Håvard Moksnes

Functional and radiological outcomes following a non-operative treatment algorithm after ACL injuries in skeletally immature children

DISSERTATION FROM THE NORWEGIAN SCHOOL OF SPORT SCIENCES • 2013

ISBN nr 978-82-502-0489-8

To Cathrine, Sofie and Ola

Out of the night that covers me,
Black as the pit from pole to pole,
I thank whatever gods may be
For my unconquerable soul.

In the fell clutch of circumstance
I have not winced nor cried aloud.
Under the bludgeonings of chance
My head is bloody, but unbowed.

Beyond this place of wrath and tears
Looms but the Horror of the shade,
And yet the menace of the years
Finds and shall find me unafraid.

It matters not how strait the gate,
How charged with punishments the scroll.
I am the master of my fate:
I am the captain of my soul.

William Ernest Henley (1875)

Acknowledgements

It is with a great feeling of pride and appreciation that I am writing the final words of this dissertation. I am honoured to have been a team member in NAR since the very beginning in 2003. The ten years have been a journey in which I have been allowed to develop skills and interests that would have never crossed my mind unless our unique research collaboration had been created. I am proud to have played my part in the development of establishing NAR as an international research group of significance.

I offer my deepest gratitude to May Arna Risberg. You brought me into clinical research on active rehabilitation, and have served as my main supervisor throughout every project thereafter. Your enthusiasm, knowledge, and availability are exceptional. I am looking forward to our continued quest for effective rehabilitation strategies and improved clinical practice.

I am also grateful to have had the honour of having Lars Engebretsen as my co-supervisor. Your clinical skills, compassion, and consistency with treatment decision making have given me insights way beyond what is accomplishable through text-books. Additionally, you and May Arna are in my opinion an unconquerable team!

Moreover, I thank all the children and their families who have been exceptionally positive and compliant throughout the projects. This dissertation would obviously not have been a reality if you had not invested your time and effort. You are contributing to the largest prospective study within this field so far, and I am looking forward to following your knee function in the years to come as well.

I am thankful to all my female colleagues in NAR. All of you prove every day that both persistence and dedication are needed to perform high quality research, and that it is possible to have fun while doing it. I am happy to have been your male alibi with regard to gender equality over the years. In particular I appreciate the problem solving conversations with Ingrid Eitzen, and I also thank the three research coordinators who have been involved with my projects; Linn Gjersing, Kristin Bølstad, and Emilie Jul-Larsen Aas, your help with logistics and guidance through the various parts of our organisation have been priceless. I also thank our Aussie friends, Ben and Adam, for valuable discussions and being my "coaches" in the English language. The master students who have contributed to the data collections are also highly valued.

I thank the Norwegian School of Sport Sciences, Department of Sports Medicine, personalised by Roald Bahr and Sigmund Alfred Andersen, for including me and my project to your inspiring organisation. The working atmosphere at SIM is without doubt branded with quality, and my fellow PhD companions in SIM3 are the best example. I have enjoyed every single day that I have been present.

Our collaboration with the Department of Radiology and Nuclear Medicine at the Oslo University Hospital is acknowledged. I know that the children experienced safe and friendly assessments, although some of them may have had their doubts about entering the gigantic MRI machine. A special thank is offered to Anne Hilde Farstad for the management of the 80 consultations. Furthermore, Tone Elise Orheim Døli, Wibeke Nordhøy, and Øivind Giertsen are acknowledged for their contribution with the development and quality assurance of the MRI investigations.

A special recognition is also offered to Tariq Rana and Arne Larmo. Your enthusiasm and devotion in the analysis of the MRIs were impressive. I have enjoyed our meetings, and my knowledge on how to interpret knee MRIs has improved substantially due to your elaborations.

Since 1999 I have had the privilege of working as a physiotherapist at NIMI, and I am glad to thank Knut Jæger Hansen for taking me in as a novice back then. It is hard to find words to describe the unique dedication and professionalism that is found in every office in our clinic. I am confident that together we will continue to develop clinical puzzles, which can be elaborated further in collaboration with NAR in the best interest of our patients.

Mum and dad; you probably did something smart when you allowed me to spend all my energy on sports for a long period of my younger years, as it feels like your strategy has somehow saved energy for academic purposes later in life. However, you also guided me adequately through all other aspects of growing up, and I am grateful for your support and encouragement. Maria and Magnus, you both have your own ways of being supportive which are highly appreciated! Furthermore, my brother in law, Magnus, is accredited for his contribution to the medical literature with his illustrations of surgical techniques.

Sofie, you have essentially been growing up parallel to the development of this dissertation. I love your enthusiasm with everything from sports to handicraft, and I enjoy taking part of your life filled with friends and fun. Ola, you are an energetic boy filled with emotions and curiosity. I am quite sure that we will continue to climb, kick, jump, and not at least extinguish fires in many years to come. Both of you can look forward to substantial amounts of knee injury prevention.

Finally, to my wife Cathrine I express my humblest gratitude. You are the pillar of our family, and even when our days are challenged by the rigors of everyday events, you always manage to convey a cool, encouraging smile. You are impressively managing your own career, and I am excited to see what the future will bring us.

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This dissertation project was performed at the Norwegian Research Center for Active Rehabilitation (NAR) in the period 2006–2012. NAR is a formal research collaboration between the Norwegian School of Sport Sciences, Department of Sports Medicine; the Oslo University Hospital, Department of Orthopaedic Surgery; and the Norwegian Sports Medicine Clinic (NIMI).

The main source of funding for this dissertation was the Norwegian School of Sport Sciences, Department of Sports Medicine. The Eastern Norway Regional Health Authority has also contributed with some funding.

The Department of Orthopaedic Surgery, and the Department of Radiology and Nuclear Medicine, Oslo University Hospital, is acknowledged for contribution with infrastructure and resources in particular for paper III and IV. Furthermore, NIMI is highly acknowledged for contribution to research through research coordinator and infrastructure.

Thank you all!

Oslo

December 10, 2012

Håvard Moksnes

Table of contents

Abbreviations

ACL	Anterior cruciate ligament
AM	Anteromedial
ANOVA	Analysis of variance
CMS	Coleman Methodology Score
ESSKA	European Society of Sports Traumatology Knee Surgery and Arthroscopy
ICC	Intraclass correlation coefficient
ICRS	International Cartilage Repair Society
IKDC	International Knee Documentation Committee
KOOS	Knee Injury and Osteoarthritis Outcome Score
KOS-ADLS	Knee Outcome Survey Activities of Daily Living Scale
LCL	Lateral collateral ligament
LSI	Leg symmetry index
MCL	Medial collateral ligament
MDC	Minimal detectable change
MRI	Magnetic resonance imaging
NAR	Norwegian Research Center for Active Rehabilitation
NKLR	Norwegian Knee Ligament Registry
Nm	Newton meter
NMT	Neuromuscular training
OA	Osteoarthritis
OUS	Oslo University Hospital
PCL	Posterior cruciate ligament
PL	Posterolateral
PT	Peak torque
RCT	Randomised Controlled Trial
ROM	Range of motion
SD	Standard deviation
SEM	Standard error of measurement
SH	The single hop test
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
T	Tesla
TCH	The triple crossover hop test
TH	The triple hop test
VAS	Visual Analogue Scale
6m-timed	The six meter timed hop test

List of Papers

This dissertation is based on the following research papers, which are referred to in the text by their Roman numerals:

I. Moksnes H, Engebretsen L, Risberg MA. Management of anterior cruciate ligament injuries in skeletally immature individuals. *J Orthop Sports Phys Ther 2012;42(3):172-183*.

II. Moksnes H, Engebretsen L, Risberg MA. The current evidence for treatment of ACL injuries in children is low: A systematic review. *J Bone Joint Surg Am 2012 June 20;94(12):1112-1119*.

III. Moksnes H, Engebretsen L, Eitzen I, Risberg MA. Functional outcomes following a non-operative treatment algorithm for anterior cruciate ligament injuries in skeletally immature children 12 years and younger. A prospective cohort with 2 years follow-up.
Submitted *Br J Sports Med* December 7, 2012. Revision submitted January 30, 2013.
Accepted February 3, 2013. *Br J Sports Med 2013 May;47(8):488-94*.

IV. Moksnes H, Engebretsen L, Risberg MA. Low incidence of new meniscus and cartilage injuries after non-operative treatment of anterior cruciate ligament tears in skeletally immature children: Prospective cohort study.
Submitted *Am J Sports Med,* October 18, 2012. Revision submitted March 10, 2013.
Accepted April 2, 2013.

Summary of Papers I-IV

Paper I was a narrative review in which the different treatment alternatives for anterior cruciate ligament (ACL) injuries in skeletally immature children advocated in the literature were outlined and discussed. Based on the literature, and the results and clinical experiences from our previously published retrospective case series, our evidence-based non-operative treatment algorithm was proposed. The treatment algorithm included a structured rehabilitation program through four phases which was described in detail. Progression guidelines for the three rehabilitation phases were specified with clinical milestones, and exercises targeted towards deficits in range of motion, neuromuscular control, and muscle strength were incorporated. The fourth phase included exercises to encourage secondary prevention of new injuries to the knee, which was encouraged when the child was released from physical therapy subsequent to passing a performance-based functional test battery. We proposed that an ACL reconstruction should not be considered unless a non-functional knee was documented despite performing adequate rehabilitation. Additionally, a symptomatic meniscus injury, or decline to an unacceptably low activity level could be secondary indications for surgical treatment before skeletal maturity.

The purpose of **Paper II** was to evaluate the methodological quality of the literature on treatment of ACL injuries in skeletally immature children using the Coleman Methodology Score (CMS). We performed a systematic review in which 31 publications and a total of 966 children who had been treated for an ACL injury were included. No randomised controlled trials, 2 prospective studies, and 29 retrospective case series were analysed. The majority of papers were on transphyseal ACL reconstructions (n=19), while physeal sparing reconstructions (n=8), and non-operative treatment (n=4) were less frequent. The methodological quality was generally low. The mean CMS was 44.7 ± 9.2; the highest score was 62 points, and the lowest score 28 points. We concluded with a recommendation that in future studies more attention should be focused towards prospective designs, the inclusion of larger sized homogenous skeletally immature populations, the reporting of rehabilitation protocols, monitoring of activity level, and the use of performance-based functional outcome measurements.

Paper III was a prospective cohort study, in which the aims were to report changes in patient-reported and performance-based functional outcomes, and to evaluate the possible changes in activity level in 46 ACL injured children following our non-operative treatment algorithm published in **Paper I**. There were 16 (35%) girls and 30 (65%) boys, with a mean age of 11.0 ±

1.5 years at time of injury included in this study. The mean follow-up time was 3.2 ± 1.1 years from injury to the last follow-up examination. Knee function was evaluated at a baseline assessment and subsequent yearly follow-ups using the same test battery; three patient-reported outcome measurements, isokinetic muscle strength measurements, four single legged hop tests, knee joint laxity measurements, and a clinical examination. The children's activity level was monitored through a monthly online activity survey, and registration of their main leisure time sport activity was done at the yearly follow-ups. The non-operative treatment algorithm proposed in **Paper I** was implemented. An ACL reconstruction was considered before skeletal maturity only if the child reported multiple giving way episodes, a symptomatic meniscus injury, or a substantially reduced activity level. The main findings were that a majority (n=36, 78%) of the included children remained non-operated with satisfactory knee function throughout the 2 years follow-up. Ninety-one per cent of the children reported consistent participation in pivoting sports and physical education classes in school; still 38% of the non-operated children reported a reduction in performing Level 1 activities as their main leisure time sport activity. The results of the patient-reported outcome measurements showed statistical significant changes for the KOOS subscale *Activity of daily living* which increased from baseline to the 1 year follow-up, and declined from the 1 year to the 2 years follow-up. The changes were, however, small and of questionable clinical significance. Knee function measured with the single legged hop tests showed a statistically significant change for the single hop test which increased from baseline to the 1 year follow-up, and the six meter timed hop test which declined from the 1 year to the 2 years follow-up. However, these changes were also minor and of questionable clinical significance. The isokinetic knee extension and flexion muscle strength significantly improved over the course of the study. Ten of the ACL reconstructed children reported abandoning a Level 1 activity as main leisure time sport activity from pre-injury to the 2 years post-operative follow-up. We concluded that a non-operative treatment algorithm may be appropriate for ACL injured skeletally immature children, although a reduced participation in Level 1 activities may be necessary for some children.

The aim of **Paper IV** was to prospectively investigate the incidence of new injuries to the menisci and articular cartilage in non-operatively treated ACL injured skeletally immature children using bilateral 3.0Tesla magnetic resonance imaging (MRI). The first 40 children who were included in the prospective cohort study were consecutively recruited to this part of the investigation. There were 14 girls (35%) and 26 boys (65%), with an age of 11.0 ± 1.4 years at time of injury. All children underwent a bilateral MRI investigation at a mean time of 2.2 ± 1.4 years after their

ACL injury. Subsequently, a second bilateral MRI investigation was performed at an average of 1.7 ± 0.1 years after the first MRI. Thirty children had not undergone ACL reconstruction at the first MRI, and we found the prevalence of meniscus and articular cartilage injuries in these children to be 32.2% and 9.7%, respectively. The incidence of new meniscus injuries during the follow-up period between the first and second MRI was 3.2% (n=1), while the corresponding incidence for new articular cartilage injuries was 3.2% (n=1). We concluded that the incidence of new injuries to the menisci and articular cartilage in skeletally immature children was low following a non-operative treatment algorithm after ACL injury. The mean follow-up time from injury was 3.8 ± 1.3 years. The results may encourage more orthopedic surgeons to consider recommending a non-operative treatment algorithm with regular follow-ups to skeletally immature children with ACL injury. However, longer follow-up is needed to document the long-term outcomes.

Introduction

The incidence of ACL injuries in skeletally immature children is unknown.[195, 221] The 2012 annual report from the Norwegian Knee Ligament Registry (NKLR) documented that approximately 50 children between the ages of 10 and 14 years underwent an anterior cruciate ligament (ACL) reconstruction (Figure 1) in 2011.[2] It is likely that a majority of these individuals were skeletally immature at the time of ACL reconstruction, although skeletal maturity is not registered in the NKLR.

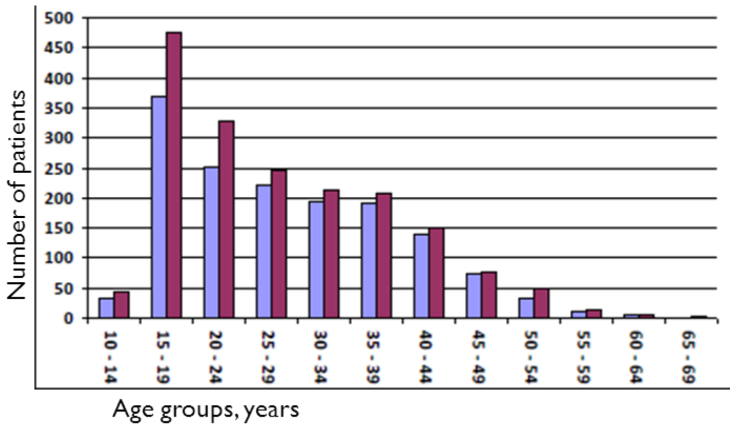

Figure 1 *Age distribution of primary ACL reconstructions performed in Norway in 2011[2]. Blue bars are average annual numbers 2004-2010, and purple bars are numbers from 2011.*

Intercondylar tibial eminence avulsion fractures involving the ACL are frequent and have long been assumed to be the most common injury involving the ACL in skeletally immature children.[136] Since a paper on surgical treatment of tibial spine avulsion injuries with involvement of the ACL from Roth in 1928,[209] consensus have developed affirming that the majority of these injuries should be treated surgically with fixation to the bone.[136, 150] Instability and functional impairments following intrasubstance ACL tears in skeletally immature children have, however, been increasingly recognised over the last 30 years.[228] These injuries were not commonly acknowledged until the early 1980s, and there is still considerable controversy with regard to their treatment.[54, 63, 118, 157, 230, 247] Historically, ACL injuries in adult athletes have been treated with surgical reconstruction to enable return to sport with a functionally stable knee joint.[186, 187] However, knowledge on the vulnerability of the epiphyseal growth plates have required a more cautious approach with regard to treatment decision making of ACL injuries in skeletally immature children.[29, 127] Consequently, one of three different treatment algorithms is traditionally recommended to skeletally immature children after ACL injury: a transphyseal surgical reconstruction, a physeal sparing ACL reconstruction, or non-operative treatment with active rehabilitation. Specific decision criteria with regard to which of these algorithms a child should be recommended have not been established, and treatment decisions are traditionally based on the experiences and practice of the individual orthopaedic surgeon or institution. Additionally, current knowledge from long-term studies on adult ACL injured subjects have demonstrated an increased risk of post-traumatic knee osteoarthritis (OA) following an ACL injury.[188] As a consequence, intrasubstance ACL injuries in children and adolescents have been especially worrisome in the paediatrics orthopaedic community due to the possibility of persistent functional disabilities at a very young age.[81, 118] Furthermore, epidemiological studies have stated that high levels of physical fitness at young ages decrease future mortality and morbidity,[60, 61, 222] and that the participation of children in organised and leisure time sport activities is increasingly popular and widespread.[41] However, there is a concern that increased participation in sport exposes children to higher risks of musculoskeletal injuries. Knee injuries may have a detrimental effect on long term health,[152, 200] as they can indirectly counter the beneficial health effects from sports participation at a young age.[152] Interestingly, the challenges with regard to treatment decision making in ACL injured skeletally immature children was addressed by Stanitski already in 1995; *"An ACL injury in this age group is not a surgical emergency; therefore, time for discussion with the patient and his or her parents is available, so that all appropriate options can be considered"*.[229]

Our institutions have traditionally advocated primary non-operative treatment for ACL injuries in skeletally immature children. The results from the first eight years of advocating a consistent non-operative treatment approach were published in 2008,[174] and became the catalyst for the development of the more detailed non-operative treatment algorithm which has been presented and evaluated in the work with the present dissertation.

