than boys. Mean age at diagnosis is about 11 years for girls and 13 years for boys (range 7–17 years) [2, 5, 8, 9]. Obesity has been identified as a strong risk factor, particularly among boys. The majority of affected children have a body mass index (BMI) in the upper 95th percentile[10].

Classification

SCFE can be classified based on clinical or radiographic findings. Clinically, the slip may be classified as stable or unstable. The slip is considered stable if the child is able to bear weight on the affected leg, with or without crutches[11]. A stable slip is correlated with significantly less risk of avascular necrosis than an unstable slip[11-15], probably due to the risk of vascular damage during the period of instability.

Symptom duration can be used to classify the slip as acute, chronic or acute-on-chronic. An acute slip (10%) causes pain, with relatively sudden onset, during less than three weeks. These slips are often unstable. A chronic slip (80–90%) is normally stable and has been present for at least three weeks, possibly for years, usually with initially vague and intermittent pain [7, 16, 17]. An acute-on-chronic slip includes the presence of symptoms for more than three weeks, with a marked aggravation across the last three weeks (i.e., from stable to unstable.) This classification may also predict the outcome.

Radiologically, the slip may be defined as acute or chronic based on the prevalence of signs of bone remodeling. In chronic slippage, the bone will continuously remodel by resorbing bone from the anterior metaphyseal "bump" and build new bone along the femoral neck posteriorly [18]. This results in the typical appearance of a "pistol grip deformity." In acute slippage, there will be no signs of remodeling and the slip will appear sharper.





Figure 6Left: Chronic SCFE, signs of bone remodeling by bone resorption anteriorly and new bone formation posteriorly. Right: Acute SCFE, sharp metaphyseal ends with no signs of remodeling.

Etiology

The etiology of SCFE is not well-established, but a few biological and mechanical theories have been presented. In biopsies from the physis, the proliferative and hypertrophic zones are thickened and disarranged, with signs of altered chondrocyte maturation. The slip is located mainly in the hypertrophic zone. Enchondral ossification is scarce and irregular with large clusters of cartilage in the metaphysis[19].

SCFE is related in some way to the hormonal context. Testosterone reduces the stability of the physis, in contrast to estrogen, which makes it stronger[20]. Hypothyroidism, hypopituitarism and hypogonadism reportedly increase risk, generally at a relatively early age and more often bilaterally[21].

Mechanical factors such as increased physeal obliquity, reduced femoral anteversion and increased femoral coverage have been correlated with increased risk of slippage [22, 23]. Obesity is a strong risk factor [10], explained by the increased mechanical stress on the physis.

A multifactorial theory of etiology is probably the most adequate. Because SCFE occurs exclusively during puberty when physeal longitudinal growth culminates, and when multiple hormonal changes occur, it may result from a combination of stress from mechanical factors, which lead to slippage.

A few sporadic cases of familial SCFE have been reported, suggesting that a hereditary factor may also be involved [24]. Increased risk of SCFE has also been established after radiation treatment of malignant disease in the hip region [25].

Diagnostics

Symptoms and clinical evaluation

The most frequent presentation of stable SCFE is limping and pain from the region around the hip, groin or thigh[26]. About a third of patients report referred pain from the knee, and in 15–20% this is the only location affected[27]. Because of the posterior orientation of the epiphysis, the slip normally leads to secondary outtoeing but other gait abnormalities can be seen [28]. Because symptoms may initially be mild and intermittent, many children often remain physically active for a long time [2]. In unstable SCFE, the symptoms are similar though more intense.

On clinical examination, impaired gait and leg length discrepancy (LLD; i.e., shortening of the slipped side) may be noted [29]. When examining the hip range of motion, internal rotation is decreased compared with the contralateral hip [30].

External rotation may be increased, but often to a lesser extent [31]. In severe cases, an external rotation contracture can be seen. When flexion of the hip is performed, the hip may rotate externally, called a positive Drehmann sign [32]. For evaluation of impaired hip rotation, the prone position has superior sensitivity over the supine or sitting positions and is therefore recommended [33, 34].

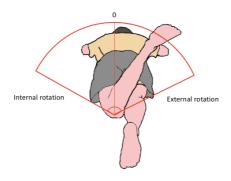


Figure 7
Prone position is superior to supine position for evaluating impaired hip rotation in SCFE. Author's own illustration.

Imaging

SCFE diagnosis is confirmed and categorized using conventional radiography. In general, the hip is evaluated in two projections using two radiographs: anterioposterior (AP) and frog-leg (Lauenstein) views. The AP radiograph is taken in the supine position with straight legs and toes touching, with hips slightly internally rotated. The frog-leg view is obtained in the supine position, with knees flexed (30–40°), hips abducted (45°) and externally rotated with foot soles together (Figure 8). In some cases, due to severe pain or different hospital standards, the lateral projection is a "cross-table lateral" taken in the neutral position with x-ray beams horizontally directed. The Billing lateral is also used, though less frequently; it is similar to the frog-leg view but with less abduction and flexion of the hip. To determine the slip angle, frog-leg and cross-table lateral views are less sensitive to measurement error from rotational discrepancies compared with the Billing lateral [35].



Figure 8
Lauenstein (frog-leg) view positioning during radiographic examination. Authors own picture.

Different measurement methods are used to assess the degree of a slip. Southwick's head–shaft angle (HSA)[36] is regarded as the international gold standard[37, 38]. It is defined as the angle between the longitudinal axis of the femoral shaft and a line perpendicular to the inferior and superior edges of the physis in the femoral head. The Southwick angle is most often measured in the frog-leg projection, but can also be assessed in the AP view. As originally described by Southwick, the head–shaft angle of the contralateral hip can be subtracted from the head–shaft angle in the affected hip. In modern research and clinical practice, the measured angle alone is commonly used [39]. Other methods, such as defining the landmark of calcar femorale, as described by Hansson[40], or defining the neck-head angle[41, 42], as described by Billing, are also used.

The slip is often classified as mild ($<30^{\circ}$), moderate ($30-50/60^{\circ}$) or severe ($>50/60^{\circ}$) and is mainly used in attempts to predict the outcome, such as the risk of developing osteoarthritis (OA) in adulthood and to determine adequate treatment.

Klein's line[43] is used to diagnose SCFE, rather than assess its severity. In this method, a line is drawn along the superior border of the femoral neck, in both AP and frog-leg views. In every radiographic view, this line should intersect with some part of the femoral epiphysis [44]. If not, or if only a small part of the epiphysis is intersected, a slip should be suspected.

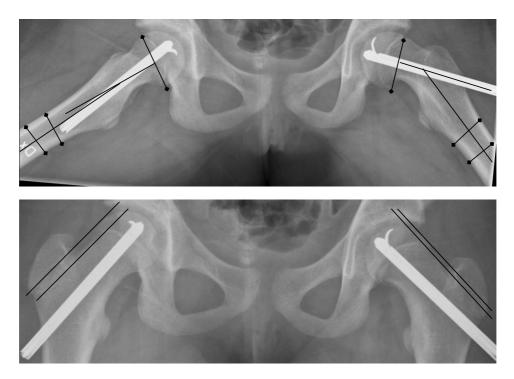


Figure 9
Schematic of measurements of HSA and Klein's line.

Ultrasound has no clinical value in the diagnosis of SCFE. Use of magnetic resonance imaging (MRI) has been described as differentiating between stable and unstable slips, and to be more sensitive for detecting very subtle slippages[45, 46], but is not generally indicated or recommended.

Diagnostic challenges

Because the epiphyseal slippage in SCFE is progressive, symptom duration is correlated with slip severity[6, 47] and early treatment is considered crucial to reducing the risk of persistent deformity [48, 49]. Unfortunately, symptoms of stable SCFE are often initially vague and intermittent, and are therefore ignored by the child, parents, teachers and health care providers. Reported duration of diagnostic delay varies between a mean of 8 and 33 weeks (Table 1). Isolated knee pain (with an absence of hip pain) is the major risk factor for delay[50, 51]. According to some reports, boys are diagnosed later than girls[2, 3]. The time between symptom onset and diagnosis appears to have been constant over the last 70 years [3, 52-56].

Table 1Previous studies of delayed SCFE diagnosis

Reports on delayed SCFE diagnosis	Region	Number of patients	Total Delay (weeks)
Herngren, et al. 2007–2013	Sweden	356	8 (median)
Matava, et al. 1985–1994	North America	106	33 (Group 1) 26 (Group 2)
Green, et al. 1989–97	North America	102	20
Siegel, et al. 1985–1987	North America	45	12
Loder, et al. 1975–1989	North America /Europe	2582	20 (Group 1) 32 (Group 2)
Wilson, et al. 1936–1960	North America	300	13 (Mild) 21 (Severe)
Hägglund, et al. 1984	Sweden	532	20
Dreghorn, et al. 1987	Scotland	72	16

Treatment

The treatment goal is to minimize subsequently impaired hip function and minimize the risk of additional complications. From a longer-term perspective, the main goal is to reduce the risk of developing degenerative joint disease (i.e., OA). A high degree of slippage at the time of treatment is correlated with inferior long-term outcome, though this relation is not fully understood[57, 58]. The natural history of untreated SCFE has been determined to have a poor outcome[54, 59]. Indication for surgical treatment is undisputed, but opinions diverge regarding the type of fixation, degree of urgency, indication of osteotomy/reduction and indication of contralateral fixation [60, 61].

There are currently two primary treatment strategies: in situ fixation with the intent to inhibit further slippage and corrective osteotomy to restore the hip anatomy immediately. Presently, in situ fixation is considered the gold standard [61, 62].

In situ fixation

In situ fixation is considered safe and with low risk of complications[31, 61, 63], as long as it is not combined with an attempt at forceful intraoperative closed reduction, which increases the risk of avascular necrosis[64]. The surgery is performed under general anesthesia lead by fluoroscopy.

In situ fixation is performed using two principal methods.

First, with the intention of creating a permanent physiodes: with a screw with threads over the physis or a bone peg [30, 65, 66]. This have been shown to be reliable for preventing further slippage and have a low risk of complication[67]. However, physiodesis may result in a relative shortening of the femoral neck and LLD, especially in younger patients with potentially longer periods of growth remaining. A short femoral neck may also decrease the femoral offset, which in turn leads to a shorter lever arm for the abduction muscles, creating a risk of Trendelenburg gait [68, 69]. Possible shortening of the femoral neck has been used as an argument for refraining from the prophylactic fixation of the contralateral, nonslipped hip[70, 71].



Figure 10 Screw with threads over the physis. Reprint used with permission from Synthes.

In contrast, fixation can be performed with the intent to allow continued physeal growth. Advocates of this method argue that it leads to less residual femoral neck shortening, which causes LLD and suboptimal conditions for hip biomechanics. It is also argued that continued growth may provide conditions for femoral neck remodeling, reducing the initial deformity. There are several devices used to allow such growth, all of which are designed for fixation in the epiphysis with a smooth surface passing the physis. Screws with extra short threading, nails with only proximal threading, telescoping nails, pin with a hook in the epiphysis and multiple K-wires or Steinmann pins with short threading have been used. However, the presence of continued growth with these methods has not been fully established. Only a few, minor studies on smooth devices have been performed, indicating growth of approximately 10% of the femoral neck length[72-75]. The relevance of this growth is not yet fully understood.



Figure 11
Unthreaded fixations. From left: Hansson hook pin, multiple K-wires, nail with proximal threading and telescoping nail.
All devices have a smooth surface passing the physis. Reprints with permission from Swemac and Pega Medical.

The Hansson hook pin

The Hansson hook pin was first introduced in the orthopedic department of Lund in 1976 by Lars Ingvar Hansson (1937–1987)[76]. In the first published paper on the hook pin, Hansson stated that "Premature closure of the growth plate and shortening of the femoral neck have also been registered and should be avoided." The nail was designed with a smooth surface to minimize the risk of physeal affection when stabilizing SCFE.





Figure 12
Dr. Lars Ingvar Hansson (1937–1987) and the Hansson hook pin. Reprints with permission from Swemac.

After cannulated drilling led by a fluoroscope, the pin is placed in the drill hole and the hook is pushed into the epiphysis via a threaded device on the lateral aspect of the nail. If needed, the nail can be removed by pulling back the hook into the nail and then the rest of the smooth nail can be retracted. In Hansson's first evaluation in 1982, among 38 cases there were no signs of avascular necrosis (AVN) or reslip and no radiological signs of early physiodesis[76]. A few years later, the Hansson hook pin was introduced as a fixation device for femoral neck fractures in adults (using two pins) and today is the standard treatment for undisplaced femoral neck fractures and fractures in younger patients in many centers in Sweden and worldwide.

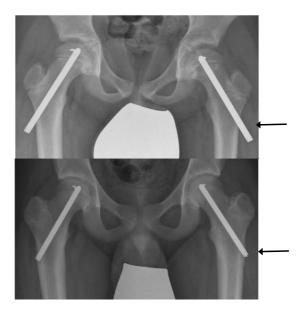


Figure 13
Growth of the femoral neck after fixation with the Hansson hook pin of a left-sided stable SCFE. Right hip pinned prophylactically. Above: Postoperative radiograph. Below: Radiograph at physeal closure, 26 month later. Growth can be confirmed by the reduced protrusion of the pin laterally.

Contralateral prophylactic treatment

When diagnosed with unilateral SCFE, the risk of contralateral slippage during remaining growth is estimated at 20–60%[16, 77, 78]. Because the originating risk is approximately 1 in 2000 (0.5‰) this risk is about 1000 times higher than the risk for a healthy child of having one slip. Young age and endocrinopathies are associated with increased risk of contralateral slippage[79, 80]. There are two principally different strategies for responding to this increased risk: immediate prophylactic fixation of the contralateral hip or monitoring the contralateral hip

regularly with radiographic follow-up. Both strategies have advantages and disadvantages and the treatment decision is often governed by local convention. Prophylactic fixation requires fewer resources due to reduced follow-ups and radiographic examinations. The risk of iatrogenic complications, such as local pain and soft tissue infections, secondary to prophylactic pinning have been evaluated to be rare but must be considered[71]. When performing a physiodesis by unilateral threaded fixation, the risk of LLD obviously becomes higher if contralateral physiodesis is excluded[70].

In Sweden, 43% of all 352 unilateral cases from 2007 to 2013 were prophylactically pinned contralaterally[6], which is high compared with North America and Europe[17, 29, 38]. Hägglund et al. have advocated prophylactic pinning based on a study in which the risk of OA at follow-up (6–66 years) was 25% in slipped contralateral slips compared with 9% in the unilateral cases. Kocher has recommended an individually based model of doctor–patient shared decision-making in which both the outcome probabilities and the patient preferences are considered[17].

Realignment surgery

Realignment surgery for SCFE is performed exclusively on moderate and severe slips. It can be performed at the subcapital[81], basocervical[82], intertrochanteric[83] and subtrochanteric levels[84]. The goal of realignment procedures is to restore an anatomic shape to the proximal femur. To achieve this, the osteotomy is preferably placed at the level of the deformity, close to the physis. Unfortunately, the risk of iatrogenic avascular necrosis of the epiphysis has been described as almost inversely proportional to the distance of correction from the physis[85, 86]. This relationship is explained by the vulnerability of the blood supply from the retinacular vessels to the epiphysis[87].

The subcapitular osteotomy via "safe surgical dislocation," often described as the modified Dunn osteotomy, has become popular over recent decades. The approach originates from a procedure first described by Ganz[88] and has evolved to minimize the risk of intraoperative injury to the retinacular vessels. The major trochanter is slid anteriorly by an osteotomy, after which the remaining part of the proximal portion of the trochanter is carefully removed. This allows full access to the posterior periosteum of the femoral neck for further subperiosteal dissection along the neck. The anterior-medial periosteum of the femoral neck is incised and the entire femoral neck can be dissected subperiosteally while preserving the femoral head blood supply [81]. The epiphyseal circulation should be monitored intraoperatively to avoid straining the posterior capsula, which may have been contracted preoperatively due to the slippage[89, 90]. The osteotomy is performed and fixated and finally, the trochanter is refixated.

Over recent decades, some authors have argued for extensive surgery due to less residual head/neck deformity and a relatively low risk of AVN[91, 92]. A recently published review based on 2262 hips reported only 3.3% AVN after subcapital osteotomy (1.4% after in situ fixation)[61]. On the other hand, other studies have reported up to 20% AVN after subcapital osteotomy[93]. Consequently, there is no consensus regarding the indication for this extensive surgical procedure. However, these procedures should only be performed at major centers due to the demanding technique and potential risk of severe complications. Further, long-term results are still lacking, given that the patients who have received this operation are still relatively young. Further monitoring and additional studies are needed to establish which patients receive greater benefits from this surgery compared with in situ fixation.

Complications and outcome

There are multiple possible complications and negative impacts of SCFE. Some are related to the disease itself, others to the treatment, in some cases, both. The primary goal of treatment should be to minimize the risk of iatrogenic complications.

Chondrolysis

The pathophysiology of chondrolysis is an acute dissolution of the cartilage leading to significantly reduced joint space on a radiograph[94]. This results in hip pain and impaired range of motion. Treatment is symptomatic. Prevalence is up to 16% of patients with SCFE[95, 96]. The etiology is unknown but severe slippage and long symptom duration before treatment are identified risk factors. It has been speculated that the cause may be intraoperative penetration of the joint cartilage by pins, screws or guide wires, which may occur to a greater extent during surgery on more severe slips because of the more technically demanding conditions[31].

Avascular necrosis

Avascular necrosis is the most significant, and dreaded, complication from SCFE. In stable SCFE, the risk is significantly lower than with unstable SCFE, but increases in relation to slip severity[37, 97, 98]. Risk calculations across studies vary from 0 to 15%[94, 98, 99] in stable and 5 to 60% in unstable slips[12, 15, 100-102]. AVN in unstable SCFE seems more likely to develop in younger patients with shorter symptom durations[15]. Optimal treatment of unstable SCFE to reduce AVN risk is controversial. Most authors advise avoiding anything but gentle reduction[12,

100] due to the risk from additional stress on the retinacular vessels in the posterior capsula. This is particularly true in acute-on-chronic cases in which these vessels are expected to be relatively short due to adaptation during the period of chronic slippage. Further, intraarticular joint pressure in unstable slips has been investigated and found to be greatly increased, similar to the level of pressure in compartmental syndromes[103, 104]. This emphasizes the importance of intraoperative joint decompression, which should be considered urgent. Several recent risk analyses have also shown a significantly increased risk of AVN in unstable slips if surgery is performed from 24 hours to 7 days after acute symptom onset[100-102, 105]. The reason for this "unsafe window" is unclear.

Symptoms and radiologic signs of AVN normally develop several months after treatment. Patients suffer from pain in the groin or thigh and the range of motion is impaired. Radiographic evaluation reveals a deformity, normally flattening, initially of the epiphysis. Unfortunately, reossification (as seen in Perthes' disease) is not usually seen in AVN after SCFE. The treatment is symptomatic and, when the pain is unacceptable, generally ends up in total hip arthroplasty (THA).



Figure 14
Avascular necrosis 8 month after acute unstable SCFE.

Leg length discrepancy

Some LLD after SCFE can be expected. Because the epiphysis generally slips posterior and inferior in relation to the metaphysis, this leads to a relative shortening of the leg. The discrepancy is thereby logically correlated with the degree of slippage. Further, depending on the in situ fixation technique, a surgically induced physiodesis may cause progressive LLD during remaining growth. In particular, this is expected when treating younger patients with extensive residuary growth. LLD after SCFE should be monitored and distal knee physiodesis of the contralateral leg performed when indicated.

Femoroacetabular impingement

In recent years, interest in femoroacetabular impingement (FAI) and its possible role as a mediator of OA[71, 106-110] has increased. FAI is caused by mechanical interference between the anterolateral aspect of the femoral neck and the acetabular rim during hip flexion and internal rotation[111] leading to decreased range of motion and pain. With time, such abutment may cause cartilage degeneration and eventually manifest as OA[112, 113]. The impingement is usually caused by either an abnormal shape of the femoral neck (CAM deformity) (Figure 15) or a prominent acetabular rim (PINCER-type). After physeal slippage, the dislocation between the epiphysis and metaphysis often results in a deformity of the femoral head-neck junction similar to a CAM deformity. Several studies have shown that SCFE is associated with an increased incidence of FAI[114, 115]. In recent years, some authors have argued for early arthroscopic intervention for FAI after SCFE to reduce the risk of developing future OA[91, 114, 116, 117]. Still, reports of long-term outcomes after interventional arthroscopic surgery are lacking and it can be argued that further knowledge about the mechanisms leading to OA after SCFE is needed before recommending such an aggressive treatment. In addition, positive remodeling of the femoral neck after in situ fixation may spontaneously reduce the prevalence of impingement[39].



Figure 15

A CAM-deformity after SCFE causing femoroacetabular impingement by mechanical interference between the anterolateral part of the femoral head-neck junction and the acetabular rim.

Osteoarthritis

OA is a chronic, noninflammatory, degenerative joint disease leading to progressive deterioration of joint cartilage and causing stiffness and pain. OA is primarily considered a joint cartilage disease with secondary changes in bone and other joint tissues. Treatment usually includes pharmacological analgesics and physiotherapy. In severe OA, when other treatments are insufficient, hip arthroplasty is indicated.

Radiographic criteria, such as joint space narrowing and osteophytes, are central to this diagnosis. However, the association between radiographic signs and hip symptoms is weak, particularly in mild and moderate OA[118]. The American College of Rheumatology has proposed a combined clinical, biochemical and radiographic diagnostic criteria[119].

An increased risk of developing OA after SCFE is undisputed. Hansson reported a 50% risk of radiographic OA 30 years after mild-to-moderate slip treated in situ among 53 patients[96]. Hägglund reported a 25% risk 16–66 years after in situ fixation of stable SCFE[78]. Some observations report up to 100% risk of subtle radiographic OA before 40 years of age[120]. The degree of slip severity has been correlated with risk of developing OA, but this relation is imperfect and some with mild slips will also be affected[97]. No gender differences have been reported.

Reports using data from registers on hip arthroplasty have verified SCFE as a common cause of OA. In a study from the Norwegian Arthroplasty Register, about 10% of the total hip replacements before 40 years of age were due to SCFE[121]. THA seems to be a good surgical option in the management of OA after SCFE, with functional outcomes and revision rates comparable to THA performed for primary OA[122].

The theory of FAI as a possible mediator of OA after SCFE has evolved over recent decades[106, 108, 113, 123].

Delayed gadolinium-enhanced magnetic resonance imaging of cartilage

The articular cartilage matrix consists of hyaluronic acid (attached with proteoglycans) contained in a collagen network. The proteoglycans consist of a core protein and multiple anionic molecules called glycosaminoglycans (GAGs). The strong negative electrochemical charge of GAGs gives the cartilage a negative fixed charge density (FCD). The negative FCD attracts positively charged sodium ions from the joint fluid, which results in an osmotic gradient that causes water diffusion from the joint into the cartilage. This creates a "swelling pressure" in the cartilage that is essential for its load bearing properties. GAGs' quantity and FCD are decreased in OA[124].

Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC) is a contrast-enhanced MRI technique for assessing the chemical composition of cartilage. Gadolinium diethylene triamine pentaacetic acid (GD(DTPA²⁻)) is a negatively charged, water-soluble MRI contrast agent. Because water is freely exchangeable in cartilage, Gd(DTPA²⁻) will distribute in cartilage in inverse relation to negatively charged GAGs[125].

Gd(DTPA²⁻) shortens the MRI relaxation time (T1) so that quantitative T1 analysis can be used to estimate the GAG concentration in cartilage. Low GAG concentration results in a high concentration of Gd(DTPA²⁻) and therefore a low T1. The average T1 in a specific cartilage region, the region of interest (ROI), is referred to as the dGEMRIC index.