Anatomy of the knee and the anterior cruciate ligament

The knee joint is a complex joint in which motion and stability are controlled by passive (ligaments, bones and cartilage) and active (neuromuscular) structures. The stabilising systems of the knee ligaments include intra- and periarticular collagen structures (Figure 2), in addition to the dynamic stability provided by the neuromuscular systems. The intraarticular structures are the ACL, the posterior cruciate ligament (PCL), and the menisci, while the periarticular structures are comprised of the joint capsule, the medial collateral ligament (MCL), the lateral collateral ligament (LCL), and the posterior ligaments and tendons.[119, 137] The ACL has been documented to be the primary restraint to anterior displacement of the tibia relative to the femur, and is a secondary restraint to knee rotation and frontal plane angulations.[28]

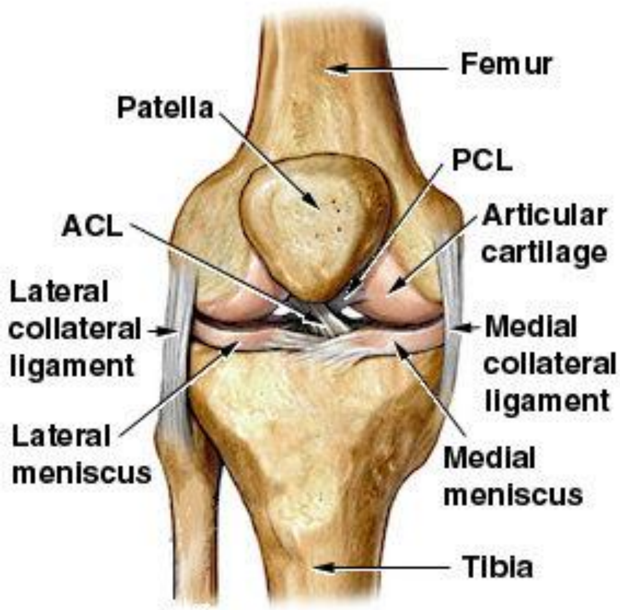

Figure 2 *The structures of the knee (right knee in a frontal view). Derived and modified from Netter.*[183]

The ACL consist of two bundles; the anteromedial bundle and the posterolateral bundle.[119, 197] The anteromedial bundle is located proximal and anterior in the femoral intercondylar notch, while the posterolateral bundle originates in the distal and posterior aspect.

At the tibial insertion the ACL fans out and the anteromedial bundle insertion is located in the anterior part of the tibial ACL footprint, whereas the posterolateral bundle is located in the posterior part.[197] The anteromedial and posterolateral bundles stabilise the knee joint in response to anterior tibial loads and combined rotational loads in a synergistic way. The anteromedial bundle is the primary restraint against anterior tibial translation, while the posterolateral bundle stabilises the knee near full extension, particularly against rotation.[254, 256]

The skeletally immature knee

As a consequence of the continuous skeletal growth in children the anatomy and physiology is in constant development. The epiphyseal growth plates are situated between the epiphyseal and metaphyseal bone (Figure 3). Within the growth plate, immature cells lie toward the epiphysis, with more mature chondrocytes in the proliferating zone, and large chondrocytes located in the hypertrophic zone adjacent to the proliferating zone.[62] During childhood, the growth plate matures; its total width decreases, and at the end of puberty it disappears with complete replacement by bone which marks the completion of vertical growth.[62] Tanner and Davies[236] stated that the adolescent growth spurt begins at an average of 10.5 years in girls and 12.5 years in boys, with peak velocity at 11.5 years in girls and 13.5 years in boys. Maturation through puberty is highly individual and large variations are normal.[237] Radiological measures of skeletal maturity are typically derived into the three categories: wide open (skeletally immature), open (adolescent) and closed (mature or adult), [20, 23, 94, 139, 159] based on assessments where x-rays of the wrist are compared to atlas of a normal population [90, 163]. Biological maturity is usually reported as Tanner stages typically subdivided into: stage 1 as pre-puberty, stages 2 and 3 as puberty, and stages 4 and 5 as adolescence.[144]

The distal femoral physis is the most active growth plate in the human body contributing approximately 1 cm of growth per year. It is responsible for 70% of the femoral longitudinal growth and 37% of the growth of the lower limb. The proximal tibial physis contribute approximately 0.7 cm of growth per year, which equals 25% of the lower limb growth and 55% of the tibial growth.[223] The epiphyseal growth plates are vulnerable to injury, and damage may result in significant angular deformities and limb length discrepancies.[40, 127] Furthermore, due largely to the constant growth and development, cartilaginous tissues in children are assumed to have an increased rate and ability of healing compared to matured tissue.[223] Consequently, the menisci and articular cartilage differ from adults with a higher amount of immature cells and vessels, which are probably creating an enhanced reparative potential.[16, 151, 164, 178]

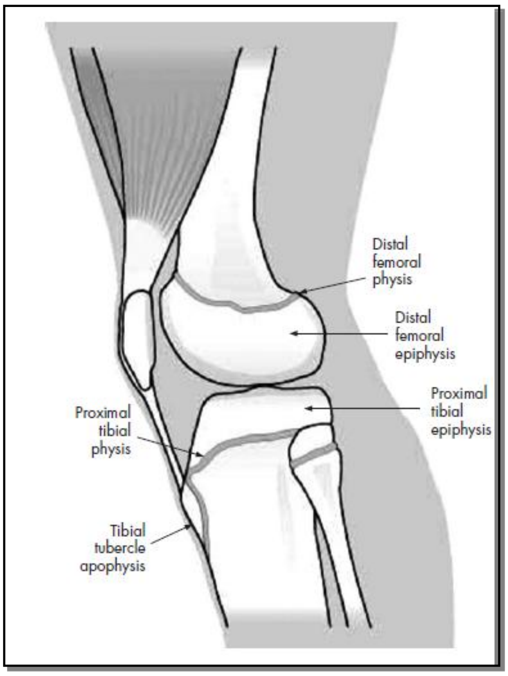

Figure 3 *Illustration of the location of the physes and epiphyses of the distal femur and proximal tibia. From Caine et al.*[40]

Behr et al.[24] and Shea et al.[219] have described the anatomy of the ACL in skeletally immature individuals, showing that the femoral origin is completely epiphyseal. Additionally, Kim et al.[122] have shown that the anatomy with regard to the angles between the tibia and the ACL increase during growth. A relatively narrow intercondylar notch also increases the technical challenge for orthopaedic surgeons with the drilling of graft tunnels when performing ACL reconstructions in skeletally immature children. However, Shea et al.[219] stated that although the ligaments in younger individuals are smaller, the anatomical landmarks for locating the appropriate tunnel placement are proportionate in the adult and skeletally immature knee.[220] To our knowledge, no anatomical or biomechanical cadaver studies have been performed to investigate the macroscopic anatomy in children.

Introduction

Several investigations have documented that paediatric knees are more loose than adult knees,[22, 66, 72, 99] and although this has not been sufficiently examined, girls are believed to have increased joint laxity compared to boys.[66, 72, 99] Knee joint laxity has been demonstrated to decrease during puberty, and the progressive decrease with age has been demonstrated by Baxter (Figure 4).[22]

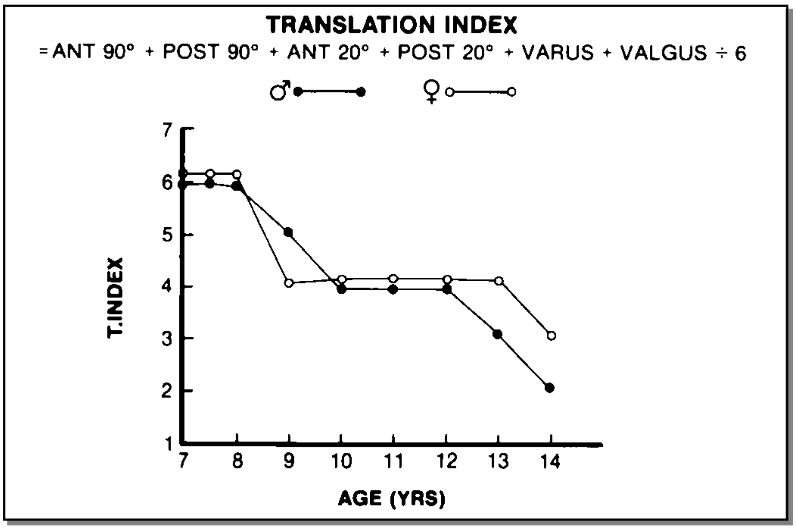

Figure 4 *Illustration showing the decrease in overall knee laxity for girls and boys from age 7 to age 14 years. From Baxter.*[22]

The combination of lower weight and joint compression forces, and the increased laxity in the knees of skeletally immature children are believed to be part of the reason why traumatic meniscal and cartilage injuries are rarely seen in children below 10 years of age.[44, 116, 163, 223] The cartilage volume and thickness also increases during growth, and this increase has been shown to correlate with levels of activity. Those who do more vigorous sports have thicker articular cartilage.[116]

Risk factors for knee injuries in children

Specific risk factors for knee injuries in children have not been firmly established, although the incidence of knee injuries in children has been reported to be increasing.[195] However, the activity patterns of children include a large proportion of non-organised activity which makes incidence calculations difficult, which is essential for risk factor estimations.[217, 227] There are no epidemiological studies identifying specific risk factors for knee injuries in skeletally immature children below the age of 13 years. However, the risk of injury among children appears to be low, and to consistently increase with age and participation at higher levels in all sports.[60, 123] The exception is injuries sustained in alpine skiing, of which a majority of injuries are reported to occur in younger and novice participants.[89, 162] Furthermore, there seems to be evidence that adolescent girls are more prone to suffer knee injuries in gymnastics, soccer, handball, and basketball compared to boys.[32, 60, 98, 149, 190] It has been shown that adolescents with poor neuromuscular control of the knee in drop landings, and those with deficits in trunk control, have increased risk of sustaining an ACL injury when performing team ball-sports.[73, 97, 98, 179, 257]

An increased long-term risk of knee OA is a well-documented consequence of ACL injury in adults.[148, 188, 246] However, the specific risk factors for the development of knee OA are not fully understood.[28, 121, 188] Concomitant or secondary meniscus and cartilage injuries seem to be important additional risk factors, while undergoing an ACL reconstruction does not seem to reduce the long-term risk of knee OA.[28, 148, 188, 206, 246] None of the risk factors for the development of knee OA have been adequately investigated in skeletally immature children after ACL injury.[76, 117, 176]

Prevention of knee injuries

Several studies have documented significantly reduced injury incidence after implementation of specific injury prevention strategies in adolescents and adults.[190, 224] However, prevention of knee injuries in children with a structured warm-up routine has not been shown to be successful to the same degree as in adolescents.[55] The development of new equipment and high-risk snow-park areas for children and adolescents may, in combination with more aggressive styles of skiing, explain the continued increase in skiing injuries among the youngest skiers.[79, 80] Additionally, the use of skiing equipment that is originally designed for adults and wrong adjustment of binding release mechanisms, may put the young skiers at risk when a fall occur.[37, 68, [89, 182] An interesting proposal on how to reduce the rates of skiing injuries in children and adolescents has been stated by Meyers et al.[162]: *"As with all high-risk sports the answer may lie in increased wisdom and responsibility of both the skier and the parent to ensure an adequate level of ability, self-control and simply common sense as they venture out on the slopes"* .[162]

Treatment of ACL injuries

Anterior cruciate ligament injuries are most frequent in young individuals who are participating in pivoting sports which involve running, cutting, hopping and landing.[15, 39] Studies utilising biomechanical evaluations suggest that a non-contact ACL tear occurs approximately 40 milliseconds after initial ground contact, and involves an immediate sudden knee valgus and knee internal rotation collapse.[131, 133, 134] A intrasubstance rupture of the ACL usually occurs at the proximal insertion site of the ACL on the lateral wall of the intercondylar notch,[254] and a distinct "pop" is often heard. The subject typically experiences pain and a feeling of the knee "giving way" when the ligament ruptures.[25, 124] The acute ACL injury is commonly followed by intraarticular effusion and impaired function, while the persistent disability after the acute phase is believed to be caused by the combination of mechanical instability and impaired neuromuscular control, resulting in dynamic knee joint instability.[143] To counter the dynamic knee instability, ACL injured subjects go through rehabilitation including neuromuscular and strength exercises to restore the muscular components of dynamic knee stability.[42, 108] Further treatment of ACL injuries may be surgical with arthroscopic reconstruction of the ligament followed by extensive rehabilitation. However, in some cases dynamic stability may be achieved through extensive rehabilitation alone.[107, 250] Recent studies have shown that patients undergoing non-operative treatment may in many cases return to their pre-injury activity level, and also experience good knee function in the long-term.[74, 84] Additionally, medium-term follow-up studies of ACL reconstructed athletes have demonstrated that the true return to pre-injury level sports rates are probably lower than previously expected.[11, 14]

Treatment algorithms for ACL injuries in skeletally immature children

The recognition of intrasubstance ACL injuries in children has added a new dimension to the treatment of patients with ACL injury. Skeletally immature children represent a population which is unique in two ways compared to the adult population of ACL injured individuals: (1) they have open growth plates which have implications related to surgical treatment,[127, 163] and (2) they have a high natural activity level through play and daily activities.[227] There is today no consensus on decision making criteria to decide whether a skeletally immature child with ACL insufficiency should undergo surgical treatment or not.[95, 172] The main challenge in the treatment of children with ACL injuries is, therefore, to balance the risk of iatrogenic growth disturbance and the uncertain development of the graft following surgical treatment, to the risk of sustaining secondary meniscus or cartilage injuries from possible repetitive giving way episodes. Adding to this clinical conundrum is the challenge to meet the wishes of the child, the parents, and society as a whole with regard to upholding an active lifestyle throughout childhood.

The risk of iatrogenic growth disturbance due to damage to the distal femoral physis or the proximal tibial physis has meant that orthopaedic surgeons need to be extra cautious with regard to advising ACL reconstructions in skeletally immature children.[43, 125, 127] Based on ovine studies Wilmes et al.[251] have suggested the period at the end of skeletal growth to be the time for peak risk of growth disturbance after injury to, or surgical drilling through, the growth plates (Figure 5).

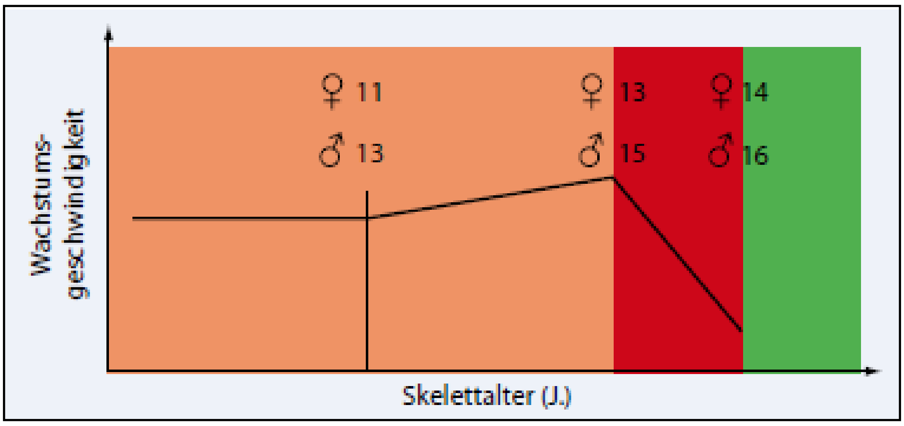

Figure 5 *Illustration showing the speed of skeletal growth on the y-axis, and the skeletal bone age at the x-axis. The red area illustrates the end of skeletal growth where the danger of growth disturbances is believed to be highest. From Wilmes et al.*[251]

However, the development of new and allegedly safer surgical techniques has increased the number of orthopaedic surgeons who advocate early ACL reconstructions also in children with open growth plates.[20, 125, 139, 215] Hence, the risk of growth disturbances is more frequently regarded acceptable compared to the disadvantages of possible secondary injuries and activity modification – leading increasing numbers of surgeons to advocate surgical treatment to skeletally immature children.[7, 45, 69, 105, 129, 144, 166, 215] More conservative algorithms usually consist of non-operative treatment with physical therapy, activity limitations, and bracing until the individual is skeletally mature.[23, 28, 158] One of the following three treatment algorithms is usually recommended to patients with ACL injury: (1) Transphyseal surgical reconstruction (adult technique) of the ACL with post-operative rehabilitation, (2) Physeal sparing surgical reconstruction of the ACL with post-operative rehabilitation, or, (3) Non-operative treatment with active rehabilitation, and a delayed ACL reconstruction if specific criteria are met.