The dGEMRIC index correlates with quantitative analyses of GAG concentration in histologically stained tissue samples in vitro[126]. Mechanical stiffness of cartilage has also been correlated with lowered dGEMRIC index in vitro[127].

During the past two decades, hundreds of human in vivo studies have been performed, confirming the validity of dGEMRIC as a sensitive method for identifying early hip and knee cartilage degeneration [109, 128, 129].

Clinically, Gd(DTPA²⁻) diffusion into the cartilage from the synovial fluid is time-dependent[130], hence a standardized time protocol is essential.

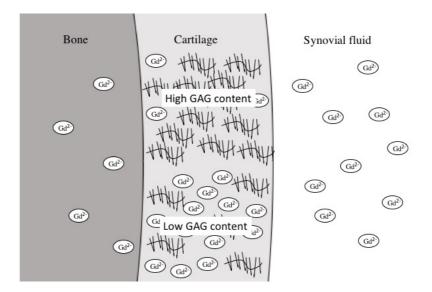


Figure 16Intravenously injected Gd(DTPA²⁻) diffuses from the synovial fluid into the cartilage. After 1–2 hours (delay), the distribution will be inversely related to the concentration of the negatively charged GAGs. Areas with different concentrations of Gd(DTPA²⁻) will give different T1 values. The average T1 in a specific ROI is defined as the dGEMRIC index. ROIs with low GAG concentrations have lower dGEMRIC indices than ROIs with higher GAG concentrations. There is a decreased GAG concentration in early OA.

A case report



Figure 17
Radiograph (Lauenstein view) of a 12 year old girl, active in handball, diagnosed with left-sided stable SCFE after 8 month of intermittent limping and progressive pain from the hip region. Internal rotation was significantly impaired. The slip was classified moderate/severe, HSA 56°. Alpha angle was 98° which implies severe FAI.



Figure 18
Six weeks postoperative radiograph after in situ fixation with the Hansson hook-pin. The right hip was pinned prophylactically. Full load on the left leg was allowed after 6 weeks.



Figure 19
First radiograph after physeal closure, 19 months later. The girl was fully active in handball and reported no subjective symptoms. Due to remodeling, alpha angle was reduced to 64°. The pins were removed according to the local standard protocol.

Twelve years later, at 25 years of age, patient reported no hip related symptoms. Hip range of motion was slightly impaired regarding internal rotation (20° vs 40°). Cartilage status of the left hip (evaluated by dGEMRIC) was not significantly decreased when compared to the right hip (512 ms vs 533 ms).

Thesis purpose

The primary objective of this thesis was to increase our understanding of the outcomes of unthreaded fixation of stable SCFE with the Hansson hook pin. To improve future SCFE outcomes, we also investigated how various factors affect these outcomes.

Specific aims:

- I. To quantify the longitudinal growth of the femoral neck and its relation to femoral offset after unthreaded in situ fixation.
- II. To study femoral neck remodeling after unthreaded in situ fixation and investigate whether remodeling correlates with growth.
- III. To assess cartilage quality in young adults affected by SCFE during childhood and study clinical and radiographic risk factors for early hip cartilage degeneration.
- **IV.** To evaluate patients' and doctors' delays in diagnosis of SCFE and identify factors leading to this delay.

Material and Methods

The cohort

All four studies were performed on a cohort of 54 consecutive children treated for stable SCFE in the hospitals of Malmö (n = 36), Lund (n = 5) and Kristianstad (n = 13) between January 1, 2001 and December 31, 2009. Children were identified through the common database of surgical records, Ortreg®, which became comprehensive starting January 1, 2001. Stable slips were defined as weightbearing, with or without crutches, per Loder[11]. There were 19 girls and 35 boys in this sample. All children received in situ fixation using the Hansson hook pin. None were excluded due to receiving another surgical method. Three children were treated for bilateral slippage; 49 were contralaterally pinned prophylactically. For **studies I**, **II** and **IV**, the complete cohort was included. For **study III**, 22 of the children were included (Figure 20).

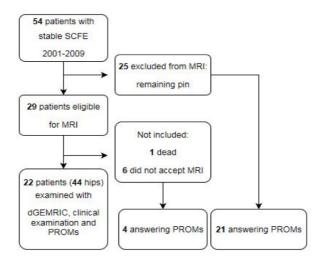


Figure 20 Flowchart of patient inclusion in study III.

Study design

- I. Retrospective, longitudinal radiographic study of 54 children with stable SCFE, operated on using the Hansson hook pin. Their first postoperative radiographs and first radiographs after physeal closure in the AP view were evaluated. Measurements of lateral nail protrusion and femoral offset were performed on both occasions. Differences were defined as femoral neck growth and increased femoral offset.
- II. Retrospective, longitudinal radiographic evaluation of 54 children operated on with the Hansson hook pin for stable SCFE. Postoperative radiograph and first radiograph after physeal closure were analyzed in the AP and frog-leg views. Head–shaft angle (slip degree), alpha angle (FAI) and displacement from Klein's line were determined on both occasions. Differences were analyzed and correlated with the amount of neck growth.
- III. An observational study including 22 children from the main cohort investigated at an average of 11 years after treatment with the Hansson hook pin. Subjects were examined with dGEMRIC to evaluate cartilage status. Alpha angle (Nötzli) was measured using anatomic MRI images to evaluate FAI. Clinical evaluation was performed by examination of ROMs and PROM (HAGOS).
- IV. Retrospective evaluation of symptoms prior to treatment was made using chart reviews (hospitals, general practitioners and school health) and personal interviews with 54 children treated for stable SCFE. Data about symptoms and their durations, medical visits and type of medical contacts were collected. Slip angle (Southwick head–shaft angle) was measured.

Radiographs

All radiographic measurements for **studies I** and **II** were performed using Orthopedic Studio® (Spectronic Medical AB, Helsingborg, Sweden). For calibration, the Hansson hook pin (diameter 6.5 mm) was used as a reference.

In **study I** AP was evaluated in the first postoperative and first postphyseal closure radiographs. All radiographs were taken in the supine position with straight legs and toes touching, slightly internally rotated. Nail protrusion and femoral offset were measured. Rotational measurement error between radiographs was analyzed by comparing the actual nail length (retrieved from surgery reports) with the length measured in the image. All measurements were performed independently by two researchers. Data are presented as the mean of the two measurements. Interobserver variability was analyzed.

In study II, AP and Lauenstein views were evaluated in the first postoperative and first postphyseal closure radiographs. The frog-leg lateral view was obtained in the supine position, with knees flexed (30–40°), and hips abducted (45°) and externally rotated with foot soles together. Displacement from Klein's line was measured in the AP view. Head-shaft angle (Southwick) and alpha angle (Nötzli) were measured in the Lauenstein view (Figure 9 and 21). The head-shaft angle was defined as the angle between the longitudinal axis of the femoral shaft and a line perpendicular to the inferior and superior edges of the physis in the femoral head. The alpha angle was measured as the angle between two lines from the center of a circle matched along the margins of the femoral head; one line was longitudinal with the femoral neck, the other crossed the point at which the contour of the femoral head/neck breaks the circle anteriorly (Figure 21). Displacement from Klein's line was defined as the distance between two parallel lines drawn at the superior margin of the femoral neck and at the superior margin of the femoral head. All measurements were performed independently by two researchers. Data are presented as the mean value of the two measurements. Interobserver variability was analyzed.

In **studies III** and **IV**, slip angles (Southwick head–shaft angles) were determined by lateral measurements as described above.

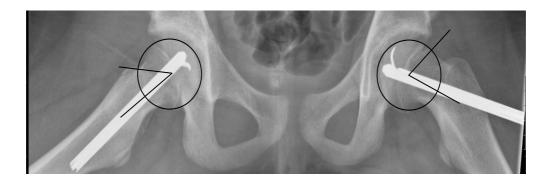


Figure 21
Schematic measureument of alpha angles.

Clinical evaluation

PROMs

In **study III**, patient-related outcome was assessed using the Copenhagen Hip and Groin Outcome Score (HAGOS)[131]. HAGOS is a self-administered, hip-specific questionnaire developed for use with young-to-middle-aged, physically active patients with longstanding hip and/or groin pain (Appendix 1). This instrument has been validated in accordance with the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) recommendations[132]. HAGOS consists of six subscales (37 items) assessing pain (10 items), symptoms (7 items), physical function in daily living (5 items), physical function in sport and recreation (8 items), participation in physical activities (2 items) and hip and/or groin-related quality of life (5 items). A score is calculated from 0 to 100 on each subscale, where 0 is the worst and 100 the best possible.

Clinical examination

In **study III**, a clinical examination for the range of motion was performed on all subjects, in connection with the dGEMRIC and PROM evaluations. Flexion, abduction and adduction were examined in the supine position. Extension and internal and external rotations were examined in the prone position, and rotation with the knee flexed. Measurements were rounded to the nearest 10th of a degree. A goniometer was used for measurements.

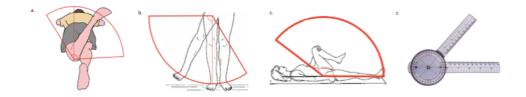


Figure 22
Positionings for clinical examinations. Right: goniometer.

dGEMRIC

Patients in **study III** were investigated using a standard 1.5 T MRI system (MAGNETOM Avanto, Siemens AG, Erlangen, Germany) with two flexible body matrix coils positioned directly over the hips. Patients received 0.2 mg/kg $Gd(DTPA)^{2-}$ (Magnevist®, Schering AG, Berlin, Germany) intravenously, followed by a 10 min timed walk. dGEMRIC imaging was performed 60 min postinjection. The variable flip angle method with two 3-D gradient echo sequences was used for image acquisition for T1 calculation (MapIt, Siemens Healthcare, Erlangen, Germany). The two sequences had flip angles 5° and 30°. Other scan parameters were: FOV = 160 mm; slice thickness = 3 mm; 22 slices; matrix 256 × 256; TE/TR = 3.39/20 ms; parallel imaging (GRAPPA) = 2. Total acquisition time for each hip was 3:48 min. T1 was calculated offline. From the two acquisitions, S1 and S2, with flip angles α 1 and α 2, T1 were calculated on a voxel-by-voxel basis using MATLAB (v. R2013b, MathWorks, Natick, USA).



Figure 23 MRI examination

The respective hips were imaged separately but during the same session, with the subject lying still in the scanner throughout the session. The right hip was investigated first. Care was taken to keep the time between the scans as short as possible. A standard clinical MRI scan of both hips was performed during the same imaging session.

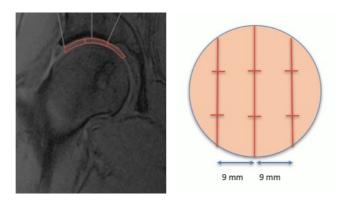


Figure 24
Left: Schematic of ROI drawing in a central slice of the hip. Right: Nine ROIs were drawn for each hip, 9 mm between slices.

Regions of interest

ROI drawings were performed using in-house-developed software (Medmap, department of medical radiation physics, Lund University, Malmö, Sweden). ROIs were drawn on anatomical images and the dGEMRIC index was calculated as the mean T1 of all voxels in the ROI. From the 3-D volume, three parallel coronal slices were chosen for analysis: a central slice, a dorsal slice (9 mm dorsal from the central

slice) and an anterior slice (9 mm ventral to the central slice). In each of the three slices, T1 was calculated for three separate ROIs: medial, central and lateral. Mean T1 of the nine ROIs in each hip was calculated as the total dGEMRIC index. All dGEMRIC indices were adjusted for BMI to correct for differences in distribution volume[133].

The alpha angle was measured on T1 parasagittal images as defined by Nötzli[134] (Figure 25).