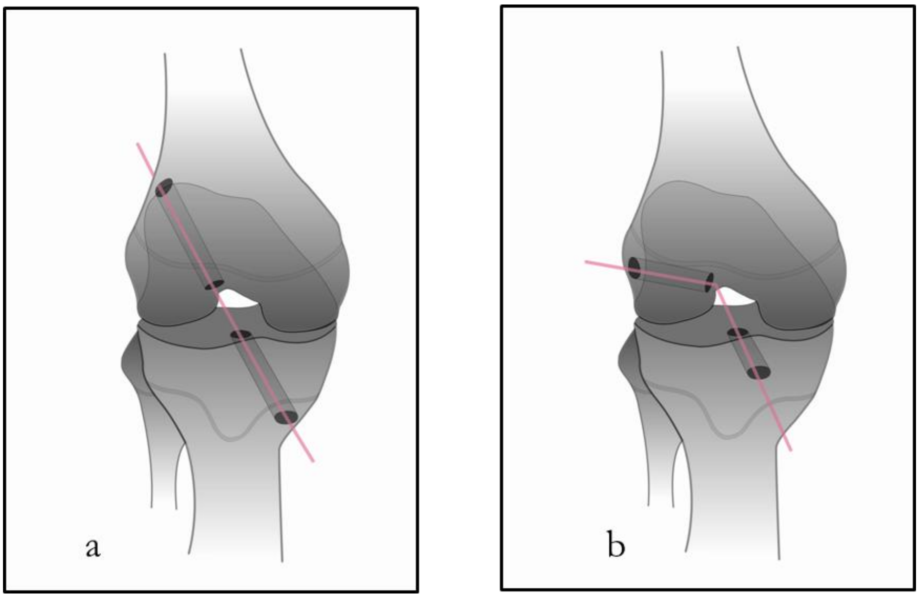

Figure 6 *Illustration of transphyseal (a) and physeal sparing (b) ACL reconstruction. From Moksnes et al.*[175]

Transphyseal ACL reconstructions

Transphyseal ACL reconstruction techniques are standard for surgical treatment of ACL injuries in adults (Figure 6a). The most prominent argument for advocating transphyseal ACL reconstructions in skeletally immature children is the increased possibility of a functional stable knee through an anatomical placement of the ACL graft, and the wish to minimise the risk of secondary injuries to the menisci or articular cartilage.[50, 106, 129, 201, 216] There is consensus in the literature and paediatric orthopaedic community that soft tissue grafts from the hamstrings tendons should be utilised in skeletally immature subjects to reduce the risk of growth disturbances.[117, 172] There are few studies in which a pre-defined treatment algorithm advocating transphyseal ACL reconstructions have been performed in skeletally immature children. Kocher et al.[129] used transphyseal technique in 59 children classified to Tanner stage 3, Liddle et al.[144] performed transphyseal reconstruction in 17 children Tanner stage 1 and 2, while Nikolaou et al.[184] chose transphyseal reconstruction in 94 patients regardless of skeletal maturity. Courvoisier et al.[50] used a transphyseal technique in 38 children. Among these four studies 209 transphyseal ACL reconstructions have been performed with good results. Twelve (5.8%) re-ruptures and no growth disturbances were reported. The re-rupture rate been shown to be higher for transphyseal reconstructions than physeal-sparing reconstructions (4.2% versus 1.4%) in a meta-analysis.[76]

An interesting, although poorly investigated issue, is the development of the ACL graft within the growing knee after surgical treatment in skeletally immature children. Kim et al.[122] have described that the angle between the tibial plateau and the native ACL increases during growth in uninjured children. Additionally, in a prospective MRI series on five ACL reconstructed skeletally immature children Bollen et al.[29] documented a large increase in the length of the graft through maturity, although the diameter of the graft did not change during growth. They concluded that some neogenesis had to take place in the ACL grafts after ACL reconstruction in skeletally immature individuals. Bollen et al.[29] also hypothesised that the remodelling of the graft due to the strain of skeletal growth after ACL reconstructions might lower the graft strength due to reduced biomechanical properties. Additionally, Park et al.[194] have suggested that the youngest patients are likely to have a graft with a smaller diameter than mature patients, and even though longitudinal growth of the graft has been demonstrated the lack of increase in the width may be problematic in the long term. Hence, there will be a risk that the result of an ACL reconstruction in an immature knee may be a thin graft with lower strength in adulthood.

Physeal sparing ACL reconstructions

The development of different physeal sparing ACL reconstruction techniques is based on the ambitions of orthopaedic surgeons to minimise the potential damage of the physeal growth plates.[88, 125, 126, 253] The general aim of the different physeal sparing reconstruction techniques is to avoid drilling through the epiphyseal growth plated (Figure 6b). Consequently, the most commonly raised argument against performing physeal sparing reconstruction is the inability of these techniques to place the ACL graft in an anatomical position.[31, 126, 129] Various techniques have been described, and among the eight largest studies on physeal sparing techniques, ten different surgical techniques were described.[7, 31, 78, 114, 126, 145, 165, 231] The ability of ACL grafts inserted using physeal sparing techniques to withstand the rigors of growth, time, and use, were questioned from an early point[157, 228] Stanitski[228] commented on the importance of long-term studies for extra-articular surgical procedures already in 1988. A study from Chotel et al.[43] highlighted that growth disturbances cannot be excluded even with the intended physeal sparing approach. This is supported by Frosch et al.[76] who found that the rate of growth disturbances was higher in studies on physeal sparing reconstructions compared to studies on transphyseal reconstructions (5.8% versus 1.9%). Kocher et al.[125] concluded that the physeal sparing surgical procedure provided excellent functional outcome with a low revision rate and minimal growth disturbance in a population of children in Tanner stages 1 and 2. Bonnard et al.[31] reported adequate function and 5.4% re-ruptures in a study in which physeal sparing reconstruction with a bone-patella tendon-bone graft was performed. Thus, the physeal sparing techniques appear to result in more growth disturbances, although the studies are few and reasons still unclear.

Non-operative management

The importance of rehabilitation after ACL injury and reconstruction is uncontroversial, and the evidence supporting the implementation of active rehabilitation programs for adults with ACL injury is strong.[204, 239] Despite the amount of published literature concerning different aspects of rehabilitation after ACL injury and reconstruction, there is no clear consensus on type or dose of exercises to include in rehabilitation programs.[204] However, there seems to be consensus that exercises that are focused on increasing muscle strength, neuromuscular control, and range of motion are recommended.[42, 59, 70, 210, 250] Systematic reviews on exercise therapy after isolated ACL injuries have identified in total only eight studies that have evaluated different aspects of non-operative management after ACL injury in adults.[49, 204] None of the studies involved rehabilitation of ACL injuries in skeletally immature individuals.

In general there seems to be a trend that rehabilitation programs for adult ACL injured subjects have moved in a more aggressive direction including early weight-bearing, more powerful strength training, and challenging neuromuscular and plyometric exercises.[35, 42, 59, 74, 135] In contrast, the sparse descriptions of rehabilitation programs in skeletally immature subjects are limited to brief overviews of post-operative rehabilitation protocols. They advocate a more conservative approach with longer periods of non-weight bearing, bracing, and a delayed return to sport in comparison to the more functional based adult protocols.[144, 145, 234] In studies on primary non-operative treatment in children, rehabilitation programs are generally absent or insufficiently described.[81, 170, 252] Furthermore, there seems to be a consensus on the use of a knee brace during sports activities, although no solid studies has been published within the area of bracing and ACL injuries in children. In studies on non-operative treatment no growth disturbances have been reported.

Aims of the dissertation

The main aims of this dissertation were to evaluate changes in knee function, and to explore the incidence of new intra-articular injuries, in skeletally immature children 12 years and younger following an evidence-based non-operative treatment algorithm after ACL injury.

Several specific aims have been addressed in the four papers:

I. To propose a treatment algorithm for the management of ACL injuries in skeletally immature children based on the current available evidence, our clinical experience, and our previously published study (**Paper I**).

II. To systematically review the literature on the treatment of anterior cruciate ligament injuries in skeletally immature children with regard to methodological quality (**Paper II**).

III. To prospectively investigate the changes in knee function in ACL injured skeletally immature children following our proposed non-operative treatment algorithm, using patient-reported outcome measurements, performance-based functional tests, and clinical outcome measurements (**Paper III**).

IV. To prospectively investigate changes in the types of physical activity skeletally immature children 12 years and younger were participating in following our non-operative treatment algorithm after ACL injury (**Paper III and IV**).

V. To prospectively investigate the incidence of new injuries to the menisci and articular cartilage in ACL injured skeletally immature children following our proposed non-operative treatment algorithm (**Paper IV**).

Related to the main aims of the prospective cohort study the following hypotheses were generated:

I. There will be significant improvement in knee function from baseline to a 1 year and a 2 year follow-up following our non-operative treatment algorithm.

II. A majority of the ACL deficient children will achieve leg symmetry indices above 90% for muscle strength at the 2 year follow-up.

III. A majority of the ACL deficient children will achieve leg symmetry indices above 90% in the four single legged hop tests at the 2 years follow-up.

IV. A majority of the ACL deficient children will continue regular physical activity and return to their main pre-injury activity.

V. The incidence of new meniscus and articular cartilage injuries will be acceptable following our non-operative treatment algorithm.

Material and Methods

Ethical considerations

The Declaration of Helsinki[1] describes special considerations with regard to ethical questions when children are included in research projects. Concretely, children are defined to be a vulnerable group and their ability to deliver an informed consent is controversial. All children in the materials included in this dissertation signed a written consent together with their parents. Children between the ages of 12 and 13 years signed a consent form written in more common language, because children in this age group are encouraged to take a more active part in the consent decision than children under the age of 12. The rights of all participants were protected by the Declaration of Helsinki,[1] and the studies were approved by the Regional Committee for Ethics and the Data Inspectorate.

Ethical considerations are extremely important when a research group is aiming to investigate children. When the current investigation on evaluating treatment algorithms in skeletally immature children was planned, our first action was to get an overview of the literature with regard to the topic. The literature was skewed in the direction of studies on surgical treatment algorithms, and we could not find documentation that non-operative treatment would subject children to unacceptable risk after an ACL injury. Additionally, we had to consider the likelihood that our projects would be beneficial for the population with an acceptable risk of harm. Based on the literature, we concluded that children should not be considered small adults, and that we could not generalize results from studies on adults to skeletally immature children. Consequently, our ethical viewpoint was that although children with ACL injuries are a vulnerable group, the implementation of a non-operative treatment algorithm was ethically acceptable. Furthermore, we concluded that recommendations of surgical treatment without having explored the outcomes of non-operative treatment would be unethical.

Moreover, throughout the studies we have sought to provide information in common language, and have had very open communication channels with all children and their parents. There are few orthopaedic surgeons and physiotherapists with specialised knowledge on treatment of ACL injuries in skeletally immature children. Thus, we have been aware of the potential pressure the involved families may have felt to participate in our studies because our research group is known to be among the few experienced in this field. Consequently, we have emphasised the fact that they would be offered identical treatment regardless of their participation in the studies, and their right to withdraw consent to participate at any time without reprisal.

Study designs

Paper I was a narrative review in which the literature on the management of ACL injuries in skeletally immature children was presented. The aim was to extract the available evidence relevant to the population, as a base for the development of a detailed evidence-based non-operative treatment algorithm. Evidence-based practice has been defined as clinical decision-making based on sound research evidence, combined with individual clinical expertise and the needs of the patient.[30] Thus, in addition to the current literature, we used the knowledge from our previous retrospective study and clinical experience, to describe our proposed treatment algorithm and rehabilitation program. In **Paper II** a structured literature search was performed in PubMed to build a systematic review on the methodological quality of studies on treatment of ACL injuries in skeletally immature children. The methodological quality of the studies was evaluated using the Coleman Methodology Score, which is an established method frequently used to evaluate the orthopaedic literature.[46] The papers which met the inclusion criteria were categorized related to the three most commonly reported treatment algorithms (transphyseal ACL reconstructions, physeal sparing ACL reconstructions, and non-operative treatment).[46] No randomised controlled trials, two prospective studies, and 29 case-series were included. Hence, the systematic review revealed that the evidence for treatment of ACL injured skeletally immature children was placed low in the hierarchy of study designs (Table 1).

Level	Properties of study design
I	Evidence obtained from at least one properly randomized, controlled trial.
II-1	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one centre or research group.
II-3	Evidence obtained from multiple time series with or without the intervention.
III	Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

Table 1 *Grades of evidence for the quality of study design.*[48]

The knowledge gaps related to non-operative treatment algorithms discovered in **Paper I** and **Paper II** gave direction with regard to the aims for papers III and IV. The current level of evidence suggested that prospective observational studies were appropriate, to potentially generate hypothesis for future experimental studies on effects of the different treatment algorithms. Prospective cohort study designs have been suggested to be particularly valuable to investigate questions concerning results from current clinical practice, prognosis, and discovery of potential adverse outcomes.[104, 244] Therefore, a prospective cohort study (Level II-2) was designed (**Paper III)**, in which the functional outcomes after ACL injury were evaluated using patient-reported outcome measurements, performance-based functional tests, knee laxity measurements, and a clinical evaluation. For the performance-based tests and knee joint laxity measurements, the results of the uninjured leg were used to evaluate the leg symmetry indexes. Further, the prospective cohort study was the base of **Paper IV** in which the integrity of the intraarticular structures was evaluated using 3.0T MRI. To subject the children to comparable amounts of exposure in activities between the two follow-up assessments, a standardised time interval between the two imaging sessions was scheduled and executed. Bilateral imaging was performed, and the uninjured knees of the children served as control knees.

Subjects

Paper I and II included data from structured literature searches. In **Paper III and IV** skeletally immature children with an ACL injury sustained at ages 12 years and younger were included. All eligible children referred to the Oslo University Hospital, Department of Orthopaedics, and the Norwegian Sports Medicine Clinic (NIMI) between March 2006 and October 2010 were requested for inclusion. Based on data from the NKLR we estimated an inclusion rate of 10-20 children with ACL injury per year to the prospective cohort. Thus, in the planning of the studies we estimated a total inclusion of maximum 60 children within the timeframe of three years. Based on the current literature at the time we decided to include a minimum of 40 children to be able to perform relatively large studies within this topic.

The inclusion criteria for the prospective cohort (**Paper III and IV**) were that a traumatic ACL injury should have been suffered at ages 12 years and younger. The diagnosis of an ACL rupture was confirmed through conventional diagnostic MRI,[140, 153] a positive Lachman test,[124] and an instrumented measured sagittal side-to-side knee laxity measurement difference of 3 mm or more using maximum manual force (KT 1000, Med-Metric, San Diego, California, USA).[51] Skeletal immaturity was established from identifying open epiphyseal growth plates in tibia and femur on the diagnostic MRIs.[212] No determination of skeletal age was performed in the studies. Children with tibial or femoral ACL avulsion fractures were not included in any of the studies, and posterior cruciate ligament injury or intraarticular fractures were also excluded. In **Paper III** 46 skeletally immature children with a mean age of 11.0 (±1.5) years at the time of injury were included, while the first 40 children were consecutively recruited to **Paper IV**. There were 35% girls and 65% boys included in both studies. A flow-diagram of children included in **Paper III** and **IV** is outlined in figure 7.

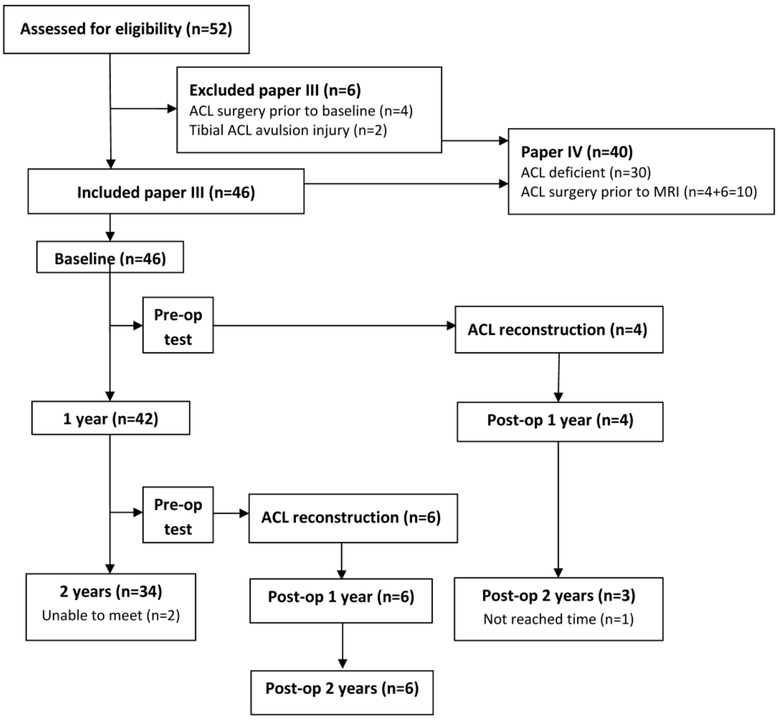

Figure 7 *Flow diagram of subjects included in* ***Paper III*** *and* ***IV****.*

Assessments of knee function

The importance of implementing functional outcome measures at different levels has been advocated to produce a broader evaluation of knee function after ACL injury.[47, 147] However, particularly the use of performance-based functional tests have been limited in the literature on ACL injuries in skeletally immature patients.[19, 26] In the present dissertation patient-reported outcome measurements, performance-based functional tests, knee laxity measurements, and a clinical examination were included to evaluate knee function in skeletally immature children after ACL injury.

There are several instruments available to evaluate outcomes of knee function in ACL injured subjects, and they are frequently administered in studies. Still, none of the available instruments were adequately validated on a population of skeletally immature children when the studies included in this dissertation were initiated. Therefore, the most optimal starting point of our studies would have been to develop and validate functional outcome measures to be used in the subsequent series of studies. However, based on our previous clinical experience with the test battery, and through considerations about the available instruments, we decided that they would provide adequate and clinically relevant information in relation to the research questions that had been defined. Additionally, to increase the possibility of a valid interpretation of the patient-reported outcome measurements we prompted the parents to assist the children answers the questions to a degree they felt appropriate. The new patient-reported outcome measurements KOOS-Child[191] and the Pedi-IKDC[128] have recently been published, although not in time to be utilised in the papers included in this dissertation. Further, isokinetic muscle strength measurements using the peak torque value, with test velocities between 30 and 180 degrees per second (°/s), have been documented to be reliable in healthy children,[52, 160] although the reliability and validity has not been investigated in a paediatric ACL injured population. The four single legged hop tests are valid for evaluation of knee function in adults following ACL injury or reconstruction, but their performance in ACL injured children had not been established.[71, 85, 111, 146, 185, 202]

Patient-reported outcome measurements

The patient-reported functional outcome measurements included the Knee injury and Osteoarthritis Outcome Score, Norwegian version LK 1.0 (KOOS) (**Paper III**),[205] the International Knee Documentation Committee Subjective Knee Form, Norwegian version (NAR 2005) (IKDC 2000) (**Paper III**),[109] and the Knee Outcome Survey Activities of Daily Living Scale, Norwegian version (NAR 2005) (KOS-ADLS) (**Paper III**).[110] Additionally, a visual analogue rating scale (VAS) of knee function was registered by asking the children to draw a vertical line across a 10 cm horizontal line. The borders were marked with "cannot do daily activities" (0) and "normal knee function" (100) (**Paper III**). The KOOS contains 42 items in five domains, which are reported as five separate subscales.[91, 205] The five subscales provide information related to *Pain, Symptoms, Activities of daily living, Sports and recreational activities*, and *Knee related quality of life*. Each subscale is scored from 0 to 100, where 100 represents perfect knee function for the subscale. The IKDC 2000 assesses symptoms, knee function, and sports activities through 18 items. A total score is reported in percentage from 0 to 100, where 100 denotes no symptoms, unlimited activities, and knee function at pre-injury level.[109, 147] The KOS-

ADLS consists of 7 items as a measure of patient-related functional limitations and impairments of knee function in activities of daily living.[110] A score of 100% indicates no limitation with activities of daily living. The use of a VAS has been shown to be a valid and reliable measure of knee function in adults,[47, 110] although no investigations with regard to its properties has been performed in skeletally immature children with ACL injury.