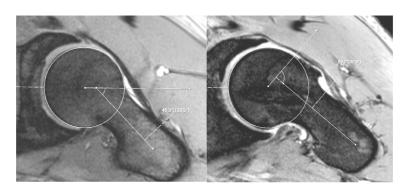


Figure 25
Alpha angle measured in T1 parasagittal images. Left: Normal (47°), Right: Severe FAI (89°)

Chart review

For **study IV**, medical records from hospitals, general practitioners and school health systems were retrieved. All doctor appointments were noted. Data regarding symptom duration, symptomatology, medical visits and type of medical contacts were retrieved. All durations were rounded to whole weeks. A patient interview via telephone was conducted with 51 patients using a questionnaire (Appendix 2). An additional guardian interview was conducted in 36 cases. Results from the chart review were available during the interviews. In 14 cases, the medical records were missing information about symptoms that were supplemented by the interview. In two cases, history of symptoms differed between the medical records and the interview; these subjects were excluded from the symptom analyses.

Statistics

SPSS (version 21; IBM, Armonk, NY) was used to analyze data for **studies I**, **II** and **III**. In **study III**, SigmaPlot 11.0 (Systat Software Inc., Richmond, CA, USA) was also used. Statistical analyses for **study IV** were performed using R-studio (R-studio, Boston, MA) and Excel 2016 (Microsoft, Redmond, WA). A *P* value less than 0.05 was considered statistically significant for all analyses. The Shapiro–Wilk test was used to test for normality.

For **studies I** and **II**, paired samples *t*-tests were used for comparisons between postoperative and postphyseal closure radiographic measurements. Correlation analyses were performed using Pearson correlation. Interobserver variability was analyzed by calculating the coefficient of variation (CV%), where CV% = (RandomError/Overallmean) × 100 and RandomError = standard deviation of ((measurement1 – measurement2)/ $\sqrt{2}$)

For **study III** paired samples *t*-tests were used to test for differences between contralateral hips. Student's *t*-tests (independent samples) were used to compare all SCFE hips (including bilateral cases) to unaffected hips. Alpha angle subgroups (nonparametric) were compared using the Mann–Whitney test. Pearson correlation was used to test correlations between dGEMRIC index and parameters for which normality could be assumed (BMI, alpha angle, age and slip angle). Spearman rank correlation was used when normality could not be assumed (HAGOS-score). The intraobserver analysis was performed by calculating the coefficient of variation, as described above.

For **study IV** the Mann–Whitney test was used to determine statistical significance between binary data, the Kruskal–Wallis test was used with categorical data and the Spearman correlation was used for continuous data.

Ethics

Ethical approval was granted by the Medical Research Ethics Committee at Lund University for **studies I** and **II** (2014/99) and for **studies III** and **IV** (2015/1).

Main results

The detailed results are described in each paper (see attachments).

Demographics

Table 2
Cohort demographics.

Girls (n)	19 (35%)	
Boys (n)	35 (65%)	
Age (years)	12.5 (7–17)	
Bilateral slippage (n)	3 (6%)	
Pinned prophylactically (n)	49 (92%)	
Slip angle (°)	35.2	
	(range 9–72)	
Mild <30°	25 (44%)	
Moderate 30-60°	29 (51%)	
Severe >60°	3 (5%)	
Time to physeal closure (months)	33.6	
	(range 10.8–73.2)	
Right hip	21 (39%)	
Left hip	36 (67%)	
Malmö	36 (67%)	
Lund	5 (9%)	
Kristianstad	13 (24%)	

The growth of the femoral neck

Mean longitudinal growth of the femoral neck in the slipped hips was 7.1 mm, compared with 10.0 mm in the contralateral hips. In the 11 children under 11 years of age at the time of surgery, the mean femoral neck growth was almost three times higher (12.1 mm) than in the eight children 14 years or older (4.2 mm) (P = 0.002). Femoral offset in SCFE hips increased from a mean of 30.0 mm to 35.2 mm (30.1 mm to 34.9 mm in unaffected hips). There was a positive correlation between the longitudinal growth of the neck and the femoral offset (R = 0.51, P < 0.001).

Remodeling of the femoral neck

Significant improvements were measured on all assessed radiographic parameters in the SCFE hips. The mean postoperative HSA decreased by 9.0°. The alpha angle improved by a mean of 14.5°. Displacement from Klein's line increased by a mean of 1.6 mm. Significant correlations were found between reduction of the alpha angle and age (R = 0.48, P < 0.001) and longitudinal growth of the femoral neck (R = 0.67, P < 0.001). Significant changes were also found in the unaffected hips with regard to alpha angle and HSA, but not displacement from Klein's line.

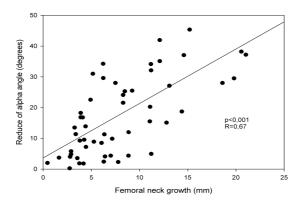


Figure 26
Correlation between alpha angle reduction by remodeling and femoral neck growth.

Cartilage quality and clinical assessment

The dGEMRIC index was lower in SCFE hips than unaffected hips, 456 ms vs 521 ms (P = 0.03).

The difference was larger in anterior (mean 21 ms) than posterior regions of the hip (P = 0.038). In the frontal plane, the magnitude of the index differences between SCFE and unaffected hips were similar in the three regions.

The alpha angle was higher in SCFE hips, 61.5° vs 45.6° , (P < 0.001). The alpha angle, but not the slip angle, was negatively correlated with the dGEMRIC index in SCFE hips (R = -0.40, P = 0.046). SCFE hips were further divided into three subgroups based on the alpha angle: $<50^{\circ}$, $50-65^{\circ}$ and $>65^{\circ}$ (Figure 27). The original slip angle, age and BMI did not correlate with the dGEMRIC index.

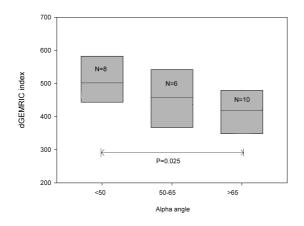


Figure 27
Mean dGEMRIC index in alpha angle subgroups.

HAGOS, separated into subscales, is presented in Diagram 1. There was a positive correlation between HAGOS and the dGEMRIC index (R = 0.41, P = 0.012).

ROM was significantly lower in SCFE hips than in unaffected hips at all ranges of motion, with the exception of adduction.



Diagram 1HAGOS separated in subscales.

Delay in diagnosis

The median delay from symptom onset to surgery was 26 weeks (range 1-109 weeks). Patients' delays were significantly longer than doctors' delays: 10 weeks (range 1-57 weeks) vs 4 weeks (range 0-57 weeks) (P=0.002).

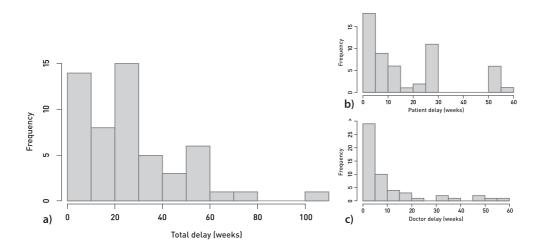


Figure 28 Histograms of a) total delay, b) patients' delays and c) doctors' delays.

Boys had significantly longer patients' delays compared with girls (13 vs 6 weeks, respectively, P = 0.021) but not doctors' delays. Children with a predominance of knee pain had significantly longer doctors' delays (14 vs 4 weeks, P = 0.002) but not patients' delays. Total delay duration was significantly correlated with slip severity.

Table 3Factors' influences on the diagnostic delay of SCFE.

Factor	Category	Value	Total delay, median (range)	Patients' delays, median (range)	Doctors' delays, median (range)	Significance of correlation to delayed diagnosis (P value)
Total group			26 (1–109)	10 (1–57)	4 (0–57)	
Age at diagnosis, mean years (range)		12.5 (7–16)				0.041
Age at symptom onset, mean years (range)		11.6 (7–15)				0.4
Gender, % (n)	Girls	35 (19)	20 (3-53)	6 (2–46)	4 (0-31)	0.038
	Boys	65 (35)	31 (1–109)	13 (1–54)	4 (0–57)	
Dominant location of pain, % (n)	Hip	72 (39)	22 (1–68)	10 (1–54)	4 (0–36)	0.003
	Knee	22 (12)	41 (4–109)	11 (0–57)	14 (0-57)	
First contact, % (n)	General practitioner	80 (43)	25 (1–109)	9 (1–57)	5 (0–57)	0.35
	School health	11 (6)	29 (10–60)	24 (8–54)	4 (2–69)	
	Orthopedic surgeon	9 (5)	39 (21–58)	39 (4–52)	3 (0–17)	

General discussion

The main objectives of this thesis were to increase our knowledge about the outcome after unthreaded fixation of SCFE and to investigate how various factors affect this outcome.

It is important to emphasize that no surgical method other than in situ fixation with the Hansson hook pin was evaluated for this thesis. All comparisons with other devices and surgical alternatives should, therefore, be seen as theoretical. Further, all discussions and conclusions herein are based on stable SCFE because unstable SCFE was not investigated.

In decision-making about treatment for SCFE, it is optimal to follow an algorithm customized for each individual situation, wherein every surgical treatment would lead to a minimized risk of sequelae and add the minimum risk of iatrogenic complications. However, because every patient is unique and includes multiple factors, this should be considered a utopian scenario. The goal of this thesis was to move a bit closer to such a utopia.

It has long been Swedish tradition to use unthreaded devices for in situ fixation, over at least the last 40-50 years[5]. During 2007-2013 only 24 of 379 SCFE hips in Sweden were operated on using threading over the physis[6]. From a Swedish perspective, the global tradition of screw physiodesis is difficult to understand. To my understanding, the main reason might be the risk of reslippage after screw fixation, which has been described [135, 136]. According to literature, such an event is rare and has mainly been an issue with unstable slips, endocrinopathies and in cases where the screw has been removed before skeletal maturity, which is strictly discouraged. No studies of the risks of reslippage from unthreaded devices have been reported. A Swedish radiostereometric analysis on SCFE hips after pinning with the Hansson pin detected discrete latitudinal movement (<2 mm) of the epiphysis in relation to the metaphysis during remaining growth, but these movements also occurred in the contralateral nonslipped hips[137]. There were no signs of reslippage in our observations, nor have there been reported in previous studies of unthreaded devices. However, it is possible that reslippage, to some extent, is underdiagnosed. If so, it has not been connected to any significant negative clinical impacts and the risk of reslippage should not be used as an argument to avoid the use of unthreaded fixation. No other possible negative effects of unthreaded fixation compared with screw physiodesis have been described.

Longitudinal growth

In **study I**, we established that there was longitudinal growth of a mean 7 mm in SCFE hips and 10 mm in the contralateral hips. These values are similar to earlier observations with smooth devices, such as short-threaded screws and multiple Kwires[72, 73, 138]. Our contralateral difference finding has also been reported in earlier observations and may indicate that SCFE per se leads to impaired growth in the physis. Potential extent of continued growth after intended screw physiodesis has not been evaluated, but a relative decreased femoral offset has been established[139]. The intentional physiodes is successful in about 90% of cases[65]. The impact of a femoral shortening of 7 mm can be debated. Still, it must be considered that this is an average value and that some of the children (in particular the youngest) grew up to 20 mm, which would mean a significant LLD if growth were inhibited. From a clinical perspective, perhaps the focus of this discussion should be on the impact of impaired femoral offset. We found that the SCFE hips did not have significantly decreased offset at skeletal maturity compared with the unslipped hips. Further, femoral neck growth correlated positively with the increase in femoral neck offset. Because decreased offset may result in an impaired joint reaction force while standing and walking, which long-term may predispose to Trendelenburg gait[69], it should be avoided whenever possible. After hip arthroplasty, it has been shown that a 15% decrease in femoral offset leads to increased risk of gait disturbance [69]. Our cohort increased their offset by a mean of 16% during remaining growth. The impact of impaired femoral offset after SCFE requires further evaluation, including clinical testing of abductor strength and PROM evaluation.

Remodeling

Study II was performed parallel to a similar radiographic observation in Sydney, Australia by Dawes et al. on remodeling after screw physiodesis[39]. There are some differences in study designs, but both established significant remodeling of the radiographic signs of FAI. Dawes et al. studied a population of milder slips and included a mix of different radiographic projections. The amounts of alpha angle decrease were comparable, implying that some femoral neck remodeling occurs regardless of femoral neck growth. This is also expected based on basic principles of appositional remodeling, which occurs independently of the physis. In the Dawes' study, age and growth correlations were lacking. However, it is difficult to predict the amount of remaining longitudinal growth and, based on our experiences, there is no reason to believe that the use of growth-allowing devices would have any negative effect.

Measurement of the alpha angle is an objective yet blunt method for evaluating the interference between the femoral neck and acetabular rim. After analyzing many radiographs, there seem to be two primary features that cause a decreased alpha angle. First, the disappearance of the metaphyseal bump by remodeling. Second, a distal displacement of the bump, probably caused by longitudinal growth, away from the acetabular rim. Both result in a decreased alpha angle. Whether the remaining distalized bump may have negative effects is up for speculation and requires investigation.

One issue central to the debate over SCFE treatments is how to handle the exposed anterior metaphysis causing impingement to the anterolateral rim and labrum. Some authors advocate in situ fixation combined with immediate arthroscopic osteoplasty of the femoral neck[114, 140]. This procedure has been evaluated only in small cohorts, with short follow-up, and needs to be further investigated. Another way to address the deformity is to perform an osteotomy, with considerable risk of iatrogenic AVN. Our observations demonstrate that the alpha angle normalizes in many patients during remaining growth when using the Hansson hook pin. With this knowledge, it seems unwise to support immediate arthroscopic osteoplasty of the metaphyseal bump.

Though desirable, it is difficult to predict the alpha angle at skeletal maturity. Given slip severity and age, the probability of ending up with a high alpha angle can only be estimated. In our observations, the risk of ending up with radiographic FAI (alpha angle $>60^{\circ}$) at skeletal maturity is low if the slip angle $<40^{\circ}$, irrespective of age at onset. In those younger than 11 years, the limit is instead $50-60^{\circ}$, particularly in girls. Similar observations with threaded devices[141, 142] have reported that a slip angle of approximately $30-35^{\circ}$ is the threshold at which FAI appears more regularly. This difference might be explained by the growth-promoted remodeling process.

Advocates of immediate, aggressive treatment of FAI in SCFE argue that damage to the anterior acetabular cartilage, labrum and rim is universal and occurs very early, prior to diagnosis. This argument is largely based on a study of 13 intraoperative observations in adolescents with SCFE who received an immediate open procedure[143]. In that study, labral erosions and varying grades of cartilage loss were present in the majority of the cases and it was concluded that OA in SCFE is triggered by early mechanical damage to the acetabular cartilage. Our results from **study III** may shed light on this issue. The dGEMRIC index was negatively correlated with the alpha angle in adulthood, but *not* with the initial slip angle. This indicates that the chondral damage at diagnosis may recover during remaining growth and that the main risk factor contributing to future OA is the alpha angle in adulthood. Instead of performing arthroscopy in children, I, therefore, suggest that this procedure be delayed until adulthood. Furthermore, the potential risks of

additional surgery must be considered. It must also be emphasized that there is currently no evidence that any treatment other than minimally invasive in situ fixation improves long-term outcome after SCFE.

FAI and OA

The results of **study III** support the theory of cartilage degeneration secondary to FAI in young adulthood. This is consistent with earlier noninvasive observations[144, 145]. It should be noted that the mean cartilage degeneration in our sample was mild and would not be detected on plain radiographs, likely for several years[109]. The clinical impact was also still mild. When comparing the means in each HAGOS subgroup, they were all within the upper 95th percentile of healthy young adults[146]. Still, the positive correlation between cartilage quality and HAGOS implies that our dGEMRIC findings are clinically relevant.

An unexpected study finding was that the alpha angle was only weakly correlated with the degree of slip severity at the onset of the disease. This implies that the original slip severity is an insufficient prognostic tool to predict FAI and, therefore, also OA after SCFE. In support of this contention, earlier observations have also found the considerable risk of radiographic FAI after SCFE in cases of mild slippage[147]. It thus appears that development of CAM deformities may also occur after reaching skeletal maturity. Potential risk factors for such development need further investigation. Whether the prevalence of FAI after SCFE should be evaluated primarily after growth is complete, or in early adulthood, is a matter of speculation.

The regional dGEMRIC analysis in our study indicated more cartilage degeneration in the anterior parts of the hip joint than posteriorly. This is probably a consequence of the location of the mechanical conflict between the anterior bump and acetabular rim and further supports the theory of FAI as a mediator of OA. Similar results have been presented from adults with FAI[109]. Regional differences also imply that cartilage degeneration at this age is incipient, before global joint affection, and that we are investigating an early phase of joint degeneration. OA is generally considered as an irreversible process[148] but maybe that isolated early focal degeneration can be reversed, or at least delayed.

In our study, the dGEMRIC index was lower in the medial than the central and lateral ROIs in both SCFE and unaffected hips. This indicates a higher GAG content in the weight-bearing (central and lateral) cartilage regions than the less weight-bearing medial portion. Similar results have been previously reported [145].

Diagnostic issues

Delay in diagnosis of SCFE is an important potentially modifiable risk factor. Results from **study IV** demonstrate that this issue is also highly relevant. During Hägglund's observations of delay from 1910 to 1982, there was a slight decrease in delay (about 1 month) over time, with a mean of 3.4 and 4.8 months in girls and boys, respectively. In our data, the median delay was 6 months (5 in girls, 7 in boys). It is noteworthy that delay in SCFE diagnosis in Sweden seems unaltered, possibly even longer, than it was at the beginning of the 18th century, despite the massive expansion in health care services. Interestingly, patients' delays accounted for the vast majority of the delay. To the best of our knowledge, this has not been previously evaluated. In the literature, patients' responsibility for delays tends to be a secondary focus, perhaps due to measurement difficulty. Our results imply that increased awareness of SCFE is important, not only among health care providers but even more so among parents, teachers, coaches, etc. In Sweden, there is a trend to consider musculoskeletal pain as the domain of physiotherapists within health care centers. This profession is, therefore, a potential target for future educational efforts.

It is noteworthy that no child who had delayed diagnosis of fewer than 20 weeks had a slip angle >40° (Figure 29). Because 40° of slippage was also the threshold at which FAI appeared more regularly at skeletal maturity, it may be concluded that children diagnosed within the first five months of symptom onset are at lower risk for eventual FAI.

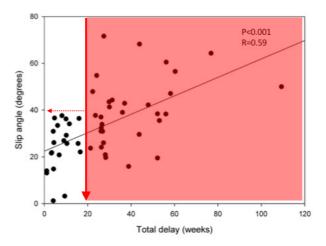


Figure 29
No case delayed fewer than 20 weeks had a slip angle >40°.

Previous observations have shown that one-third of patients with SCFE initially present with knee symptoms and that this leads to increased risk of delayed diagnosis. We were able to confirm this, though interestingly only doctors' delays, not patients' delays, were prolonged. This emphasizes that hip status should be routinely assessed in all children with knee pain to improve time to SCFE diagnosis. Future educational efforts targeted at different health care providers should include this information.

Boys' diagnoses were delayed more than girls', due to longer patients' delays. We can only speculate about the possible reasons for this. Different social expectations and variations in lifestyle may be one reason. Because boys also seem to have a reduced ability to remodel the residual femoral neck deformity, it could be assumed that boys would have worse outcomes than girls. This contention was not supported by **study III**, in which we found no gender differences in cartilage quality. However, it should be noted that our sample was relatively small, increasing the risk for type II error.

After reviewing the details of 54 stable SCFE cases with regard to symptoms before diagnosis, my experience has been that information about symptom duration from hospital medical records is, in many cases, deficient and untrustworthy. If school health and general practitioner records had not been included in this study, the delay in diagnosis would have been severely underestimated. This may be one reason for the relatively long delay in our observation, compared with others. This should be considered in future studies.

Limitations

The limitations of **study I** are mainly issues of measurement error due to rotational discrepancies. The rotational discrepancies were determined to be a mean of 4° and 5° , respectively (range 0– 11°). Applying a 5° rotational discrepancy to a hypothetical 10 mm nail protrusion would change the measured protrusion by 0.9 mm ($\sin(5^{\circ}) = 9\%$). Further, by increasing the severity of the slip, where the nail is inserted from anterolateral to posteromedial, the orientation of the nail will be less perpendicular to the x-ray beam compared with the contralateral hip. In such cases, the nail protrusion is from the lateral cortex; hence, the longitudinal growth appears shorter. This would result in an underestimation of the measured growth. In conclusion, there are no reasons to believe that different rotations of the nail between examinations influenced these results.

There are also potential issues with measurement precision in **study 2**. A mixture of projections may lead to errors, which is why cross-table projections were excluded. In addition, the dorsal slip of the epiphysis theoretically improves the ability to rotate the hip externally. This could potentially cause different rotations between the Lauenstein projections on the postoperative radiographs compared with postphyseal closure radiographs. It should be noted that earlier reports on hip ROM in SCFE diverge and that external rotation may even be impaired, despite slippage. Furthermore, Lauenstein projection is not meant to be taken during a forced maximal external rotation. It has been shown that 10° of rotational discrepancy leads to a mean 1.8° difference in alpha angle in the AP view[149]. In summary, we do not expect that any significant or systematic measurement error influenced our results.

In **study III**, the major limitation is a small sample size, which may have caused type I and II errors. Selection bias must also be considered. Only subjects who had undergone pin removal were eligible for MRI. At the hospitals included as data collection sites, some surgeons remove hardware as a matter of clinical routine, whereas others remove hardware only when it causes local tenderness. This problem was addressed by comparing PROMs between the MRI group and the rest of the cohort (with hardware remaining), between which no significant differences were found. In addition, the contralateral hip was used as an internal reference. Another potential limitation was the lack of information regarding the patients' levels of physical activity because individuals with high activity levels have higher dGEMRIC indices than sedentary individuals[150]. However, using the

contralateral hip as an internal reference should have minimized this potential source of error. Furthermore, the dGEMRIC index in the unaffected hips in our study was similar to previous data from young, healthy volunteers[151].

Study IV is limited by its retrospective nature because covariates were dependent on pre-existing medical records. The patient and guardian interviews were performed to improve data quality, but recall bias must be considered. Two subjects gave information that contradicted the charts with regard to symptoms and were excluded from the symptom analyses. It should be noted that earlier reports on diagnosis delay have exclusively reviewed hospital medical records, without a supplemental interview. Another limitation is the lack of information about BMI, which could not be retrieved from the charts.

Conclusions

Unthreaded in situ fixation of stable SCFE with the Hansson hook pin is safe and leads to the continued growth of the femoral neck. Remaining growth enables the hip to achieve an almost anatomic femoral offset. Young children grow more than older children, implying that they benefit more from growth-allowing fixation. In prophylactic pinning, unthreaded fixation can be used with minimal risk of negative effects to the hip.

In situ fixation of stable SCFE using the Hansson hook pin results in substantial remodeling of the femoral neck. Correlations between longitudinal growth and decreased alpha angle support the use of a surgical device that permits continued growth to minimize the risk of persistent FAI, especially in young patients. Older age, high degree of slippage and male sex are negative prognostic factors for persistent FAI.

The contralateral hip also undergoes substantial remodeling during growth, which should be taken into account in longitudinal studies of SCFE.

Signs of early cartilage degeneration with correlated impaired clinical satisfaction can be seen as early as the mid 20s in patients who received surgery for stable SCFE in childhood. Degenerative changes appear related to the current presence of FAI rather than the initial degree of slippage. Results support focusing on FAI after SCFE to improve future outcomes.