Performance-based outcome measurements

To evaluate knee muscle function we included isokinetic muscle strength measurements in **Paper III**. Isokinetic muscle strength test equipment (Biodex 6000, Shirley, New York, USA) was used to evaluate quadriceps and hamstrings muscle performance. In **Paper III** we reported the strength measurements as the peak torque values adjusted to body weight, and thereby enabled assessments of changes in isokinetic muscle strength over time.[52, 173] A standard 10 minutes warm-up on a stationary bike was performed prior to the isokinetic strength measurement. A correction of gravity was performed with weighing of the tested limb at 10° of knee flexion. The isokinetic strength measurements were performed with 5 maximal effort repetitions with a test velocity of 60°/s. A trial session with 4 repetitions at the same velocity was performed prior to the maximum effort test to familiarise the child with the testing equipment. Additionally, verbal encouragement was employed during the test to enhance the ability of the child to perform a maximum effort.[52] The peak torque value from the best repetition, adjusted to bodyweight as (Nm/kg) x 100, was recorded. The change in this value between follow-ups was used as a measure of muscle strength development. Additionally, the leg symmetry index (LSI) was reported in per cent; (injured leg/uninjured leg) x 100.

Following a 5 minute break after the isokinetic strength measurement four single legged hop tests (the single hop test (SH), the triple crossover test (TCH), the triple hop test (TH), and the six meter timed hop test (6m-timed)) were performed (**Paper III**). All tests were completed without a knee brace. For each hop test each child performed three attempts on each leg, and the longest hop on each leg was recorded. The attempt was considered valid when the child managed a firm landing without excessive stabilising movements. For the 6m-timed hop test each child hopped 6m at maximum speed while the time was manually recorded with a handheld digital stopwatch to the nearest 100th of a second. Results were presented as the LSI. For three of the single legged hop tests (SH, TCH, and TH) the LSI was calculated as the result of the injured leg divided by the result of the uninjured leg, multiplied by 100. LSI for the 6m-timed hop test was calculated as the fastest time hopped on the uninjured leg divided by the fastest time on the injured leg, multiplied by 100. To increase the children's sense of confidence one of the parents was always in attendance at the performance based tests.

Additionally, an evaluation of the intra-tester and inter-tester reliability for the isokinetic muscle strength measurements and single legged hop tests with two of our experienced testers was performed in a master thesis in our research group in 2011.[115] Twenty-six healthy soccer players and alpine skiers aged between 12 and 13 years were included. The participants underwent testing at three occasions, distributed over two test days with one week interval. The inter-rater reliability was calculated from the measures of the two testers at day 1, while the intrarater reliability was calculated from the three measures of each child performed by one tester (HM) at day 1 and day 2.

Clinical outcome measurements

The inclusion criteria for all four studies included a measurement of anterior sagittal knee laxity by use of a knee arthrometer (KT 1000, Med-Metric, San Diego, California, USA).[51] Knee laxity measurements with an arthrometer have been shown to be a valid and reliable measurement tool when performed by experienced investigators in adults.[27, 34] To our knowledge no evaluations of validity or reliability have been performed in children. The side-to-side differences measured using the maximal manual test was reported at all follow-ups in **Paper III**.

In **Paper III** the pivot shift test was used to assess rotational knee laxity. One experienced orthopaedic surgeon (LE) performed all pivot shift tests. The pivot shift test is an anterolateral subluxation test for ACL integrity which is assumed to mimic the pivoting motion associated with ACL injury, and also subsequent giving way episodes in the ACL deficient knee.[141] A positive pivot shift test is characterised by anterior subluxation of the tibial plateau out from beneath the lateral femoral condyle,[64, 77] and a negative test has been associated with adequate functional stability in adults.[130, 141] The pivot shift test was graded as grade 0 (absent), grade I (slight), grade II (definite subluxation), and grade III (subluxation and momentary locking).[9]

Magnetic Resonance Imaging

All children included in the four studies had their ACL rupture initially diagnosed using conventional MRI. Magnetic resonance imaging has been recommended to diagnose acute knee injuries in children and adolescents.[124, 140, 153] Additionally, the first 40 children included in the prospective cohort were consecutively recruited and assessed with two bilateral 3.0T MRI investigations in **Paper IV**. All the 160 MRI procedures were administered by one MRI-physicist at the Section of Neuroradiology, Department of Radiology and Nuclear Medicine, Oslo University Hospital. One MRI unit (GE Medical, Signa HDxt 3.0T, United Kingdom) using a standardised protocol with a transmit/receive eight-channel phased-array knee coil was utilised. All patients had sagittal, coronal, and axial proton-density (PD)-weighted fat-suppressed (FS) images.[171, 226] The sagittal PD-weighted images had a slice thickness of 3mm, while the coronal and axial slice thickness was 2 mm. Additionally, oblique T2-weighted sagittal images with a slice thickness of 2mm were obtained.[100] All MRIs were analysed with regard to the integrity of the knee ligaments, menisci, and articular cartilage, by two independent musculoskeletal radiologists experienced in reading MRIs. Subsequently, a consensus meeting was held to generate agreement with regard to the presentation of the results.

Activity level

In **Paper III** all children were asked at the baseline assessment to define their primary pre-injury leisure time sports activity. At the baseline and subsequent follow-ups they were asked to define their present main leisure time sports activity, which was used to evaluate possible changes in their activity level throughout the study. The activity level was classified as Level I, II, III, or IV according to the classification system by Hefti el al.[93], modified to European Sports activities (Table 2).

Level	Sports activity	Occupational activity
I	Jumping, cutting, pivoting (Soccer, handball, basketball, floorball)	Activity comparable to level I sports
II	Lateral movement, less pivoting than level I (racket sports, alpine skiing, snowboard, gymnastics)	Heavy manual labor, working on uneven surface
III	Straight ahead activities, no jumping or pivoting (running, cross-country skiing, weightlifting)	Light manual work
IV	Sedentary	Activities of daily living

Table 2 *Activity level classification from Hefti el al.*[93] *Modified to European sport activities.*[177]

Furthermore, an online activity survey was e-mailed to the participants every month throughout the prospective cohort study, and data were used to monitor participation in physical activity during physical education classes in school and leisure time activities (**Paper III and IV**). The purpose of the online activity survey was to enable a prospective assessment of possible changes in participation. Additionally, all children were asked to report all giving way episodes they had experienced during the previous month. If a giving way episode was reported, a subsequent automatic follow-up question on whether the knee brace was worn or not was asked.

Treatment algorithm

The treatment algorithm developed, implemented, and evaluated in this dissertation is based on extensive clinical experience and the current available evidence. The algorithm was published in **Paper I**,[175] and is outlined in Figure 8. The algorithm advocates primary non-operative management until skeletal maturity is reached for children with open growth plates. We advocated that immature children with ACL injury were treated with a structured and monitored rehabilitation program to explore the possibility of returning adequate dynamic knee stability. Children with ACL injuries were monitored and assessed by an orthopaedic surgeon (LE) and a physical therapist (HM) who worked closely together. An ACL reconstruction before skeletal maturity was not considered before it had been established that a structured rehabilitation program had not been successful in establishing a functionally stable knee, or if a secondary symptomatic meniscus injury occurred, or if an unacceptable decrease in the child's activitylevel was reported.

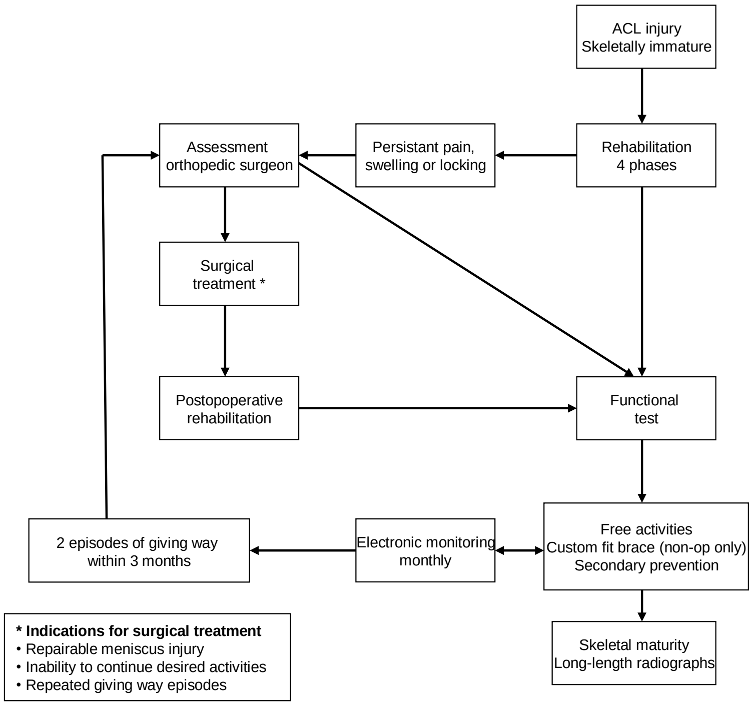

Figure 8 *The treatment algorithm for anterior cruciate ligament injury in skeletally immature children.*[175]

A supervised rehabilitation program consisting of a variety of neuromuscular, plyometric, and muscle strengthening exercises was implemented. Exercises similar to those that have been successful in preventing knee injuries in adolescents in previous studies were selected for the functional rehabilitation program,[181, 190, 224] with the intention of challenging neuromuscular control of the lower limb. Additionally, all children were given a custom fit functional knee brace which they were encouraged to use when they were participating in pivoting sports and physical education classes in school.

	Aims	Rehabilitation milestones
Phase 1	Regain active and passive knee extension	Straight leg raise without extension lag
	Resolve intraarticular effusion	Weight bearing single leg terminal extension
	Reactivate quadriceps muscle	Normal gait pattern
Phase 2	Normalise activities of daily living	Normal bilateral stair walking
		Daily activities without instability or subsequent intraarticular effusion
Phase 3	Running without asymmetry and subsequent intraarticular effusion	Running 15 minutes with symmetry and without subsequent intraarticular effusion
	Ability to adequately perform a single leg landing in all planes	Adequate single leg hop from a 30 cm height with satisfactory stable landing
Phase 4	Prevent giving way episodes and secondary injuries	

Table 3 *The aims and progression milestones in the four phases of the rehabilitation program.*

The aims and progression milestones of the rehabilitation program are outlined in Table 3. The rehabilitation program was divided into 4 phases and consisted of exercises targeted towards regaining range of motion, neuromuscular control, and muscle strength. Children were prompted to consult their physical therapist once a week throughout phase 1 and 2, and once a month in phase 3. Rehabilitation exercises were primarily performed at home and limited to a maximum of three exercises. Exercises were reviewed and progressed at each physical therapy session. Children were progressed to the next rehabilitation phase when specific functional milestones were reached during each phase. The three exercises selected at each clinical follow-up were combined with one exercise from each of the three categories; range of motion, neuromuscular training, and muscle strength (Figure 9). A functional examination was performed at the end of phase 3 – provided that the milestones of running 15 minutes without subsequent intraarticular swelling and single legged hops with adequate landings had been achieved. The functional tests consisted of an isokinetic muscle strength test with five repetitions at 60°/sec,[52, 56] and the four single legged hop tests.[185] In clinics where isokinetic muscle strength equipment was not available, a 1 repetition maximum test in a leg press machine was performed. Children were allowed to return to their preferred activities wearing a custom fit functional knee brace when the LSI of the isokinetic muscle strength measurements and all four single leg hop tests were at least 90%. When the children were released from physical therapy a secondary prevention program was instructed and encouraged. Additionally, all included children were encouraged to visit the www.skadefri.no website, in which information and training programs designed to prevent sports injuries are available for free. Subsequently, they were also free to contact their physiotherapist and their orthopaedic surgeon to schedule follow-up consultations.

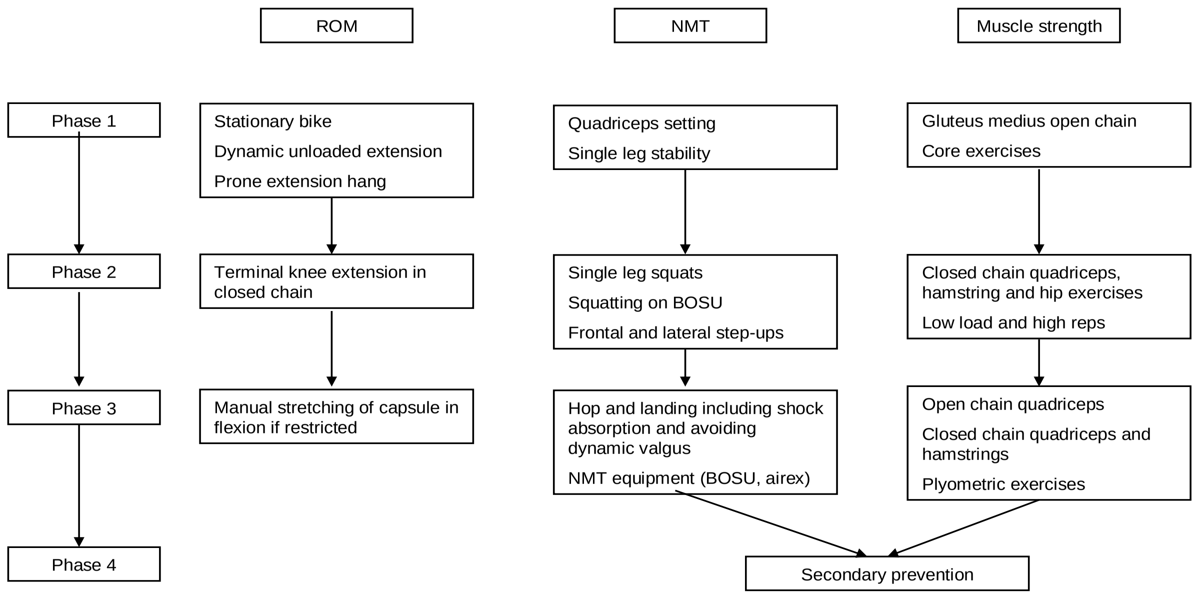

Figure 9 *Proposed guide for the rehabilitation of anterior cruciate ligament injury in skeletally immature individuals. Progressions through the 4-phase program were determined by the functional progression milestones presented in* Table 2. *(ROM, Range of motion; NMT, neuromuscular training.*[175]

Surgical treatment

Children who suffered or developed a symptomatic meniscus injury underwent meniscus repair with a concomitant ACL reconstruction. Additionally, perceived inability to be active in preferred activities, or repetitive episodes of giving way, led to an assessment by the orthopaedic surgeon for surgical treatment of the ACL before skeletal maturity. All surgical ACL reconstructions were performed with a transphyseal technique, and a quadrupled hamstring tendon autograft was preferred. When a decision on a recommendation of ACL reconstruction had been made, the child and parents were given thorough information with reference to the risks involved. The option of continuing sports involving less pivoting motions until skeletal maturity was part of the information. During surgery emphasis on centrally placed vertical drill holes through the tibial physis was made. The fixation devices were placed proximal to the femoral epiphysis, and distal to the tibial epiphysis. A post-operative rehabilitation program was carried out with a protocol identical to the non-operative rehabilitation with four phases. Individually adjusted time based precautions were included in phase 1 and 2 to ensure a safe incorporation of the ACL graft and healing of meniscus sutures with attention on avoiding undesirable strains and share forces. Muscle strength deficits were specifically targeted. The medial hamstring muscle group was given specific attention, with emphasis on restoring optimal neuromuscular and stabilising function.[17, 18, 258] Training induced strength gains in children are believed to be facilitated through neural adaptive mechanisms and not hypertrophy,[65] thus, the exercises were directed towards challenging neuromuscular knee stabilising strategies and plyometric exercises. The intention was to facilitate increased motor unit activation, and enhancements in motor unit coordination, recruitment, and firing. We deliberately advocated four specific actions different from adult post-operative rehabilitation: (1) a slower progression towards jumping and running to reduce the impact loading of the graft and the physis, (2) less use of external loads, (3) primarily home based functional exercises, and (4) later return to pivoting sports at 9-12 months.