Delayed diagnosis leads to increased slip severity, emphasizing the importance of early diagnosis to reduce the risk of sequelae. The majority of delays was caused by late presentation to health care. Boys were diagnosed later than were girls, due to longer patients' delays. The predominance of knee pain increased the risk of misdiagnosis and therefore caused longer doctors' delays. To improve outcomes for future patients, education of various health care providers is essential, as is increased awareness about SCFE among the general population.

Future perspectives

"There is nothing permanent except change"

-Heraclitus (Greek philosopher)

This thesis encourages global change of in situ fixation of stable SCFE. With no additional risks, there are multiple advantages in using a device that allows continued femoral neck growth. Based on these findings, pediatric orthopedic surgeons should avoid a permanent physiodesis to optimize offset and provide optimal conditions for remodeling. Skeptics might opine that a randomized controlled study should be performed to legitimize the use of unthreaded fixation globally. However, this would likely be impossible in Sweden, for ethical reasons.

In the future, more focus should be drawn to the association between FAI and future OA. At present, we do not know when and how to deal with FAI after SCFE. In particular, surgical treatment for FAI needs further evaluation. Longitudinal, randomized trials to evaluate long-term clinical and radiographic outcomes following arthroscopic osteoplasty for persistent FAI after SCFE are essential.

Currently, there is no convincing evidence that development of irreversible cartilage damage occurs during childhood that can motivate osteoplasty before skeletal maturity. In addition, the risks of iatrogenic side effects must be considered. Until further evidence exists, unthreaded in situ fixation with optimal conditions for remodeling is adequate. For the future, I would suggest clinical and radiographic evaluation of SCFE patients early after completed growth (around 18 years). In patients with clinical and radiographic signs of FAI, an additional evaluation of the cartilage status would be advisory.

Considerable delay in diagnostics of SCFE occurs in Sweden, with the major cause being patients' delay. Late diagnosis causes more severe deformities and increases the risk of life-long sequelae. Efforts to increase awareness of SCFE should be directed at both the general community and health care providers to improve future outcomes.

Acknowledgements

It is with great honor I want to highlight those who made this thesis possible. Special thanks to the following.

Carl-Johan Tiderius, my dear friend and supervisor. You made all this possible by guiding me through endless work with countless laughs, in-depth conversations and mutual pep-talks, as well in Lund as in Glimminge, the Pyrenees or Honolulu. You are truly a role model, always full of joy to discover something new. Somewhere along this road you became one of my very best friends. I can't wait to see what's around the next corner.

Jonas Svensson, my co-supervisor, for invaluable guidance in the mazy world of MRI physics.

Lina Björklund-Sand and **Malin Engbom** for an impressive work and great collaboration with measurements for paper I and II.

Johan Österman for dedicated work with hunting down information of diagnostic delay for paper IV. Your future is so bright you have to wear shades.

Anetta Bolejko and **Ann-Sofi Sjökvist** for conducting dGEMRIC examinations with great accuracy in many late nights and early mornings.

Håkan Lövkvist, Jonas Ranstam and Jan Åke Nilsson for invaluable statistical consulting.

Josefin Örtegren for cover layout with artistic elegance, as always. A lot have changed since you and I shared room and explored the world together, but you are always in my heart.

Although not directly involved in this thesis I also want to address a special gratitude to:

Henrik Düppe for opening the door to the world of pediatric orthopaedics and for making me want to enter it. Your own door is always open for staunch guidance in everything from progressive surgical techniques to cycle gadgets, or just for a chat.

Henrik Lauge-Pedersen for your uniquely generous and supportive personality combined with genuine orthopaedic wisdom that makes you an inspiring role model and a really good friend. With your winning personality and "thick forehead" everything is possible, both in the ski track and in the operating room.

Gunnar Hägglund for impeccable and humble guidance in all aspects of research and pediatric orthopedic issues. Also for your own solid contribution to SCFE research and for sharing the important history of pediatric orthopedics in Lund.

Lennart Landin for inspiration and heavy support during my early career. You are the real spirit of pediatric orthopaedics. Your quotes will live forever.

My colleagues in the board of the Swedish Pediatric Orthopadic Society (SBOF) and in the steering committee of the Swedish Pediatric Orthopaedic Quality Register (SPOQ) for constantly hard work with the ambition to develop and improve pediatric orthopedics in Sweden and abroad.

My colleagues at the Orthopaedic department of Skåne University Hospital, and in particular **Per B, Olof** and **Måns** for all great moments we share.

Jesper Banck and Iman Ghanei for brotherhood through poverty and prosperity.

And last but not least, my colorful and sprawling family:

Dolores for coming to us, and being just perfect.

Bodil for holding my hand through this life. I love you.

Elisabeth for your eternal support and for making me really believe that I was something special.

Michael for your uncompromised warmth and goodness. You are truly unique.

Johan for genuine brotherhood.

Louise and Hjördis for lifelong support and love.

- 1. White, J.R., et al., *Histomorphometric analysis of an adolescent distal tibial physis prior to growth plate closure.* J Child Orthop, 2008. **2**(4): p. 315-9.
- 2. Loder, R.T. and E.N. Skopelja, *The epidemiology and demographics of slipped capital femoral epiphysis*. ISRN Orthop, 2011. **2011**: p. 486512.
- 3. Hagglund, G., L.I. Hansson, and G. Ordeberg, *Epidemiology of slipped capital femoral epiphysis in southern Sweden*. Clin Orthop Relat Res, 1984(191): p. 82-94.
- 4. Loder, R.T., *The demographics of slipped capital femoral epiphysis. An international multicenter study.* Clin Orthop Relat Res, 1996(322): p. 8-27.
- 5. Hansson, L.I., G. Hagglund, and G. Ordeberg, *Slipped capital femoral epiphysis in southern Sweden 1910-1982*. Acta Orthop Scand Suppl, 1987. **226**: p. 1-67.
- 6. Herngren, B., et al., *Slipped capital femoral epiphysis: a population-based study*. BMC Musculoskelet Disord, 2017. **18**(1): p. 304.
- 7. Koenig, K.M., et al., *Does skeletal maturity predict sequential contralateral involvement after fixation of slipped capital femoral epiphysis?* J Pediatr Orthop, 2007. **27**(7): p. 796-800.
- 8. Lehmann, C.L., et al., *The epidemiology of slipped capital femoral epiphysis: an update.* J Pediatr Orthop, 2006. **26**(3): p. 286-90.
- 9. Loder, R.T., et al., *Narrow window of bone age in children with slipped capital femoral epiphyses.* J Pediatr Orthop, 1993. **13**(3): p. 290-3.
- 10. Manoff, E.M., M.B. Banffy, and J.J. Winell, *Relationship between Body Mass Index and slipped capital femoral epiphysis*. J Pediatr Orthop, 2005. **25**(6): p. 744-6.
- 11. Loder, R.T., *Unstable slipped capital femoral epiphysis*. J Pediatr Orthop, 2001. **21**(5): p. 694-9.
- 12. Dietz, F., *How best to treat acute or unstable slipped capital femoral epiphysis with great interest.* Clin Orthop Relat Res, 1997(340): p. 281-3.
- 13. Kalogrianitis, S., et al., *Does unstable slipped capital femoral epiphysis require urgent stabilization?* J Pediatr Orthop B, 2007. **16**(1): p. 6-9.
- 14. Loder, R.T., et al., *Acute slipped capital femoral epiphysis: the importance of physeal stability.* J Bone Joint Surg Am, 1993. **75**(8): p. 1134-40.
- 15. Sankar, W.N., et al., *The unstable slipped capital femoral epiphysis: risk factors for osteonecrosis.* J Pediatr Orthop, 2010. **30**(6): p. 544-8.
- 16. Castro, F.P., Jr., J.T. Bennett, and K. Doulens, *Epidemiological* perspective on prophylactic pinning in patients with unilateral slipped capital femoral epiphysis. J Pediatr Orthop, 2000. **20**(6): p. 745-8.
- 17. Kocher, M.S., et al., *Prophylactic pinning of the contralateral hip after unilateral slipped capital femoral epiphysis*. J Bone Joint Surg Am, 2004. **86-A**(12): p. 2658-65.

- 18. Bellemans, J., et al., *Slipped capital femoral epiphysis: a long-term follow-up, with special emphasis on the capacities for remodeling.* J Pediatr Orthop B, 1996. **5**(3): p. 151-7.
- 19. Ippolito, E., M.R. Mickelson, and I.V. Ponseti, *A histochemical study of slipped capital femoral epiphysis*. J Bone Joint Surg Am, 1981. **63**(7): p. 1109-13.
- 20. Morscher, E., Strength and morphology of growth cartilage under hormonal influence of puberty. Animal experiments and clinical study on the etiology of local growth disorders during puberty. Reconstr Surg Traumatol, 1968. **10**: p. 3-104.
- 21. Mann, D.C., J. Weddington, and S. Richton, *Hormonal studies in patients with slipped capital femoral epiphysis without evidence of endocrinopathy*. J Pediatr Orthop, 1988. **8**(5): p. 543-5.
- 22. Kitadai, H.K., et al., *Wiberg's center-edge angle in patients with slipped capital femoral epiphysis*. J Pediatr Orthop, 1999. **19**(1): p. 97-105.
- 23. Mirkopulos, N., D.S. Weiner, and M. Askew, *The evolving slope of the proximal femoral growth plate relationship to slipped capital femoral epiphysis*. J Pediatr Orthop, 1988. **8**(3): p. 268-73.
- 24. Rennie, A.M., *Familial slipped upper femoral epiphysis*. J Bone Joint Surg Br, 1967. **49**(3): p. 535-9.
- 25. Loder, R.T., et al., *Slipped capital femoral epiphysis associated with radiation therapy.* J Pediatr Orthop, 1998. **18**(5): p. 630-6.
- 26. Kelsey, J.L., *Epidemiology of slipped capital femoral epiphysis: a review of the literature.* Pediatrics, 1973. **51**(6): p. 1042-50.
- 27. Ledwith, C.A. and G.R. Fleisher, *Slipped capital femoral epiphysis* without hip pain leads to missed diagnosis. Pediatrics, 1992. **89**(4 Pt 1): p. 660-2.
- 28. Katz, D.A., Slipped capital femoral epiphysis: the importance of early diagnosis. Pediatr Ann, 2006. **35**(2): p. 102-11.
- 29. Krauspe, R. and S. Weinstein, *Special symposium issue: slipped capital femoral epiphysis (SCFE)*. J Child Orthop, 2017. **11**(2): p. 85-86.
- 30. Gholve, P.A., D.B. Cameron, and M.B. Millis, *Slipped capital femoral epiphysis update*. Curr Opin Pediatr, 2009. **21**(1): p. 39-45.
- 31. Aronson, D.D. and W.E. Carlson, *Slipped capital femoral epiphysis*. *A prospective study of fixation with a single screw*. J Bone Joint Surg Am, 1992. **74**(6): p. 810-9.
- 32. Drehmann, F., [Drehmann's sign. A clinical examination method in epiphysiolysis (slipping of the upper femoral epiphysis). Description of signs, aetiopathogenetic considerations, clinical experience (author's transl)]. Z Orthop Ihre Grenzgeb, 1979. 117(3): p. 333-44.
- 33. Han, H., et al., *Hip rotation range of motion in sitting and prone positions in healthy Japanese adults.* J Phys Ther Sci, 2015. **27**(2): p. 441-5.

- 34. Kouyoumdjian, P., et al., *Clinical evaluation of hip joint rotation range of motion in adults*. Orthop Traumatol Surg Res, 2012. **98**(1): p. 17-23.
- 35. Loder, R.T., Effect of femur position on the angular measurement of slipped capital femoral epiphysis. J Pediatr Orthop, 2001. **21**(4): p. 488-94.
- 36. Southwick, W.O., *Slipped capital femoral epiphysis*. J Bone Joint Surg Am, 1984. **66**(8): p. 1151-2.
- 37. Carney, B.T. and J. Liljenquist, *Measurement variability of the lateral head-shaft angle in slipped capital femoral epiphysis*. J Surg Orthop Adv, 2005. **14**(4): p. 165-7.
- 38. Loder, R.T., *Controversies in slipped capital femoral epiphysis*. Orthop Clin North Am, 2006. **37**(2): p. 211-21, vii.
- 39. Dawes, B., J.L. Jaremko, and J. Balakumar, *Radiographic assessment of bone remodelling in slipped upper femoral epiphyses using Klein's line and the alpha angle of femoral-acetabular impingement: a retrospective review.* J Pediatr Orthop, 2011. **31**(2): p. 153-8.
- 40. Hansson, L.I., et al., *The calcar femorale as a landmark in hip physiolysis*. Acta Orthop Scand, 1988. **59**(2): p. 134-8.
- 41. Billing, L., Roentgen examination of the proximal femur end in children and adolescents; a standardized technique also suitable for determination of the collum-, anteversion-, and epiphyseal angles; a study of slipped epiphysis and coxa plana. Acta Radiol Suppl, 1954. 110: p. 1-80.
- 42. Billing, L., H.G. Bogren, and J. Wallin, *Reliable X-ray diagnosis of slipped capital femoral epiphysis by combining the conventional and a new simplified geometrical method.* Pediatr Radiol, 2002. **32**(6): p. 423-30.
- 43. Klein, A., et al., *Roentgenographic features of slipped capital femoral epiphysis*. Am J Roentgenol Radium Ther, 1951. **66**(3): p. 361-74.
- 44. Loder, R.T., Correlation of radiographic changes with disease severity and demographic variables in children with stable slipped capital femoral epiphysis. J Pediatr Orthop, 2008. **28**(3): p. 284-90.
- 45. Harland, U. and F.A. Krappel, [Value of ultrasound, CT, and MRI in the diagnosis of slipped capital femoral epiphysis (SCFE)]. Orthopade, 2002. **31**(9): p. 851-6.
- 46. Tins, B., V. Cassar-Pullicino, and I. McCall, *The role of pre-treatment MRI in established cases of slipped capital femoral epiphysis*. Eur J Radiol, 2009. **70**(3): p. 570-8.
- 47. Rabenhorst, B.M. and J. Aronson, *Do Not Miss This Diagnosis: Slipped Capital Femoral Epiphysis (SCFE)*. J Ark Med Soc, 2015. **112**(7): p. 114-5
- 48. O'Connor, S.J. and J.C. Ivanoff, *Slipped upper femoral epiphysis; early recognition and treatment.* J Mich State Med Soc, 1956. **55**(2): p. 188-91.

- 49. Samson, A. and L. Jarry, *Early and late treatment of slipped upper femoral epiphysis*. J Bone Joint Surg Br, 1948. **30B**(1): p. 221.
- 50. Brenkel, I.J., A.J. Prosser, and M. Pearse, *Slipped capital femoral epiphysis: continuing problem of late diagnosis*. Br Med J (Clin Res Ed), 1986. **293**(6541): p. 256-7.
- 51. Perry, D.C., et al., *A nationwide cohort study of slipped capital femoral epiphysis*. Arch Dis Child, 2017. **102**(12): p. 1132-1136.
- 52. Hosseinzadeh, P., et al., *Delay in the Diagnosis of Stable Slipped Capital Femoral Epiphysis*. J Pediatr Orthop, 2017. **37**(1): p. e19-e22.
- 53. Kocher, M.S., et al., *Delay in diagnosis of slipped capital femoral epiphysis*. Pediatrics, 2004. **113**(4): p. e322-5.
- 54. Ordeberg, G., L.I. Hansson, and S. Sandstrom, *Slipped capital femoral epiphysis in southern Sweden. Long-term result with no treatment or symptomatic primary treatment.* Clin Orthop Relat Res, 1984(191): p. 95-104.
- Wilson, P.D., B. Jacobs, and L. Schecter, Slipped Capital Femoral Epiphysis: An End-Result Study. J Bone Joint Surg Am, 1965. 47: p. 1128-45.
- 56. Schur, M.D., et al., Continuing Delay in the Diagnosis of Slipped Capital Femoral Epiphysis. J Pediatr, 2016. 177: p. 250-254.
- 57. Boyer, D.W., M.R. Mickelson, and I.V. Ponseti, *Slipped capital femoral epiphysis*. *Long-term follow-up study of one hundred and twenty-one patients*. J Bone Joint Surg Am, 1981. **63**(1): p. 85-95.
- 58. Dreghorn, C.R., et al., Slipped upper femoral epiphysis--a review of 12 years of experience in Glasgow (1972-1983). J Pediatr Orthop, 1987. 7(3): p. 283-7.
- 59. Carney, B.T. and S.L. Weinstein, *Natural history of untreated chronic slipped capital femoral epiphysis*. Clin Orthop Relat Res, 1996(322): p. 43-7.
- 60. Moriarity, A., et al., Levels of Evidence in the Treatment of Slipped Capital Femoral Epiphysis: A Systematic Review. Orthop Rev (Pavia), 2016. **8**(2): p. 6303.
- 61. Naseem, H., et al., *Treatment of stable slipped capital femoral epiphysis: systematic review and exploratory patient level analysis.* J Orthop Traumatol, 2017. **18**(4): p. 379-394.
- 62. Millis, M.B., *SCFE: clinical aspects, diagnosis, and classification.* J Child Orthop, 2017. **11**(2): p. 93-98.
- 63. Givon, U. and J.R. Bowen, *Chronic slipped capital femoral epiphysis:* treatment by pinning in situ. J Pediatr Orthop B, 1999. **8**(3): p. 216-22.
- 64. Lim, Y.J., et al., *Management outcome and the role of manipulation in slipped capital femoral epiphysis.* J Orthop Surg (Hong Kong), 2007. **15**(3): p. 334-8.

- 65. Peck, K. and J. Herrera-Soto, *Slipped capital femoral epiphysis: what's new?* Orthop Clin North Am, 2014. **45**(1): p. 77-86.
- 66. Ward, W.T., et al., *Fixation with a single screw for slipped capital femoral epiphysis.* J Bone Joint Surg Am, 1992. **74**(6): p. 799-809.
- 67. Uglow, M.G. and N.M. Clarke, *The management of slipped capital femoral epiphysis*. J Bone Joint Surg Br, 2004. **86**(5): p. 631-5.
- 68. Cassidy, K.A., et al., *Effect of femoral offset on pain and function after total hip arthroplasty*. J Arthroplasty, 2012. **27**(10): p. 1863-9.
- 69. Sariali, E., et al., *The effect of femoral offset modification on gait after total hip arthroplasty*. Acta Orthop, 2014. **85**(2): p. 123-7.
- 70. Hansson, G. and J. Nathorst-Westfelt, Management of the contralateral hip in patients with unilateral slipped upper femoral epiphysis: to fix or not to fix--consequences of two strategies. J Bone Joint Surg Br, 2012. **94**(5): p. 596-602.
- 71. Sankar, W.N., et al., What are the risks of prophylactic pinning to prevent contralateral slipped capital femoral epiphysis? Clin Orthop Relat Res, 2013. **471**(7): p. 2118-23.
- 72. Guzzanti, V., F. Falciglia, and C.L. Stanitski, *Slipped capital femoral epiphysis in skeletally immature patients*. J Bone Joint Surg Br, 2004. **86**(5): p. 731-6.
- 73. Hagglund, G., et al., *Bone growth after fixing slipped femoral epiphyses: brief report.* J Bone Joint Surg Br, 1988. **70**(5): p. 845-6.
- 74. Lehmann, T.G., et al., *In situ fixation of slipped capital femoral epiphysis with Steinmann pins*. Acta Orthop, 2011. **82**(3): p. 333-8.
- 75. Sailhan, F., et al., Continued growth of the hip after fixation of slipped capital femoral epiphysis using a single cannulated screw with a proximal threading. J Child Orthop, 2011. 5(2): p. 83-8.
- 76. Hansson, L.I., Osteosynthesis with the hook-pin in slipped capital femoral epiphysis. Acta Orthop Scand, 1982. **53**(1): p. 87-96.
- 77. Cousins, G.R., et al., *Prophylactic pinning for slipped capital femoral epiphysis: does it affect proximal femoral morphology?* J Pediatr Orthop B, 2016. **25**(3): p. 202-6.
- 78. Hagglund, G., et al., *Bilaterality in slipped upper femoral epiphysis*. J Bone Joint Surg Br, 1988. **70**(2): p. 179-81.
- 79. Riad, J., G. Bajelidze, and P.G. Gabos, *Bilateral slipped capital femoral epiphysis: predictive factors for contralateral slip.* J Pediatr Orthop, 2007. **27**(4): p. 411-4.
- 80. Stasikelis, P.J., et al., *Slipped capital femoral epiphysis. Prediction of contralateral involvement.* J Bone Joint Surg Am, 1996. **78**(8): p. 1149-55.
- 81. Dunn, D.M., *The Treatment of Adolescent Slipping of the Upper Femoral Epiphysis*. J Bone Joint Surg Br, 1964. **46**: p. 621-9.

- 82. Kramer, W.G., W.A. Craig, and S. Noel, *Compensating osteotomy at the base of the femoral neck for slipped capital femoral epiphysis*. J Bone Joint Surg Am, 1976. **58**(6): p. 796-800.
- 83. Muller, M.E., [Planning of a complex intertrochanteric osteotomy (author's transl)]. Z Orthop Ihre Grenzgeb, 1979. **117**(2): p. 145-50.
- 84. Southwick, W.O., Osteotomy through the lesser trochanter for slipped capital femoral epiphysis. J Bone Joint Surg Am, 1967. **49**(5): p. 807-35.
- 85. Diab, M., M.T. Hresko, and M.B. Millis, *Intertrochanteric versus* subcapital osteotomy in slipped capital femoral epiphysis. Clin Orthop Relat Res, 2004(427): p. 204-12.
- 86. Gage, J.R., et al., Complications after cuneiform osteotomy for moderately or severely slipped capital femoral epiphysis. J Bone Joint Surg Am, 1978. **60**(2): p. 157-65.
- 87. Gautier, E., et al., *Anatomy of the medial femoral circumflex artery and its surgical implications.* J Bone Joint Surg Br, 2000. **82**(5): p. 679-83.
- 88. Ganz, R., et al., Surgical dislocation of the adult hip a technique with full access to the femoral head and acetabulum without the risk of avascular necrosis. J Bone Joint Surg Br, 2001. **83**(8): p. 1119-24.
- 89. Jackson, J.B., 3rd, et al., Restoration of Blood Flow to the Proximal Femoral Epiphysis in Unstable Slipped Capital Femoral Epiphysis by Modified Dunn Procedure: A Preliminary Angiographic and Intracranial Pressure Monitoring Study. J Pediatr Orthop, 2018. 38(2): p. 94-99.
- 90. Rubin, L.E., et al., *Direct intraosseous pressure monitoring of the femoral head during surgery for slipped capital femoral epiphysis*. Orthopedics, 2008. **31**(7): p. 663-6.
- 91. Abdelazeem, A.H., et al., The anatomical reduction of a moderate or severe stable slipped capital femoral epiphysis by modified Dunn subcapital osteotomy using the Ganz approach: functional and radiological outcomes. Bone Joint J, 2016. **98-B**(9): p. 1283-8.
- 92. Ziebarth, K., et al., *Capital realignment for moderate and severe SCFE using a modified Dunn procedure.* Clin Orthop Relat Res, 2009. **467**(3): p. 704-16.
- 93. Souder, C.D., J.D. Bomar, and D.R. Wenger, *The role of capital realignment versus in situ stabilization for the treatment of slipped capital femoral epiphysis*. J Pediatr Orthop, 2014. **34**(8): p. 791-8.
- 94. Loder, R.T., et al., *Slipped capital femoral epiphysis*. Instr Course Lect, 2008. **57**: p. 473-98.
- 95. Hagglund, G., et al., Slipped capital femoral epiphysis in southern Sweden. Long-term results after femoral neck osteotomy. Clin Orthop Relat Res, 1986(210): p. 152-9.
- 96. Hansson, G., et al., Long-term results after nailing in situ of slipped upper femoral epiphysis. A 30-year follow-up of 59 hips. J Bone Joint Surg Br, 1998. **80**(1): p. 70-7.