Statistical analysis

In **Paper I** no statistical analysis was performed. In **Paper II, III, and IV** data were analysed using the Predictive Analytics SoftWare (PASW) Statistics (version 18.0.2 (April 2, 2010); SPSS Inc., Chicago, IL, USA). In **Paper II** basic calculations of means and standard deviations was performed. In **Paper III** analyses of variance (ANOVA) were used to test changes over time with a significance level of .05. If the assumption for the ANOVA with repeated measures was violated statistical differences were calculated using the Friedman test. A paired t-test was used to calculate differences from the pre-operative test to the 2 year post-operative test for ACL reconstructed subjects. The leg symmetry indices were calculated as (injured/uninjured) x 100 for isokinetic strength measurements and three of the single legged hop tests (SH, TCH, and TH), while the LSI for the six meter timed hop was calculated as (uninjured/injured) x 100. In **Paper IV** descriptive statistics with means and standard deviations were calculated for subject characteristics and time intervals between injury, MRI1, and MRI2. To evaluate the frequency of observed menisci with high signal without rupture between the ACL injured and the non-injured knee the Fisher's Exact test was used. The interobserver agreement was calculated as kappa (ϰ) coefficients (Cohen's kappa), which is the recommended statistical analysis for the purpose of evaluating interobserver agreement in diagnostically assessments with nominal data.[132] Kappa values were interpreted as; poor (ϰ = 0.0–0.20), fair (ϰ = 0.21–0.40), moderate (ϰ = 0.41–0.60), good (ϰ = 0.61–0.80) or excellent (ϰ = 0.81–1.0).[132, 259]

Discussion

The results from our retrospective study[174] encouraged our research group to initiate a prospective cohort study on skeletally immature children who had sustained a traumatic ACL injury at ages 12 years and younger. However, there was an absence of thoroughly described rehabilitation protocols and treatment algorithms in the literature. Thus, a detailed evidence-based description of a treatment algorithm and a rehabilitation program was developed based on the available literature, our retrospective study, and our clinical experience (**Paper I**). Furthermore, the systematic review (**Paper II**) disclosed that the methodological quality of the literature on this topic was generally low. The results of the systematic review highlighted the need for higher quality prospective studies with emphasis on descriptions of treatment algorithms, detailed rehabilitation programs, and evaluations of changes in knee function in the population of ACL injured children. Consequently, the prospective cohort study (**Paper III and IV**), in which our proposed non-operative treatment algorithm and rehabilitation program were implemented, was launched in 2006. The prospective cohort studies showed that the knee function measured with patient-reported and performance-based outcome measurements was consistent without clinical relevant changes over the 2 years follow-up. Seventy-eight per cent of the children did not undergo an ACL reconstruction. The vast majority remained physically active in school and leisure time sport activities, although a significant reduction in participation in Level 1 activities was observed. Furthermore, the incidence of new injuries to the menisci and articular cartilage was found to be acceptable in ACL injured skeletally immature children following the non-operative treatment algorithm.

Study designs

This dissertation consists of a narrative review (**Paper I**), a systematic review (**Paper II**), and two prospective cohort studies (**Paper III and IV**). The two first papers were logical consequences of the previously described lack of evidence-based treatment decision making criteria and rehabilitation protocols. For the assessment of functional outcomes following the implementation of our proposed treatment algorithm we decided to use observational designs. The importance of observational research designs have been highlighted in the development of Evidence Based Medicine over the last two decades.[154, 155] Well-designed prospective cohort studies are said to deliver valuable knowledge with high external validity that are more likely to provide an implication for clinical practices than many experimental studies.[36, 155] Additionally, detection of rare or late adverse effects of interventions is more likely in observational studies, and cohort studies are proposed to be the best studies for determining the incidence and natural history of a condition or an injury.[104, 155] The direct analogy to the studies included in this dissertation is the possibility of detecting adverse effects, such as high incidences of meniscus or articular cartilage injuries in **Paper III and IV**. Consequently, as the prospective study showed a low incidence rate of meniscus and articular cartilage injuries comparable to previous studies on early ACL reconstructions, new hypotheses for experimental studies can be generated. Furthermore, the results on functional outcomes in **Paper III** document the results of our clinical practice and may serve as a foundation to generate hypotheses regarding the choice of treatment algorithms and outcome measures in future studies. However, before a comparative study to evaluate the effectiveness of different interventions is pursued, significant predictive factors for outcomes should also be established in high quality prospective studies.

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative have published a checklist (The STROBE checklist) of 22 items with the intention of providing guidance on how to report observational research well.[244] The statement especially emphasises the importance of reporting the explicit inclusion and exclusion criteria in observational studies, and also suggests that confounding variables have previously not been sufficiently reported.[242, 244] Additionally, Bryant et al.[36] have described the importance of appropriate selection of participants and control groups, the management of confounders, the use of outcomes with established properties, inclusion of blinded testers, and the impact of patients lost to follow-up. A major strength of **Paper III and IV** compared to the current literature is the inclusion of a homogenous population of skeletally immature children. Additionally, the standardised test intervals, specific criteria for surgical treatment, and the inclusion of functional outcome measures as well as a described rehabilitation program aimed at different properties of knee function, strengthen the data. In **Paper III** we do not have a control group to which we could have compared the results of our study. The numbers of ACL injuries in skeletally immature children in Norway are low and we decided that it was more important to include all eligible patients to undergo the proposed non-operative treatment algorithm than to include a control group. The inclusion of a control group may be more appropriate if a future multicentre study is started. In such a study different centres could advocate different treatment algorithms and serve as control groups to each other, provided that standardised inclusion criteria and outcome measurements are incorporated. In **Paper IV** the children's uninjured leg served as control with regard to changes in the integrity of the intra-articular structures. The contralateral leg has been exposed to the same activities as the injured leg without suffering injury to the ACL, and the inclusion of bilateral MRIs is a major strength of that study. To increase the external validity and to optimise the possibility of recruitment of the prospective cohort we decided not to exclude children with associated non-symptomatic injuries to the menisci at baseline. All functional tests and clinical examinations in **Paper III** were performed by members of the research group who were not blinded. Conversely, the radiologists who described the MRIs in **Paper IV** were blinded with regard to which side the ACL injury was present and also to treatments performed prior to the MRI investigations. There were no drop-outs with children who abandoned from the prospective cohort study. Data from two children who were unable to meet at the 2 years follow-up are missing, however, the children have been assessed at subsequent follow-ups which are not within the scope of this dissertation.

Approximately 90% of papers in clinical speciality journals describe observational research, which demonstrate that much of the knowledge on clinical and public health originates from observational studies.[242, 244] Within the concept of evidence-based medicine it has been highlighted that evidence-based practice is not restricted to randomised controlled trials (RCTs) or meta-analyses, although these are ranked highest in the hierarchy of evidence to evaluate the effect of different treatment modalities.[211, 232, 233] **Paper II** in this dissertation is a systematic review of the literature on treatment of ACL injuries in skeletally immature children. The systematic review does not evaluate the effects of different treatments based on RCTs, but the methodological quality of published literature within this field. No RCTs and only two prospective studies were identified. Still, there are eight systematic reviews,[67, 69, 117, 158, 172, 218, 243] and one meta-analysis published on the treatment of ACL injuries in skeletally immature children.[76] Three of the systematic reviews concluded quite strongly that transphyseal ACL reconstructions should be the treatment of choice for skeletally immature children,[76, 117, 243] four recommended ACL reconstruction in selected cases,[67, 69, 158, 218] while Mohtadi & Grant[172] stated that the level of evidence in the literature was insufficient to advice one treatment over the other. The main concerns with these systematic reviews are, as shown in **Paper II**, that their conclusions are based on studies with poor methodological quality, which also makes the conclusions of the systematic reviews unreliable. Consequently, the research field on treatment of ACL injuries in skeletally immature children still needs more prospective observational studies to enable higher quality knowledge with regard to the outcomes of the current recommended treatment algorithms.

Subjects

This dissertation incorporates studies which in total have included 46 skeletally immature children, who all have sustained an ACL injury at age 12 years and younger. There were 16 (35%) girls and 30 (65%) boys included, with a total of 47 ACL injuries. The majority of injuries in **Paper III** had occurred in alpine skiing and soccer (Table 4).

	n (%)
Alpine skiing	23 (48.9)
Soccer	10 (21.3)
Trampoline	3 (6.4)
Playground	3 (6.4)
Bicycle	2 (4.3)
Handball	2 (4.3)
Cross-country skiing	1(2.1)
Ski-jumping	1 (2.1)
Skateboard	1 (2.1)
Motocross	1 (2.1)

Table 4 *Activities at time of injury, n=46 (47 knees)* ***(Paper III)***

That the majority of injuries were sustained by boys (65%), and the relatively low percentage of injuries which had occurred during team ball sports (n=12, 25.6%), are marked differences from studies on ACL injuries in adolescents and adults.[189, 203, 225] The majority of injuries occurred in boys is consistent with the previous literature on skeletally immature children with ACL injury.[45, 95, 125, 184] Nikolaou[184] have published the largest population of children with 56 (60%) boys and 38 (40%) girls with a median age of 13.7 years at time of surgery. Henry et al.[95] performed physeal sparing reconstructions in 29 children (26 (90%) boys and 3 (10%) girls) with a mean age at time of injury of 11.5 ± 2.2 years, while Kocher et al.[125] included 28 (64%) boys and 16 (36%) girls with mean age of 10.3 years at time of surgery in their study on physeal sparing reconstructions. Cohen et al.[45] have reported the highest proportion of girls (n=15/26, 58%), although they also reported a higher age at time of injury (mean 13.1 years, and 21 (81%) were Tanner stage 3 or 4). Graded activity levels were not reported, but Kocher et al.[125] reported that the injuries occurred in similar sports as in **Paper III**, such as soccer, American football, basketball, gymnastics, and free play. In **Paper III** it is particularly interesting that only 2 (4.3%) injuries had occurred in handball, because adolescent girls are documented to be at high risk of ACL injuries in handball.[3, 82] Plausible reasons for the observed differences in the number of ACL injuries between children and adolescents in team ball sports are the assumption that the youngest children have not developed sport specific skills and speed sufficient to place them in high risk situations during games and practice. Additionally, the time of exposure to injury risk situations is likely to be lower because children are participating in sports less frequently during the week than their older counterparts. Furthermore, it is not surprising that alpine skiing is highly represented as especially young boys are shown to be a group with high risk of injuries in alpine skiing.[79, 162] The development of new skiing techniques in combination with the increased popularity and availability of high-risk activities in snow-parks are probably related to the number of ACL injuries observed in alpine skiing activities.[37, 80, 162] Additionally, psychological factors such as risk seeking behavior and peer pressure are suggested to be influencing the injury panorama in skiing activities.[79]

With regard to the recruitment of patients to our studies, the majority were referred to the project from orthopaedic surgeons and physical therapists in Eastern Norway, because children with ACL injuries traditionally have been referred to the Oslo University Hospital. We published information of the study in the Norwegian Journal of Sports Medicine (Norsk Idrettsmedisin), and in the member journal of the Norwegian Orthopaedic Society (Norsk Ortopedpost) in 2008, and encouraged colleagues to refer patients to the prospective cohort study.

An important limitation with the literature on ACL injuries in skeletally immature children is the heterogeneity of included populations with regard to skeletal maturity within and between studies.[20, 172] In the treatment of ACL injuries in children the determination of skeletal maturity is of significant importance with regard to the selection of treatment alternatives and study populations. Unfortunately there are no uniform definitions used with regard to the classification of skeletal maturity in the scientific literature on the treatment of ACL injuries in children and adolescents. Differentiation using age groups is common,[172, 174] although a majority of studies pool children and adolescents ranging from 8 to 18 years together in the same studies.[10, 172] We have not included radiological or biological classification of the children included in our studies. However, we have documented that all children included in the prospective cohort study were skeletally immature and grew taller (mean 11.3 (±5.0) cm, minimum 2 cm and maximum 24 cm) from the baseline assessment throughout the study. Yet, it is likely that the population we investigated consisted of children from Tanner stages 1-3.

Throughout the studies we have been seeking to educate the children and their parents with regard to understanding the function of the ACL and the possibility of dynamic knee stability through neuromuscular control. Additionally, they have had an open direct line to both Håvard Moksnes and Lars Engebretsen, and we have been liberal with regard to clinical controls and consultations. All consultations, also unrelated to the scheduled follow-ups, have been free of charge, and no financial claims have been made towards insurance companies for any consultations. However, we must also consider the possibility that the children included may have been recruited from communities in which the awareness of ACL injuries is high (for example alpine skiing). Additionally, several children were recruited into the prospective cohort study late due to incorrect diagnoses after their injury, which is visualised by the average time of 11.9 (±12.2) months, with minimum 1.1 months, and maximum 48.2 months from injury to baseline examination in **Paper III**. Thus, we cannot confidently establish that the results reported in **Paper III and IV** are representative of functional and radiological outcomes in all ACL injured skeletally immature children. Nevertheless, the results are most likely representative for children actively participating in sports.

We believe that the most important factors with regard to the high compliance were the combination of high availability of the orthopaedic surgeon and physical therapist, and the conscientious focus on plain language patient and parent information. I have, in my experience successfully, utilized an analogy of ACL function to explain the concept of dynamic knee stability. The standard information of the "seat-belt analogy" goes like this; *When you are a passenger in a car you always wear the seat-belt – but you are not using it unless a sudden stop occurs. Comparably, the ACL is worn, but not used, when you are being active – unless a sudden uncontrolled pivoting motion of the knee occurs. Driving a car without wearing the seat-belt is not allowed or recommended, but it is not dangerous as long as sudden stops are avoided. Hence, most of the time the ACL is inactive and you infrequently depend on the stability it provides, because the muscles surrounding the knee are responsible for the majority of functional stability when you are active. Performing a specific rehabilitation program will enhance the ability of your muscles to provide knee stability.*

Outcome measurements

To enable a comprehensive evaluation of knee function in ACL injured skeletally immature children, patient-reported outcome instruments, performance-based functional tests, and clinical evaluations of knee laxity and mechanical instability were included in **Paper III**. Additionally, MRI was included to evaluate a possible development of pathology in the intra-articular structures without exposing the children to radiation or surgical procedures (**Paper IV**). The incorporation of a combination of measurements which are intended to examine the features of knee function at different levels of demand is recommended when patients with knee injuries are assessed in clinical studies.[19] The functional consequences of an ACL injury are complex and affect several aspects of knee function from mechanical laxity to functional instability and fear of new injuries.[4, 238] The patient-reported outcome measurements included in this dissertation were intended to evaluate the children's knee function in daily activities (KOS-ADLS), leisure time sport activities (IKDC 2000), and to capture the more general functional difficulties (KOOS and VAS) after ACL injury. Patient-reported outcome instruments have been extensively utilised in studies on knee function after ACL injury over three decades. It is highly recommended that such instruments are standardised and patient-reported to avoid bias.[101] To enable such instruments to generate a valid measure of knee function, they should be developed with the intention of identifying aspects of knee function that are important to the patients who are participating in the study. They should be sensitive to capture changes in knee function over time.[47] Hence, if the instruments are to produce confident results of knee function the validity and reliability of the instrument should be tested in a population they are intended to evaluate. As previously stated none of the patient-reported outcome measurements included in **Paper III** have been developed with the intention of evaluating knee function in skeletally immature children with ACL injuries, due to the absence of such instruments at the start of the prospective cohort study. However, new patient-reported instruments specifically intended to evaluate knee function in children have recently been available; the KOOS-Child and the pedi-IKDC.[128, 191] The IKDC 2000 and the KOOS have been documented to be difficult for children to comprehend and answer,[112, 191] while the other instruments (KOS-ADLS and VAS) have not been evaluated in a paediatric ACL injured population. Normative results from a healthy population have been published for the KOS-ADLS and IKDC 2000, however not in persons younger than 18 years.[8, 156, 193] In **Paper III,** the children completed the patient-reported outcome measurements together with their parents to limit the difficulties attributed with understanding the items. However, both the children and their parents were aware that the questionnaires were to be analysed by the leader of the research project (HM), who also was responsible for the treatments given. Hence, to increase the strength of the data an independent person should have been responsible for all data collected. Identical arguments can be made with regard to the administration of the performance-based functional tests, although the trust and confidence experienced by the children from meeting a familiar person at the test sessions was probably important for the high compliance in the studies.

In the development of KOOS-Child, Örtqvist et al.[191] examined how the KOOS was understood among a cohort of children with knee injuries. They performed cognitive interviews of 34 Swedish children and reported that many children had problems understanding several terms and tracking items on the time frame. The children reported that several items were irrelevant, although they did understand how to use the 5 point Likert response scale. Specifically, children noted the lack of items relevant to children like spending time with friends, attending school, and playing sports. Although we have not performed any qualitative or structured registrations on how the children included in our cohort experienced filling in the KOOS, my experiences with administrating the KOOS to children are very similar to the difficulties reported by Örtqvist et al.[191] Particularly, questions related to the *Activities of daily living* subscale such as carrying groceries and domestic work were frequently commented to be irrelevant. The IKDC 2000 has also been found to be difficult to comprehend and answer for children. Iversen et al.[112] described the importance of lexical comprehension when patient-reported outcome measurements are used, and that this issue demand considerable attention when questionnaires intended for children are developed. They performed an identical evaluation of the IKDC 2000 as Örtqvist et al.[191] of the KOOS, with cognitive interviews of 30 American children with a primary knee injury. They reported that the children often read only parts of the questions and had trouble with understanding the timeframes and that the questions were primarily related to their knee injury. It was especially difficult for the children to comprehend the concepts of; strenuous/moderate activity, pivoting, locking, giving way, significant pain/swelling, and catching. Thus, the results that we have reported in **Paper III** must be considered with caution, and comparison of the scores to results from studies on adult participants should be avoided.

Isokinetic muscle strength measurements and four single legged hop tests were used to evaluate knee function in **Paper III**. These outcome measurements have been shown to be reliable and valid to evaluate knee function in adult subjects. Isokinetic muscle strength measurements using the peak torque value, with test velocities between 30 and 180°/s, have also been documented to be reliable in healthy children,[52, 160] although the reliability and validity has not been investigated in a paediatric ACL injured population. Further, normative data for isokinetic strength variables in 191 girls and 185 boys in the ages 7 to 12 years have been published.[102] To target the possible bias of low reliability all involved testers were experienced, and underwent training prior to data collection. Additionally, the intra-tester and inter-tester reliability with two of our testers was evaluated in a master thesis performed in our institution.[115] The inter-tester results at a test velocity of 60°/s showed an ICC (95% CI) for peak torque knee extension of 0.81-0.82 (0.42-0.92), and for peak torque knee flexion of 0.76-0.81 (0.49-0.91). Intra-tester results (HM) were slightly higher with 0.85-0.87 (0.62-0.94) and 0.77-0.81 (0.55-0.91) for knee extension and knee flexion, respectively. The minimal detectable changes (MDC) were estimated to 15.5 Nm (15.3-15.7%) for knee extension, and 12.5 Nm (22.8-24.6%) for knee flexion. The MDC data for children were lower than those previously published for adults (Knee extension, 22.76 Nm; and knee flexion 33.93 Nm).[161]

The four single legged hop tests were first described by Noyes et al.[185] in 1991, and have been used extensively with the purpose of evaluating knee function in healthy, ACL deficient and ACL reconstructed patients.[58, 85, 146, 208] Reid et al[202] have reported that these tests are a reliable and valid measure of knee function in adult ACL injured patients, although their reliability and validity have not been documented in children. In 2011 we also evaluated the inter-tester and intra-tester reliability of the single legged hop tests between two of our experienced testers. The inter-tester results showed an ICC of 0.72-0.91, while the intra-tester showed an ICC of 0.62-0-88. The MDC for the four single legged hop tests were: 12.8-13.8% (SH), 15.7-20.5% (TCH), 10.8-14.2% (TH), and 11.8-14.7% (6m-timed).[115]

The pivot shift test was included as a clinical outcome measure, and KT1000 measurements to evaluate knee laxity. A positive pivot shift test is characterised by anterior subluxation of the tibial plateau out from beneath the lateral femoral condyle,[64, 77] and a negative test has been associated with adequate functional stability in adults.[130, 141] The pivot shift test is performed manually, and the results highly rely on the experience of the investigator and the complete relaxation of the child.[5, 196] To optimise the consistency in the grading of the pivot shift test all tests were performed by one experienced orthopaedic surgeon (LE). The KT1000 has been shown to be valid and reliable when performed in experienced hands,[249] and the measurements were thus performed by only two experienced investigators at inclusion and the subsequent follow-ups.

Discussion

In **Paper IV** high resolution 3.0T MRIs were used to evaluate the integrity of the intraarticular tissues of the cruciate ligaments, the menisci, and the articular cartilage. 3.0T MRI has been proposed to produce images of higher quality than 1.5T MRI systems, and should thus increase the accuracy of diagnosing intra-articular knee pathologies. However, the magnetic susceptibility artefacts may be larger at 3.0T, and the possible enhancements of increased magnet fields are still not solidly confirmed.[100] The sensitivity and specificity of MRI for the detection of ACL tears in children is reported to be 95% and 88%, respectively.[140] In children under 12 years of age the sensitivity and specificity for diagnosing meniscus injuries is reported to be 62% and 78%, respectively[124]. The vascularisation and maturation of the menisci have been proposed to increase the difficulty in correctly diagnosing meniscus pathology in children[199, 255]. Yet, Sanchez et al.[212] and Major et al.[153] have described that the accuracy of MRI as a diagnostic tool for meniscus injuries in children and adolescents is acceptable.

The 160 MRIs in **Paper IV** were analysed by two experienced MRI radiologists independently in April 2012. A meeting was also held prior to the independent analysis to ensure agreement on classification criteria and the reporting of observations. A standardised scoring form was developed and utilised, and a consensus meeting was held to achieve agreement with regard to the results of the study. Additionally, although not within the scope of the aims in **Paper IV**, the inter-observer agreement was subsequently evaluated to generate knowledge for future studies. The inter-observer agreement in the children's injured knee was excellent for the diagnosis of ACL injuries and lateral meniscus injuries ($\varkappa$=0.81 and $\varkappa$=0.87, respectively), while it was moderate for medial meniscus injuries ($\varkappa$=0.47), and fair for the classification of cartilage injuries ($\varkappa$=0.38). Interobserver kappa ($\varkappa$) coefficients with 95% confidence intervals are presented in Table 5.

	Cohen's k (95% CI)
ACL	0.81 (0.70 – 0.93)
Meniscus injury, yes/no	0.57 (0.39 – 0.75)
Medial meniscus injury, yes/no	0.47 (0.26 – 0.68)
Medial meniscus sub classification	0.33 (0.21 - 0.46)
Lateral meniscus injury, yes/no	0.87 (0.75 – 0.99)
Lateral meniscus sub classification	0.51 (0.38 - 0.64)
Cartilage injury, yes/no	0.38 (0.06 – 0.71)

Table 5 *Interobserver agreement of the analysis of MRIs in ACL injured skeletally immature children (**Paper IV**).*

The ACL was classified according to criteria described by van Dyck et al.[240] as being normal, with total rupture, or partial rupture. Diagnosing partial tears of the ACL using MRI has previously been shown to be problematic, particularly because imaging characteristics overlap with those of total ruptures and mucoid degeneration of the ACL.[240] The inter-observer agreements for ACL injuries were excellent in the present study. Six ACLs were classified as partial ruptures even though all six had been diagnosed with a total rupture according to the inclusion criteria of the study. It has been proposed that children may have enhanced possibilities of healing. We could not however verify the possible partial regeneration of the ACL in the included children of the present study because arthroscopies were not performed diagnostically after the acute injury or subsequently during the follow-up period. However, all these patients had a positive pivot shift and a KT 1000 difference of more than 3 mm at inclusion for the study.

The agreement on the classification of lateral meniscus injuries was also excellent, while medial meniscus injuries and cartilage injuries seemed to be more difficult to analyse. Injuries in the menisci were classified as being normal, having a horizontal rupture, a longitudinal rupture, a radial rupture, or having high signal without rupture[124, 167, 235]. We particularly emphasised differentiating normal vascular structures known to be present in children (high-signal without rupture, grade 2) from grade 3 ruptures[235]. Nevertheless, the majority of discrepancies between the two radiologists were related to the classification of medial meniscus tears and high-signal without rupture in the medial meniscus, which highlights the difficulty with accurate diagnosis of subtle medial meniscus injuries in children. The articular cartilage was described as normal or injured (grade 0-4) based on the International Cartilage Repair Society (ICRS) classification of cartilage injuries[33]. The ICRS classification criteria were developed to be used when cartilage injuries are classified with an arthroscopic evaluation,[33] although it has also been used to classify articular cartilage from MRI.[86, 87, 213] It has been suggested that 3.0T MRI provides convincing visualisation of the hyaline cartilage with good diagnostic values,[83, 168, 241, 245] although the positive predictive values seem to be low for all grades of cartilage lesions. Again, the difficulties of diagnosing cartilage injuries were visualised by low inter-observer agreement for articular cartilage injuries.

In **Paper III and IV** we have classified the children's activity level based on registration from two different methods. The online activity surveys were submitted by e-mail monthly throughout the prospective cohort study. The surveys were e-mailed to the address that the parents registered at the baseline assessment, and they were encouraged to answer the survey together with the children. However, we have no registrations of who actually responded to the surveys, although our impression is that the vast majority were answered by one of the parents. The validity and reliability of the online activity survey has not been investigated in children, although another PhD candidate in our group is currently writing a manuscript in which the validity of the survey in adults is evaluated. At the yearly follow-up assessments the children were instructed to state which activity they regarded to be their main leisure time sports activity. In relation to the fact that children had problems with comprehending concepts like strenuous/moderate as reported by Iversen et al.,[112] we consider it a significant strength of our studies that it was the test administrator, and not the children, who performed the actual classification of activity level in accordance with the criteria.[93]

Results

The main aims of this dissertation were to evaluate changes in knee function and to explore the incidence of new intra-articular injuries in skeletally immature children 12 years and younger following a non-operative treatment algorithm after ACL injury. We have proposed a treatment algorithm for skeletally immature children (**Paper I**), and documented the methodological quality of the literature to be low (**Paper II**). The results of **Paper III** document that skeletally immature children with ACL injury were well functioning and had adequate knee function recorded with performance-based outcome measures with a total follow-up of 3.2 ± 1.1 years. The vast majority of children (91%) reported to be physically active in pivoting sports and/or physical education in school on a regular basis. However, we also found a significant reduction in the children's reports of performing a Level 1 activity as their main activity throughout the study, which indicates that the lives of skeletally immature children are affected by their knee injury. In **Paper IV** the incidences of new injuries to menisci and articular cartilage were documented to be low (3.2%) in 30 ACL deficient skeletally immature children with a total follow-up time of 3.0 ± 1.1 years.

Few authors have previously published their treatment algorithms and the rationale for treatment decision making based on the best available evidence. A research group from Boston, USA, have proposed an algorithm in which the youngest children (Tanner stages 1 and 2) are treated with physeal sparing reconstructions, and older children (Tanner stage 3) undergo a transphyseal reconstruction.[69, 125, 129] Additionally, Milewski et al.[166] recommended a comparable algorithm in which several different physeal sparing reconstruction techniques were guided by the age of the injured child.[166] Mohtadi & Grant[172] suggested that ACL deficient skeletally immature children should be treated with activity modification, rehabilitation, bracing, and monitoring. In cases where the rehabilitation failed to provide a successful outcome (unable to modify activities, recurrent effusions, and instability) they recommended a transphyseal ACL reconstruction, while those cases who were successful after rehabilitation waited until skeletal maturity when a transphyseal ACL reconstruction could be performed.[172] However, the option of recommending primary non-operative treatment has generally been discarded in the literature without a solid scientific foundation.

From **Paper I** we found that there was a major lack of high quality studies, treatment decision criteria, and in particular rehabilitation programs for skeletally immature children after ACL injury. This was further supported in **Paper II** in which the methodological quality of the literature was evaluated using the Coleman Methodology Score. Thirty-one studies were included, of which two were prospective cohorts and 29 were retrospective case series. The mean CMS was 44.7 ± 9.2 points, which is substantially lower than what has previously been reported for orthopaedic studies.[169, 188, 192, 248] In previous systematic reviews where the CMS has been used, Coleman et al[46] have reported the lowest mean CMS was 37.3 ± 15.9 points in studies on the surgical outcome of patellar tendinopathy. The highest CMS reported are from studies on different techniques on collagen meniscus implantations[92] and microfracture cartilage repair technique[169], with means of 67.1 ± 18.6 points and 58.2 ± 3.6 points, respectively. Jakobsen et al[113] reported an average CMS of 43.5 ± 12.5 in studies on cartilage repair, while Øiestad et al[188] evaluated studies on long term follow up of adult subjects with ACL injury and reported an average modified CMS of 52.2 ± 13. Thus, the quality of studies focusing on treatment of skeletally immature children after ACL injury in **Paper II** was evaluated to be low. The maximum CMS was 62 points,[144] and the lowest score was 28 points.[81] The main methodological deficiencies were related to five areas. (1) Study size: The number of children in the included studies was low. There were 10 studies with more than 40 children, and 11 studies with less than 20 children included. (2) Study design: Only two studies were prospective. (3) Description of rehabilitation programs: Rehabilitation guidelines were adequately described in only one study. (4) Inclusion of adequate outcome measures: Twenty-eight (90%) of the studies did not include adequate outcome measures for the detection of secondary meniscus and cartilage injuries at the follow-up assessments. (5) The use of established and validated outcome measurements: Outcome measurements utilised were in general not validated. The most important features in favour of prospective study designs in orthopaedic research is that prospective cohort studies allow a determination of a temporal sequence of events.[36] Additionally, follow-up times are standardised and recall bias is minimised. Thus, prospective cohort studies tend to provide substantially stronger and often more reliable data than retrospective studies. The methodological quality has been addressed in only one previous systematic review on treatment of ACL injuries in skeletally immature children,[172] although a quantification of the quality was not performed. Therefore, conclusions from systematic reviews, and the literature on ACL injuries in skeletally immature children in general, should be interpreted with high levels of caution.

The results of the patient-reported outcome measurements in **Paper III** showed statistical significant changes on the KOOS subscale *Activity of daily living*, although the changes were small and of questionable clinical relevance related to the reported minimal detectable changes reported in adults.[47] Changes that were of likely clinical relevance were found in the ACL reconstructed subjects who showed mean increases larger than the assumed clinical relevant change in adults from the pre-operative test to 2 years post-operative; IKDC 2000, 20.0 ± 13.6 points, KOOS *Sport and recreation* 17.0 ± 27.0 points, and KOOS *Knee related quality of life* 30.0 ± 32.3 points. The lack of changes found in the patient-reported outcome measurements may indicate that the skeletally immature ACL injured children maintained their knee function following the non-operative treatment algorithm. However, the lack of changes may also reflect the fact that the outcome measurements may have been irrelevant and invalid for the population, as indicated by Örtqvist et al.[191] and Iversen et al.[112]. In non-operated children the IKDC 2000 was also used in our retrospective study, showing a median score of 85 (71-95) points in 20 children with a mean follow-up of 3.1 years. The mean IKDC 2000 score in **Paper III** was 82.9 ± 17.6 points among the non-operated children at 2 years, while the mean score for the 10 ACL reconstructed children was 85.1 ± 9.4 points. Kocher et al.[125] reported the mean score of the IKDC 2000 to be 96.7 ± 6.0 points with an average follow-up of 5.3 years after performing physeal sparing ACL reconstructions. Bonnard et al.[31] reported 39 (71%) class A, 14 (25.5%) class B, two (3.6%) class C, and 1 (1.8%) class D with a mean follow-up of 5.5 years after performing transphyseal ACL reconstructions with patella tendon grafts. Liddle et al.[144] reported 100% grade A in 17 prepubescent (Tanner stage 1 and 2) children with a mean follow-up of 44 months after transphyseal reconstructions. However, Liddle et al.[144] used the old IKDC form,[93] classification grades from the IKDC 2000 have not been published (Bonnard et al.[31] categorized the results), and neither the cut-off values nor the points are described in the two latter papers. The paper from Liddle et al.[144] was the only prospective study, while the others are retrospective. None of the studies stated how the IKDC 2000 was completed (child/parent/surgeon/other). In general the IKDC 2000 scores seem to be higher than what we have reported in **Paper III**. However, a direct comparison of the scores cannot be made due to the differences in study designs, populations, and non-unison way of reporting the results. However, the results may be used to generate hypotheses, which could be investigated further in a prospective controlled study (e.g. a multicentre prospective cohort).

Isokinetic muscle strength measurements are commonly utilised to evaluate changes in muscle strength after ACL injury and reconstruction.[12, 57, 58, 120, 198, 239] However, the use of such measurements of muscle strength in ACL injured skeletally immature children is rare in the literature. Increased muscle strength is an expected feature of maturation, and both girls and boys have been shown to increase their strength significantly through puberty.[53, 65] De Ste Croix et al.[53] have investigated the longitudinal development of isokinetic leg strength in girls and boys between the ages of 10 and 14 years. They concluded that the development of peak knee extension and peak knee flexion strength could be accounted for by the increase in stature and mass. However, they did not find any independent effects of maturation, classified by Tanner staging, on isokinetic leg strength increase in the same population. The clinical relevance of increased isokinetic strength during growth in children has not been established in the literature.[52] In **Paper III** the effect of increased stature and mass was adjusted by normalising the peak torque values of the isokinetic strength measurements to bodyweight. Still, there was a statistically significant increase in isokinetic muscle strength for both knee extension and knee flexion normalised to bodyweight in the injured side from baseline to the 1 year and 2 year follow-ups. Based on the MDCs for children,[115] the changes from baseline to the 2 year follow-up seem to also be clinical relevant. The isokinetic strength of the uninjured legs showed no change from baseline to 1 year, and a significant increase from 1 year to 2 years. We may therefore assume that the increased muscle strength is partly attributed to rehabilitation from baseline to 1 year, while the increase from 1 year to 2 years may be ascribed to maturation because a number of the children probably entered maturity throughout the progression of the study. The mean adjusted peak torque values in the ACL deficient knee at the baseline (mean age 11.8 ± 1.3 years) assessment was 195.5 ± 44.9 (Nm/kg)x100 and 103.8 ± 24.3 (Nm/kg)x100, for knee extension and flexion, respectively. Holm et al. published normative data for peak torque isokinetic muscle strength with a test velocity of 60 °/s in children aged 7 to 12 years in 2008.[102] They did however report the absolute peak values (Nm), and not values adjusted for body weight (Nm/kg). Estimations based on the reported mean absolute peak torque values and the mean body weight in children aged 12 years, 31 girls and 28 boys, show mean values of 183.2 (Nm/kg)x100, and 117.9 (Nm/kg)x100, for peak isokinetic knee extension and flexion, respectively.[102, 103] Although a direct comparison to the estimated normative data is not possible, it seems that the ACL deficient children showed normal isokinetic muscle strength values at the baseline assessment. However, large variations in the results was found in our data as well as the data presented by Holm et al.[102] Furthermore, the LSIs for muscle strength in knee flexion and knee extension were above 90% at all measurements, which is comparable to the results from our previously published retrospective study.[174] The standard deviations, for knee flexion in particular, were smaller in the present study, which may reflect that the prospective study included a more homogenous population. Furthermore, based on the results from **Paper III** we found that in the total population 69.8% showed an LSI above 90% for knee extension at the 2 year follow-up, while the corresponding number for knee flexion was 53.5%.

Single legged hop tests have been shown to be valid and reliable to investigate functional knee stability in ACL deficient and reconstructed subjects.[96, 202] The use of the uninjured leg as a control to evaluate leg symmetry indices is commonly utilised and shown to be an adequate measure following rehabilitation of knee injuries.[85, 146, 198] In **Paper III** the LSI of the single legged hop tests showed statistically significant changes (SH increased from baseline to 1 year, and 6m-timed decreased from 1 year to 2 year follow-up), although the changes were minor and of questionable clinical relevance related to the MDCs of 10.8%-20.5% observed in children.[115] The single legged hop tests were performed to provide an evaluation of the functional knee stability after ACL injury or reconstruction. A LSI of 90% or more is commonly referred to as normal knee function, and also frequently used as a functional criterion in return to sports decisions.[135, 239] The mean LSIs for the four single legged hop tests were above 90% on all time points in the prospective cohort study, which again is comparable to our retrospective study on 20 non-operated children from 2008.[174] Based on the results in **Paper III** we found the proportions of children who at the 2 year follow-up performed the hop tests with LSIs above 90% to be 81.0%, 80.0%, 82.5%, and 82.9% for the SH, TCH, TH, and 6m-timed, respectively. This indicates that the majority of children were well functioning, although there is also a possibility that the four single legged hop tests were not able to distinguish those with good functional knee stability from those with poorer functional knee stability. In a case report of three skeletally immature children who underwent physeal sparing ACL reconstructions at ages 10 years, 12 years, and 12 years, Lawrence et al.[139] reported that hop tests and strength tests were performed with LSI above 90% at a one year follow up. They did not report which hop tests or what kind of muscle strength measure that was used, and no values for the tests were given. To our knowledge, no other studies have reported the detailed results from performance-based functional outcomes.