- 97. Carney, B.T., S.L. Weinstein, and J. Noble, *Long-term follow-up of slipped capital femoral epiphysis*. J Bone Joint Surg Am, 1991. **73**(5): p. 667-74.
- 98. Hagglund, G., L.I. Hannson, and S. Sandstrom, *Slipped capital femoral epiphysis in southern Sweden. Long-term results after nailing/pinning.* Clin Orthop Relat Res, 1987(217): p. 190-200.
- 99. Aronsson, D.D. and L.A. Karol, *Stable Slipped Capital Femoral Epiphysis: Evaluation and Management*. J Am Acad Orthop Surg, 1996. **4**(4): p. 173-181.
- 100. Alshryda, S., et al., Evidence based treatment for unstable slipped upper femoral epiphysis: Systematic review and exploratory patient level analysis. Surgeon, 2018. **16**(1): p. 46-54.
- 101. Kohno, Y., et al., *Is the timing of surgery associated with avascular necrosis after unstable slipped capital femoral epiphysis? A multicenter study.* J Orthop Sci, 2017. **22**(1): p. 112-115.
- 102. Kushare, I., R.E. Wiltfong, and K.E. Klingele, *Acute, unstable slipped capital femoral epiphysis with associated congenital coxa vara.* J Pediatr Orthop B, 2015. **24**(6): p. 511-4.
- 103. Crepeau, A., et al., *Intracapsular Pressures After Stable Slipped Capital Femoral Epiphysis*. J Pediatr Orthop, 2015. **35**(8): p. e90-2.
- 104. Herrera-Soto, J.A., et al., *Increased intracapsular pressures after unstable slipped capital femoral epiphysis*. J Pediatr Orthop, 2008. **28**(7): p. 723-8.
- 105. Davis, R.L., 2nd, et al., *Treatment of Unstable Versus Stable Slipped Capital Femoral Epiphysis Using the Modified Dunn Procedure*. J Pediatr Orthop, 2017.
- 106. Agricola, R., et al., *Cam impingement causes osteoarthritis of the hip: a nationwide prospective cohort study (CHECK)*. Ann Rheum Dis, 2013. **72**(6): p. 918-23.
- 107. Agricola, R., et al., Cam impingement: defining the presence of a cam deformity by the alpha angle: data from the CHECK cohort and Chingford cohort. Osteoarthritis Cartilage, 2014. 22(2): p. 218-25.
- 108. Oner, A., et al., The prevalence of femoroacetabular impingement as an aetiologic factor for end-stage degenerative osteoarthritis of the hip joint: analysis of 1,000 cases. Hip Int, 2016. **26**(2): p. 164-8.
- 109. Palmer, A., et al., Diagnostic and prognostic value of delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC) in early osteoarthritis of the hip. Osteoarthritis Cartilage, 2017. 25(9): p. 1468-1477.
- 110. Bittersohl, B., et al., *Current concepts in management of slipped capital femoral epiphysis.* Hip Int, 2015. **25**(2): p. 104-14.
- 111. Jones, C.E., et al., *Relationships Between Severity of Deformity and Impingement in Slipped Capital Femoral Epiphysis*. J Pediatr Orthop, 2017. **37**(4): p. 272-278.

- 112. Nicholls, A.S., et al., *The association between hip morphology parameters and nineteen-year risk of end-stage osteoarthritis of the hip: a nested case-control study.* Arthritis Rheum, 2011. **63**(11): p. 3392-400.
- 113. Thomas, G.E., et al., Subclinical deformities of the hip are significant predictors of radiographic osteoarthritis and joint replacement in women. A 20 year longitudinal cohort study. Osteoarthritis Cartilage, 2014. **22**(10): p. 1504-10.
- 114. Basheer, S.Z., et al., Arthroscopic treatment of femoroacetabular impingement following slipped capital femoral epiphysis. Bone Joint J, 2016. **98-B**(1): p. 21-7.
- 115. Terjesen, T. and A. Wensaas, *Prognostic factors for long-term outcome of chronic slipped capital femoral epiphysis treated with fixation in situ*. J Child Orthop, 2017. **11**(2): p. 114-119.
- 116. Azegami, S., D. Kosuge, and M. Ramachandran, Surgical treatment of femoroacetabular impingement in patients with slipped capital femoral epiphysis: A review of current surgical techniques. Bone Joint J, 2013. 95-B(4): p. 445-51.
- 117. Bali, K., et al., Subcapital osteotomy of the femoral neck for patients with healed slipped capital femoral epiphysis. Bone Joint J, 2014. **96-B**(11): p. 1441-8.
- 118. Kinds, M.B., et al., A systematic review of the association between radiographic and clinical osteoarthritis of hip and knee. Osteoarthritis Cartilage, 2011. **19**(7): p. 768-78.
- 119. Altman, R.D., *Criteria for classification of clinical osteoarthritis.* J Rheumatol Suppl, 1991. **27**: p. 10-2.
- 120. Castaneda, P., et al., *The natural history of osteoarthritis after a slipped capital femoral epiphysis/the pistol grip deformity.* J Pediatr Orthop, 2013. **33 Suppl 1**: p. S76-82.
- 121. Lehmann, T.G., et al., *Total hip arthroplasty in young adults, with focus on Perthes' disease and slipped capital femoral epiphysis: follow-up of 540 subjects reported to the Norwegian Arthroplasty Register during 1987-2007.* Acta Orthop, 2012. **83**(2): p. 159-64.
- 122. Boyle, M.J., C.M. Frampton, and H.A. Crawford, *Early results of total hip arthroplasty in patients with slipped upper femoral epiphysis compared with patients with osteoarthritis.* J Arthroplasty, 2012. **27**(6): p. 1003-7.
- 123. Sankar, W.N., et al., Femoroacetabular impingement: defining the condition and its role in the pathophysiology of osteoarthritis. J Am Acad Orthop Surg, 2013. **21 Suppl 1**: p. S7-S15.
- 124. Venn, M. and A. Maroudas, *Chemical composition and swelling of normal and osteoarthrotic femoral head cartilage. I. Chemical composition.* Ann Rheum Dis, 1977. **36**(2): p. 121-9.

- 125. Bashir, A., et al., Glycosaminoglycan in articular cartilage: in vivo assessment with delayed Gd(DTPA)(2-)-enhanced MR imaging.
 Radiology, 1997. **205**(2): p. 551-8.
- 126. Bashir, A., et al., *Nondestructive imaging of human cartilage glycosaminoglycan concentration by MRI*. Magn Reson Med, 1999. **41**(5): p. 857-65.
- 127. Samosky, J.T., et al., *Spatially-localized correlation of dGEMRIC-measured GAG distribution and mechanical stiffness in the human tibial plateau.* J Orthop Res, 2005. **23**(1): p. 93-101.
- 128. Zilkens, C., et al., *Current knowledge and importance of dGEMRIC techniques in diagnosis of hip joint diseases*. Skeletal Radiol, 2015. **44**(8): p. 1073-83.
- 129. Owman, H., et al., Association between delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) and joint space narrowing and osteophytes: a cohort study in patients with partial meniscectomy with 11 years of follow-up. Osteoarthritis Cartilage, 2014. 22(10): p. 1537-41.
- 130. Tiderius, C.J., et al., *Gd-DTPA2*)-enhanced MRI of femoral knee cartilage: a dose-response study in healthy volunteers. Magn Reson Med, 2001. **46**(6): p. 1067-71.
- 131. Thorborg, K., et al., *The Copenhagen Hip and Groin Outcome Score* (HAGOS): development and validation according to the COSMIN checklist. Br J Sports Med, 2011. **45**(6): p. 478-91.
- 132. Mokkink, L.B., et al., Protocol of the COSMIN study: COnsensus-based Standards for the selection of health Measurement INstruments. BMC Med Res Methodol, 2006. 6: p. 2.
- 133. Tiderius, C., et al., *dGEMRIC as a function of BMI*. Osteoarthritis Cartilage, 2006. **14**(11): p. 1091-7.
- 134. Notzli, H.P., et al., *The contour of the femoral head-neck junction as a predictor for the risk of anterior impingement.* J Bone Joint Surg Br, 2002. **84**(4): p. 556-60.
- 135. Engelsma, Y., et al., *Progressive slip after removal of screw fixation in slipped capital femoral epiphysis: two case reports.* J Med Case Rep, 2012. **6**: p. 405.
- 136. Sanders, J.O., et al., *Progressive slippage after pinning for slipped capital femoral epiphysis*. J Pediatr Orthop, 2002. **22**(2): p. 239-43.
- 137. Holmdahl, P., et al., *Continued growth after fixation of slipped capital femoral epiphysis.* J Child Orthop, 2016. **10**(6): p. 643-650.
- 138. Seller, K., et al., Clinical outcome after transfixation of the epiphysis with Kirschner wires in unstable slipped capital femoral epiphysis. Int Orthop, 2006. **30**(5): p. 342-7.
- 139. Abraham, E., et al., *Clinical implications of anatomical wear characteristics in slipped capital femoral epiphysis and primary osteoarthritis.* J Pediatr Orthop, 2007. **27**(7): p. 788-95.

- 140. Howse, E.A., et al., Arthroscopic treatment of slipped capital femoral epiphysis screw impingement and concomitant hip pathology. Arthrosc Tech, 2014. **3**(4): p. e515-7.
- 141. Murgier, J., et al., *The frequency of sequelae of slipped upper femoral epiphysis in cam-type femoroacetabular impingement.* Bone Joint J, 2014. **96-B**(6): p. 724-9.
- 142. Nectoux, E., et al., Evolution of slipped capital femoral epiphysis after in situ screw fixation at a mean 11 years' follow-up: a 222 case series.

 Orthop Traumatol Surg Res, 2015. **101**(1): p. 51-4.
- 143. Leunig, M., C.R. Fraitzl, and R. Ganz, [Early damage to the acetabular cartilage in slipped capital femoral epiphysis. Therapeutic consequences]. Orthopade, 2002. **31**(9): p. 894-9.
- 144. Helgesson, L., et al., *Early osteoarthritis after slipped capital femoral epiphysis*. Acta Orthop, 2017: p. 1-7.
- 145. Zilkens, C., et al., *Delayed gadolinium-enhanced magnetic resonance imaging of cartilage (dGEMRIC), after slipped capital femoral epiphysis.* Eur J Radiol, 2011. **79**(3): p. 400-6.
- 146. Thorborg, K., et al., Copenhagen hip and groin outcome score (HAGOS) in male soccer: reference values for hip and groin injury-free players. Br J Sports Med, 2014. **48**(7): p. 557-9.
- 147. Fraitzl, C.R., et al., Radiological evidence of femoroacetabular impingement in mild slipped capital femoral epiphysis: a mean follow-up of 14.4 years after pinning in situ. J Bone Joint Surg Br, 2007. **89**(12): p. 1592-6.
- 148. Bay-Jensen, A.C., et al., Which elements are involved in reversible and irreversible cartilage degradation in osteoarthritis? Rheumatol Int, 2010. **30**(4): p. 435-42.
- 149. Monazzam, S., et al., *Does femoral rotation influence anteroposterior alpha angle, lateral center-edge angle, and medial proximal femoral angle? A pilot study.* Clin Orthop Relat Res, 2013. **471**(5): p. 1639-45.
- 150. Tiderius, C.J., et al., dGEMRIC (delayed gadolinium-enhanced MRI of cartilage) indicates adaptive capacity of human knee cartilage. Magn Reson Med, 2004. **51**(2): p. 286-90.
- 151. Tiderius, C.J., et al., *Hip dGEMRIC in asymptomatic volunteers and patients with early osteoarthritis: the influence of timing after contrast injection.* Magn Reson Med, 2007. **57**(4): p. 803-5.