In **Paper IV** the incidence of new injuries both to the menisci and articular cartilage was found to be low (n=1, 3.2%) in the 30 children who were ACL deficient at the first MRI. The assumed increased risk of new injuries to the menisci and articular cartilage is the most serious statement raised to justify the indication of performing early ACL reconstructions in skeletally immature children.[69, 105, 138, 166] A concern with such an statement is that it has not been evaluated in studies with sound methodological quality. However, when an expert opinion is continuously repeated it may in the end be regarded as the truth, which may subject children with ACL injuries to undergo unnecessary treatments. **Paper II** showed no high-quality studies on non-operative treatment algorithms, and **Paper IV** documented that the incidence of such injuries following a non-operative treatment algorithm was low in our population (3.2%). The overall prevalence of knees with meniscus injuries (32.3%) was in the lower range of what has been reported in previous studies on early ACL reconstructions in similar populations.[45, 50, 95, 125, 129, 138, 170, 184] Throughout the prospective cohort study, eight (17.4%) of the 46 children underwent surgical procedures for meniscus injuries; five were repaired and three were partially resected. Currently, the largest retrospective study on ACL injuries in skeletally immature children has been presented by Nikolaou et al. They reported a prevalence of meniscus injuries of 35% in 94 children who underwent transphyseal ACL reconstruction at median 4 months after injury. The majority of meniscus injuries were repairable (85%), and located in the red zone of the medial meniscus.[184] Lawrence et al.[138] retrospectively compared the intraoperative prevalence of meniscal injuries in children who underwent ACL reconstruction more than 12 weeks after injury, to children who were operated before 12 weeks. They found a significant increased risk of meniscal and articular cartilage injuries in children who were operated more than 12 weeks after injury. However, there were 15% medial, and 40% lateral meniscus injuries in the children who underwent early surgical treatment as well. Conversely, the results from our prospective study provide data which show that a non-operative treatment algorithm does not necessarily lead to new secondary injuries to the menisci or articular cartilage. Thus, undergoing a non-operative treatment algorithm seems to be a safe option for skeletally immature children who are reluctant to undergo an ACL reconstruction before skeletal maturity. With regard to clinical decision making, the results of **Paper IV** should enable consultants and clinicians to more confidently recommend a non-operative treatment algorithm to skeletally immature children with an ACL injury and their families.

Additionally, the impact of the knee injury on the children's physical activity was imperative to monitor, as return to pre-injury activity is a commonly used success-criterion in orthopaedic literature.[14] Thus, to investigate possible changes in physical activity, the children's participation in physical activities was monitored with a monthly activity survey, and their main leisure time sport activity was registered at the yearly follow-ups. In **Paper III** the vast majority (91%) of the children reported from the online activity surveys that they were regularly participating in pivoting sports and/or physical education in school. In light of the described positive effects of physical activity on a healthy physiological and psychological development these finding are positive. No previous studies have performed prospective multi-response registrations of activity level in children after ACL injury. However, we also found a significant proportion (38%) of the children reported a reduction in performing a Level 1 activity as their main leisure time sport activity. Furthermore, among the 10 ACL reconstructed children five (50%) children discontinued performing a Level 1 activity as their main leisure time sport activity after surgical treatment. Based on the results from **Paper III**, 19 (41%) of the 46 children in the prospective cohort study reported a decreased level of main leisure time activity at the latest follow-up. Pre-injury classification was; Level 1, n=39 (85%), and Level 2, n=7 (15%), and classification at the final follow-up was; Level 1, n=23 (50%); Level 2, n=14 (30.4%); Level 3, n=9 (19.6%). Bonnard et al.[31] reported that 15 (27%) of 55 children were participating at a lower level sport than before their injury in a retrospective study with a mean follow-up of 5.5 years. All children had undergone an ACL reconstruction using patella tendon grafts with a physeal sparing technique. Liddle et al.[144] reported no significant changes (p=0.56) in the Tegnér activity scale from pre-injury to the mean 3.7 years (minimum 2.1 years, and maximum 8.3 years) follow-up. Nikolaou et al. reported that 78% of the 94 children included in their study on transphyseal ACL reconstructions reported to have returned to sports activities similar to the pre-injury activities. Additionally, 90% returned to their pre-injury level of daily activities, although the method used to obtain the data for these results are not described in the retrospective study.

Hence, from the registrations of physical activity in the prospective cohort study, we argue that an ACL injury in a skeletally immature knee is a serious injury which will burden the lives of children regardless of management option pursued. We have not investigated the reasons behind their decision for abandoning Level 1 activities as their main leisure time sport activity. In studies where return to pre-injury activity level is used as a success criterion such a change of activity would have been regarded failure of treatment.[6, 13, 21, 84, 142, 214] However, there are indications that returning to pivoting sports after an ACL injury may increase the rate of development of knee OA.[75, 148, 207, 246] Thus, the compliant individual who lowers their activity level and refrains from pivoting sports, the so-called "adapters", may have a reduced risk of future knee OA compared to those who continue Level 1 activities after ACL injury, regardless of treatment option pursued.[38, 180] It is our intention to follow the children we have studied in this dissertation and to continue to monitor their knee function, activity level, and the structural integrity of their knee joints in the long-term. Results from longer term follow-up studies may shed light on possible risk factors for the development of knee OA in skeletally immature children after ACL injury, and generate new hypotheses for experimental studies.

Conclusions

This dissertation has evaluated the functional and radiological outcomes following the implementation of a non-operative treatment algorithm for skeletally immature children after ACL injury. The body of evidence, needed for future experimental studies to investigate the effect of different treatment algorithms in this population, has been strengthened. New knowledge has been provided to assist clinical decision making. An evidence-based treatment algorithm has been developed, and the current methodological quality of the literature on the treatment of skeletally immature children has been investigated. The main conclusions which may have an impact on future clinical practice and research were:

I. The methodological quality of the literature on treatment of skeletally immature children after ACL injury was low. In particular we identified a lack of properly sized prospective cohort studies on homogenous populations, few studies including functional outcome measurements, an absence of descriptions of rehabilitation protocols and valid outcome measurements, as well as no randomised clinical trials on the effect of different treatment modalities (**Paper II**).

II. Patient-reported and performance-based outcome measurements did not show clinical relevant changes in knee function in ACL injured skeletally immature children following a non-operative treatment algorithm (**Paper III**).

III. Skeletally immature children remain physically active following a non-operative treatment algorithm after ACL injury, although 38% of the ACL deficient children abandoned a Level 1 activity as their main leisure time sport activity (**Paper III**).

IV. A low incidence of new injuries to the menisci and articular cartilage was found after implementing a non-operative treatment algorithm in ACL injured skeletally immature children (**Paper IV**).

Future perspectives

The incidence of traumatic ACL injuries in the paediatric population seems to be rising. More children are participating in high level sports and leisure time activities with high risk of knee trauma at a young age. However, the true incidence and risk factors for ACL injuries in children are unknown. Thus, there is an imminent need of properly sized **prospective epidemiologic studies** to establish the extent of the problem, and to analyse the risk factors associated with different sport activities. Subsequently, the knowledge from such epidemiological studies should be used to develop specific initiatives to enable **prevention** of ACL injuries in the paediatric population.

There is still a need for prospective studies on the different treatment algorithms recommended to skeletally immature children after ACL injury. Additionally, the effect of different rehabilitation programs emphasising structured exercises should be performed to investigate the optimal content, dose, and duration in children after ACL injury. The most appropriate study design would in our opinion be **international multicentre prospective studies**. Most institutions seem to have a tradition and culture for recommending the different algorithms to skeletally immature children after ACL injury. An international multicentre prospective study would allow the different institutions to continue their preferred treatment recommendations, which is likely to increase the adherence to contribute in the study. Furthermore, such a study would need a standardised battery of valid outcome measurements with which the included children are evaluated at standardised time intervals. Patient-reported outcome measurements, performance-based functional tests, radiological outcomes and monitoring of the children's activity level should be included.

Finally, the outcomes after paediatric ACL reconstructions should be studied further. The literature today focuses mainly on the risk of iatrogenic growth disturbances, although such adverse events are reported to be rare. In our opinion the **development of the ACL graft** within the growing knee after surgical treatment may be an equally important factor influencing long term knee function in skeletally immature children. The increased focus on anatomical ACL reconstructions in adults has evolved due to increased knowledge on the detrimental effects of non-anatomical reconstructions to the knee joint. Thus, the uncertain development of the ACL graft in skeletally immature children may be a more important factor for future knee function than whether children should be recommended transphyseal reconstruction, physeal sparing reconstruction, or non-operative treatment algorithms.

Our research group have, in collaboration with international partners in ESSKA, started to explore the possibility of starting a project which has been called the Paediatric ACL Monitoring Initiative (PAMI). The aim of the project is to establish a European registry of ACL injuries in skeletally immature children. Children should ideally be registered at the time of diagnosis, and then prospectively be evaluated from the injury and forward, which will allow prospective evaluations of both non-operative and surgical treatment algorithms.

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Paper I

[CLINICAL COMMENTARY]

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Management of Anterior Cruciate Ligament Injuries in Skeletally Immature Individuals

Musculoskeletal injuries in individuals with an immature musculoskeletal system require a different set of considerations than injuries in adult individuals. Children are not small adults. Treatment alternatives and treatment decision criteria after anterior cruciate ligament (ACL) injuries must be implemented in light of the physiological processes within children and adolescents. In this clinical commentary we describe the existing knowledge about, and best practices for, treatment of ACL injuries in skeletally immature individuals. Additionally, we present a proposal for a treatment algorithm based on the literature and our extensive clinical experience.

There is a concern that the increase in sports participation exposes children to a higher risk of musculoskeletal injuries that may negatively influence long-term health.[70,88] ACL injuries are among the most severe and most frequent activity-related injuries sustained by active children.[18] An ACL injury inevitably leads to a prolonged absence from sports and leisure activities. Lifelong knee function and quality of life may also be affected due to a probable increase in the risk of developing early knee osteoarthritis (OA).[85] Throughout the last 2 decades, an increasing number of studies on ACL injuries among children have been published.[35,53,81] There are, to our knowledge, no epidemiological studies that specifically identify the true incidence of ACL injuries in the skeletally immature population,[16,41] although reports from ACL registries document that ACL reconstructions are most frequently performed in teenagers.[41]

The main challenge for the management of ACL injuries in the skeletally immature population is 2-fold: to safely implement treatment interventions that provide the best possible long-term functional outcomes and to reduce the risk of secondary meniscus injury or harm to the epiphyseal growth plates. ACL reconstructions involve a risk of iatrogenic growth disturbances,[20,61] while nonoperative treatment may involve an increased risk of secondary meniscus and cartilage injuries.[85]

Recently, Kaeding et al[53] and Frosch et al[35] separately reviewed the literature on the outcomes and risks of surgical treatment of ACL injuries in children. They found the outcomes to be good

SYNOPSIS: Anterior cruciate ligament (ACL) injuries in skeletally immature individuals remain a challenge for the child, the parents, orthopaedic surgeons, and physical therapists. The main challenges are the potential risk of recurrent instability, secondary injuries following nonoperative treatment, and the risks involved with surgical treatment due to the vulnerability of the epiphyseal growth plates. We first present the physiological background for considerations that must be made when advising on treatment alternatives for skeletally immature individuals after ACL injury. The implications of continuous musculoskeletal development for treatment decisions are emphasized. No randomized controlled trials have been performed to investigate outcomes of different treatment algorithms. There is no consensus in the literature on clinical treatment decision criteria for whether a skeletally immature child should undergo transphyseal ACL reconstruction, physeal sparing ACL reconstruction, or nonoperative treatment. Additionally, well-described rehabilitation programs designed for either nonoperative treatment or postoperative rehabilitation have not been published. Based on the currently available evidence, we propose a treatment algorithm for the management of ACL injuries in skeletally immature individuals. Finally, we suggest directions for future prospective studies, which should include development of valid and reliable outcome measures and specific rehabilitation programs. *J Orthop Sports Phys Ther 2012;42(3):172-183, Epub 4 September 2011. doi:10.2519/jospt.2012.3608*

KEY WORDS: *ACL, children, growth plates, kids, rehabilitation, surgery*

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and the risk of growth disturbances to be low. However, no randomized controlled trials (RCTs) have compared the outcomes of different surgical techniques or compared any surgical treatment to nonoperative management. In an earlier systematic review, Mohtadi and Grant[81] evaluated studies that compared early surgical treatment to delayed surgical treatment and concluded that the study designs were inadequate to recommend one treatment algorithm or intervention over another. The description of rehabilitation protocols is generally poor throughout the literature, and no studies on structured nonoperative treatment have been published to our knowledge.

The Anterior Cruciate Ligament and the Skeletally Immature Knee

The knee is a complex joint in which motion and stability are balanced by the interplay between passive and active structures.[54] The stabilizing defense systems of knee ligaments include intra-articular and periarticular collagen structures, which are supported by the neuromuscular system.[54]

The increased healing rate and capabilities of the immature musculoskeletal system[51,96] have implications for treatment considerations. Intrasubstance ACL injuries in skeletally immature individuals have been increasingly studied and recognized since the 1980s.[67,73] Previously, the tibial eminence was considered to be the "weak link," due to its relatively lower strength compared to ligaments in the immature knee.[27] But increased awareness and technological developments have revealed that intrasubstance tears are common.[56,71] In the developing skeleton, the epiphyseal growth plates are especially vulnerable, and injuries to these may result in significant limb length discrepancies and angular deformities.[17,61] The distal femoral physis is the most active growth plate in the human body, contributing approximately 1 cm of growth per year. The femoral physis is responsible for 70% of the longitudinal growth of the femur and 37% of the growth of the lower limb.[96] The proximal tibial physis contributes approximately 0.7 cm of growth per year, which equals 55% of tibial growth and 25% of lower limb growth.[96]

Several investigations have documented that pediatric knees have more ligamentous laxity than adult knees.[8,33,34,47] Additionally, Behr et al[9] and Shea et al[94] have described the anatomy of the ACL in skeletally immature individuals and shown that the femoral origin is completely epiphyseal, which makes the drilling of graft tunnels a technical challenge for orthopaedic surgeons. However, the femoral and tibial insertion sites in children of all ages, regardless of skeletal maturity, have proven to be consistently similar to adult insertion sites.[55] Moreover, Kim et al[55] documented that the angle between the ACL and tibia is significantly smaller in younger children than in older children. They reported that the angle between the ACL and tibia increases with age in both the sagittal and coronal planes, ultimately showing that angles comparable to those in adult knees were not observed before skeletal maturity.[55]

Anterior Cruciate Ligament Injury

ACL injuries occur most frequently in persons who participate in pivoting sports that involve running, cutting, hopping, and landing.[5,16] In an ongoing prospective cohort study, we found that skeletally immature individuals with ACL injury typically present a history of high-energy trauma or contact injuries. The most common activities at the time of injury in our cohort were alpine skiing, jumping on twin-tip skis, and playing soccer. The injury rates in children for alpine skiing have been reported to be 3.9 to 9.1 injuries per 1000 skier days, with the highest rates in children aged 1 to 10 years.[43,78] Although the incidence of ski injuries has decreased in adults, it has increased in children and adolescents over the last 2 decades.[39,43]

A total rupture of the ACL is usually located at the proximal insertion site on the lateral wall of the intercondylar notch.[11] When the ligament ruptures, often a distinct "pop" is heard and the individual experiences a feeling of the knee "giving way."[10,57] Partial ruptures have been reported to be more frequent in younger individuals than in adults, although partial ruptures have not been thoroughly investigated.[57,60]

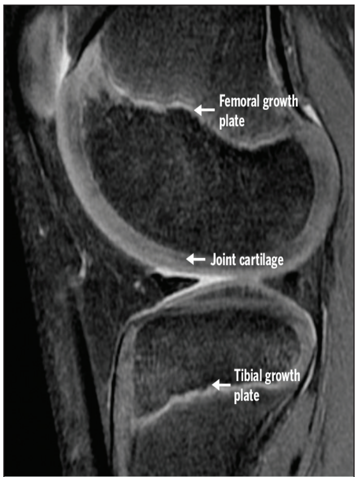

FIGURE 1. Magnetic resonance image showing thick cartilage without subchondral ossification and wide, open growth plates in a skeletally immature knee.

Acute ACL injury is usually followed by pain, intra-articular effusion, and muscular inhibition.[87] Persistent disability after the acute phase is attributed to increased knee joint laxity and altered neuromuscular function, which may lead to dynamic joint instability.

It has been documented that cartilage and meniscus tissues in children and adolescents differ from those in adults.[69] The immature meniscus and cartilage tissues have enhanced reparative potential due to high vascularity, increased thickness, and lack of subchondral ossification (**FIGURE 1**).[6,22,69] There is an increase in cartilage volume and thickness of the knee joint during growth, which correlates with levels of activity.[51] Additionally, traumatic meniscus and cartilage injuries are rarely seen in children younger than

10 years.[22,96] An increased risk of knee OA is a well-known consequence of ACL injury,[68,85,103] although specific risk factors for the development of OA are not fully understood.[85] Concomitant or secondary meniscus and cartilage injuries have been documented to be important additional risk factors for knee OA in adults, whereas ACL reconstruction has not been recognized to reduce the long-term risk of knee OA.[68,85,90] Some authors have proposed that immature children may be at little risk of developing early knee OA due to the lower forces involved in the injury trauma and the increased ability of the immature cartilage and meniscus tissues to heal and regenerate.[13,22,52] However, these theories need further investigation.

Examination and Diagnosis

The diagnostic accuracy of acute knee injuries in children is less than that in adults.[57,65,71] The increased difficulty in correctly diagnosing acute knee injuries in children has been suggested to be partly due to the naturally greater laxity in the knees of children,[57] and the reduced sensitivity and specificity of magnetic resonance imaging may also play a role.[57] Advances in technology and increased awareness of ACL injuries in this population will likely improve diagnostic accuracy in the future.[55] The combination of injury history, clinical examination (including the Lachman test and pivot shift test), and magnetic resonance imaging is recommended to optimize the diagnostic accuracy of ACL injuries in skeletally immature individuals.[10,71]

TREATMENT ALGORITHMS AND PROGNOSIS

The traditional treatment algorithm for ACL injuries in skeletally immature individuals consists of nonoperative management with active rehabilitation, activity limitations, and bracing until the child's skeleton is near the end of its growth.[58] However, the development of new surgical techniques

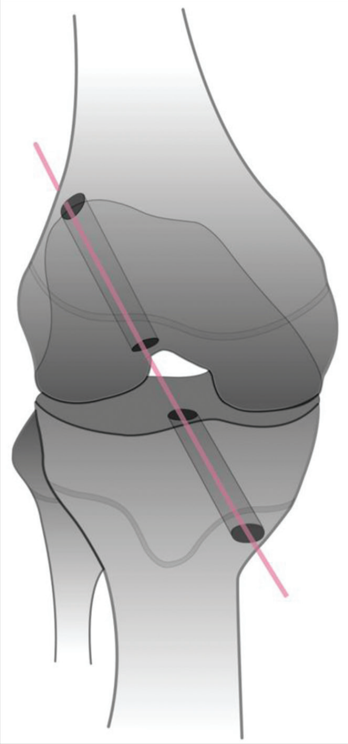

FIGURE 2. Illustration of transphyseal anterior cruciate ligament reconstruction.

has increased the number of orthopaedic surgeons who advocate treatment algorithms consisting of early ACL reconstruction.[25,38,63,66,83,99] The 3 most commonly reported treatment algorithms are transphyseal (adult) ACL reconstruction, physeal sparing ACL reconstruction, and nonoperative management. Transphyseal ACL reconstructions require the surgeon to drill a hole through both the proximal tibial physis and distal femoral physis to enable an anatomical reconstruction of the native ACL (**FIGURE 2**). An ACL reconstruction is described as physeal sparing when the surgical procedure does not involve drilling graft holes through the epiphyseal growth plates (**FIGURE 3**). To our knowledge, no RCTs comparing the outcomes of different algorithms have been published. A PubMed search for publications on the treatment of ACL in-

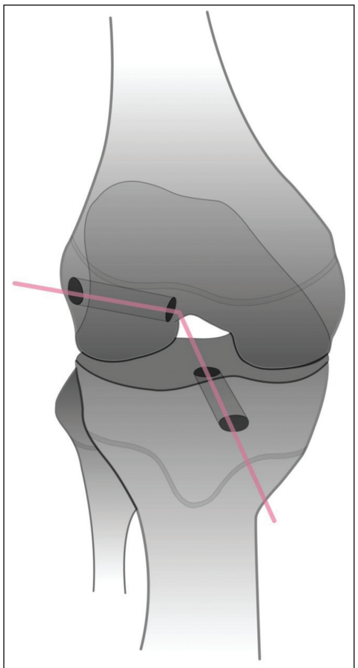

FIGURE 3. Illustration of physeal sparing anterior cruciate ligament reconstruction.

juries in skeletally immature individuals (minimum of 10 participants) identified 31 studies (**TABLE**): 19 (61%) on transphyseal reconstructions, 8 (26%) on physeal sparing reconstructions, and 4 (13%) on primary nonoperative treatment. There is agreement in the literature that the primary goals of treatment of ACL injuries in children and adolescents are to provide a functional, stable knee, to preserve the menisci, and to avoid iatrogenic growth disturbances following surgical treatment.[35,53,81] Despite the increased awareness of intrasubstance ACL injuries in children, there is still no consensus on the optimal timing of surgery, surgical technique, or rehabilitation program. Although the optimal surgical technique is still being debated, there seems to be consensus that an ACL reconstruction is necessary at some point for children and adolescents who want to continue participating in cutting and pivoting sports.

TABLE	Overview of Studies Including Treatment Algorithm			
Study	**Number of Patients**	**Treatment**	**Age at Inclusion***	**Follow-up***
Aichroth et al, 2002[1]	45	T	13 (11-15)	4.1 (1.0-8.0)
Arbes et al, 2007[4]	20	T	13.9 (9-15)	5.4 (0.5-10.5)
Aronowitz et al, 2000[7]	21	T	13.4 (11-15)	2.1 (1.0-5.0)
Cohen et al, 2009[23]	26	T	13.3 (11-15)	3.8 (2.0-7.0)
Courvoisier et al, 2011[25]	37	T	14 (11-15)	3.0 (2.0-4.0)
Edwards and Grana, 2001[29]	20	T	13.7 (11.8-15.6)	2.8 (1.4-7.4)
Fuchs et al, 2002[36]	10	T	13.2 (9-15)	3.3 (2.2-5.0)
Gaulrapp and Haus, 2006[37]	53	T	13.9 (9-16)	6.5 (3.0-11.0)
Henry et al, 2009[45]	56	T	12.4 (5.0-16.8)	2.3 (1.0-6.8)
Kocher et al, 2007[63]	59	T	14.7 (11.6-16.9)	3.6 (2.0-10.2)
Kopf et al, 2010[64]	14	T	14.4 (11-16)	7.0 (1.9-11.1)
Liddle et al, 2008[66]	17	T	12.1 (9.5-14.0)	3.8 (2.1-8.3)
Marx et al, 2009[72]	55	T	13.4 (8.4-16.6)	3.2 (1.0-7.5)
McCarroll et al, 1994[74]	60	T	13.7 (13-15)	4.2 (2.0-7.0)
McIntosh et al, 2006[75]	16	T	13.6 (11.2-14.9)	3.4 (2.0-9.3)
Nikolaou et al, 2011[83]	94	T	13.7 (11.5-16.0)	3.2 (2.0-5.0)
Seon et al, 2005[93]	11	T	14.7 (13.1-15.5)	6.5 (3.8-10.9)
Shelbourne et al, 2004[95]	16	T	14.8 (13.1-15.8)	3.4†
Streich et al, 2010[100]	31	T	11 (9-12)	5.8 (3.4-7.1)
Anderson, 2004[3]	12	P	13.3‡	4.1 (2.0-8.1)
Bonnard et al, 2011[15]	57	P	12.2 (6.8-14.5)	5.5 (2.0-14.0)
Gebhard et al, 2006[38]	40	P	11.9 (7-14)	2.8 (1.1-17.0)
Janarv et al, 1996[50]	28	P	13.1 (9.9-15.0)	⩾3.0
Kocher et al, 2005[58]	44	P	10.3 (3.6-14.0)	5.3 (2.0-15.1)
Lipscomb and Anderson, 1986[67]	24	P	13.5 (10-15)	2.9 (2.0-5.0)
Micheli et al, 1999[79]	17	P	11 (2-14)	5.5 (2.1-14.0)
Steadman et al, 2006[99]	13	P	13 (10-16)	5.8 (2.2-9.4)
Graf et al, 1992[40]	12	N	14.5 (11.7-16.3)	⩾2.0
Mizuta et al, 1995[80]	18	N	12.8 (10-15)	4.3 (0.8-8.3)
Moksnes et al, 2008[82]	26	N	10.3 (5.2-12.7)	3.8 (2.0-9.0)
Woods and O'Connor, 2004[107]	13	N	13.8 (11.0-16.0)	5.8 (1.8-24.5)

Abbreviations: N, nonoperative treatment; P, physeal sparing reconstruction; T, transphyseal reconstruction.
**Values are mean (range) years.*
†SD, ±1.1.
‡SD, ±1.3.

Complications Related to Surgical Treatment of ACL Injuries in Skeletally Immature Individuals

Skeletal growth disturbance is one of the main concerns of surgical treatment of ACL injuries in the skeletally immature individual. The problem of minimizing the risk of iatrogenic growth disturbances when performing ACL reconstructions in young patients has been addressed by several authors, and there seems to be agreement that small-diameter vertical drill holes placed centrally in the growth plate provide the least risk of physeal damage.[21,76,92] Wilmes et al[106] identified the end of skeletal growth to be the time of peak risk of growth disturbances from surgical drilling through the epiphyseal growth plates. Frosch et al[35] found the overall risk of a leg length difference or axis deviation to be 2.1% (19 of 906 knees) following ACL reconstruction in immature patients. Interestingly, they also found that the risk of growth disturbances was higher following physeal sparing reconstructions (5.8%) compared to transphyseal reconstructions (1.9%). However, these results should be considered with caution, because only a few studies have included full-length radiographs of the lower extremities at follow-up.[53] A recent publication by Chotel et al[20] reported 2 cases of skeletal overgrowth and angular deformity following physeal sparing reconstructions in children with wide, open physes. They highlighted the importance of continued attention to the potentially harmful effects of surgical treatment in children.

Treatment Decision Criteria

The majority of studies reported retrospectively on outcomes of ACL treatment, suggesting that poor outcomes of nonoperative treatment and greater risk of secondary meniscus injury are the primary reasons for performing ACL reconstruction in skeletally immature individuals. We are aware of only 2 studies in which functional preoperative outcome measurements were included,[50,66] while the majority of studies did not include any data on baseline or pretreatment knee function. To our knowledge, no well-designed studies on nonoperative management have been published, and the rates of secondary meniscus injuries in 3 of 4 case series were low.[80,82,107] There is an immense need for well-designed prospective studies with well-described inclusion criteria and long-term follow-up to develop evidence-based criteria for the treatment of skeletally immature individuals.

Transphyseal Reconstruction

The development of new and supposedly safer surgical techniques appears to have changed orthopaedic surgeons' views; they now more frequently accept the risks of growth disturbances involved with ACL reconstruction.[3,23,63,66,91] There is consensus that hamstring tendons should be utilized as ACL grafts in skeletally immature individuals to reduce the risk of growth disturbances.[53,81] With regard to following a predefined treatment algorithm, Kocher et al,[58,63] Liddle et al,[66] and Streich et al[100] used skeletal maturity as a criterion in their decisions on surgical technique. Kocher et al[58,63] used the transphyseal technique for young individuals in Tanner stage III and above, while those in Tanner stages I and II underwent ACL reconstruction with the physeal sparing technique. Conversely, Liddle et al[66] performed transphyseal reconstruction in children in Tanner stages I and II, while Nikolaou et al[83] chose transphyseal reconstruction in all patients, regardless of skeletal maturity. Streich et al[100] reported that children with isolated ACL injuries were nonoperatively treated, whereas children in Tanner stages I and II underwent transphyseal reconstruction if there were any additional injuries within the knee.

The rerupture rate of the ACL graft in children has been reported to be comparable to the rate in adult patients after transphyseal reconstruction (4.2%-11.9%).[35,53] The rerupture rate of physeal sparing reconstructions has been reported to be lower (1.4%-4.5%).[35,53] Frosch et al[35] and Kaeding et al[53] concluded that transphyseal ACL reconstructions in skeletally immature individuals demonstrated good and excellent functional results when measured with the Lysholm score and the International Knee Documentation Committee (IKDC) Subjective Knee Form score, respectively. However, we propose that the true functional outcome is unknown in this population, because no studies have included performance-based functional outcome measures at baseline or follow-up.

Another poorly investigated issue is the development of the ACL graft within the growing knee after surgical treatment. Kim et al[55] have described the increase of the angle between the tibial plateau and native ACL during growth in uninjured children. This change in the angle between the ACL and tibia during maturity presents a challenge for orthopaedic surgeons with regard to successful graft placement. Thus, if the ACL is reconstructed with the angle of adult knees in a skeletally immature knee, the graft angle is likely to become too steep and provide insufficient rotational stability when the child reaches skeletal maturity.[55] Additionally, in a prospective magnetic resonance imaging series on 5 skeletally immature individuals with ACL reconstructions, Bollen et al[14] documented a large increase in the length of the graft through maturity but no increase in the diameter of the graft during growth. They highlighted that the strain and remodeling of the graft due to skeletal growth after ACL reconstruction may lower the graft's biomechanical ability to withstand stress. Because knowledge of the physiological and biomechanical properties of the graft over time is limited, there is a need for further studies on this topic. Thus, caution should be taken during rehabilitation and return to sport for skeletally immature individuals.

Physeal Sparing Reconstruction

The most common argument against performing physeal sparing reconstruction is the inability of these techniques to place the ACL graft in the anatomically correct position.[15] Among the 8 largest published studies on physeal sparing techniques, 10 different surgical techniques were described.[3,15,38,50,59,67,79,99] Physeal sparing techniques were introduced in the 1980s, and the operated knee's ability to withstand the rigors of growth, time, and use was questioned early.[73,98] The previously mentioned study by Chotel et al[20] highlighted that growth disturbances cannot be excluded, even with the physeal sparing approach. This is supported by data from Frosch et al,[35] who found that the reported rates of growth disturbances were higher in studies on physeal sparing reconstruction than in studies on transphyseal reconstruction (5.8% versus 1.9%). Kaeding et al[53] found no differences between the 2 techniques for functional outcomes measured with the Lysholm score or the IKDC Subjective Knee Form score. Kocher et al[58] concluded that the physeal sparing surgical procedure provided an excellent functional outcome, with a low revision rate and minimal risk of growth disturbance in a population of children in Tanner stages I and II. Additionally, Bonnard et al[15] reported that 53 of 57 (93%) children achieved good or excellent outcomes as measured with the 2000 IKDC Subjective Knee Evaluation Form. In spite of the positive outcomes in some studies, a conclusive recommendation regarding this treatment algorithm cannot be made due to the diversity of physeal sparing surgical techniques.

Nonoperative Management

The importance of rehabilitation after ACL injury and reconstruction is universally recognized, and the evidence supporting the implementation of active rehabilitation programs for adults with ACL injuries is strong.[101] Despite the amount of published literature concerning different aspects of rehabilitation after ACL injury and reconstruction, there is no consensus on the type or number of exercises to include in rehabilitation programs.[101] A Cochrane review of exercise therapy after isolated ACL injuries and 2 systematic reviews of ACL rehabilitation identified only 8 studies that evaluated different aspects of nonoperative management.[24,89] None of the 8 studies included rehabilitation of skeletally immature individuals, and no RCTs of different rehabilitation programs for skeletally immature patients with ACL injuries have been published to our knowledge.

To address the potential for joint instability, individuals with an ACL injury are advised to undergo rehabilitation, which includes cyclic movements to improve joint homeostasis and neuromuscular and muscle strength exercises to restore dynamic knee stability.[19,49] In some cases, dynamic knee stability may be achieved through extensive rehabilitation alone.[105]

In general, rehabilitation programs after ACL reconstruction in adults have moved in a more aggressive direction, including early weight bearing, more powerful strength training, challenging neuromuscular and plyometric exercises, and an earlier return to sport.[12,31,42,102] In contrast, the sparse descriptions of rehabilitation programs for skeletally immature individuals appear to advocate a more conservative approach, with longer periods of non–weight bearing and bracing, and a later return to sport.[66,67,100] The slower and more conservative protocols for skeletally immature patients who undergo ACL reconstruction may be due to the uncertainty regarding the strength of the graft and the risk of growth disturbances, as well as the lack of evidence-based practice guidelines. Kocher et al[60] published a prospective cohort study of 45 skeletally mature and immature patients with partial ACL injuries that reported excellent outcomes. In that population, structured active rehabilitation without surgical treatment was recommended, although the authors did not describe the rehabilitation program. In studies on primary nonoperative treatment, the rehabilitation programs are insufficiently described.[40,80,82,107] There seems to be a consensus on the use of a knee brace during sports activities, although no RCT has been published that studies bracing and ACL injuries in children. Woods and O'Connor[107] followed the strictest algorithm, recommending bracing and activity limitations until surgical treatment at skeletal maturity, while Mizuta et al[80] and Moksnes et al[82] advocated bracing only when performing pivoting sports.

In studies using nonoperative treatment, no growth disturbances were reported. Woods and O'Connor[107] reported that the incidence of meniscus injuries at the time of surgery (46%) in the 13 included children was similar to the incidence in 116 skeletally mature adolescents treated with transphyseal reconstruction. Moksnes et al[82] reported 3 medial (11%) and 3 lateral (11%) meniscus injuries in 26 children during a follow-up period of 2 to 9 years, while Mizuta et al[80] reported 1 additional meniscus injury in a study of 18 skeletally immature patients (6%). Graf et al[40] reported 7 new meniscus injuries (88%) in 8 children who underwent delayed ACL reconstruction due to knee instability. Although the methodological quality of these studies must be taken into consideration, 3 of 4 studies did not show a high incidence of secondary meniscus injuries in nonoperatively treated children. Thus we find that the statement that nonoperative treatment will lead to a high number of secondary meniscus injuries should be interpreted with caution.

PROPOSED TREATMENT ALGORITHM

Our proposed treatment algorithm (**FIGURE 4**) is based on extensive clinical experience and the currently available evidence described in this manuscript. The algorithm advocates primary nonoperative management until skeletal maturity is reached for children with open growth plates. We advocate an initial treatment for skeletally immature individuals with ACL injuries with a structured and monitored rehabilitation program, to explore the possibility of returning good dynamic knee stability. Our previous study showed that approximately half the children with ACL injuries could be classified as copers (resumed preinjury activity level and had single-leg hop test indexes greater than 90% of the uninjured limb) without a high risk of secondary meniscus injuries.[82] Children with ACL injuries should be monitored and assessed by an orthopaedic surgeon and a physical therapist working together, and ACL reconstruction should not be considered before it has been established that a structured rehabilitation program was not successful in returning functional stability of the knee.

A supervised rehabilitation program consisting of a variety of neuromuscular, plyometric, and muscle-strengthening exercises is implemented. The neuromuscular rehabilitation component is based on the principles described in several studies on ACL injury prevention in adolescent athletes[46,86,97] and in adults with ACL injuries.[89,105] All children are given a functional, custom-fit knee brace that they are instructed to use when they are participating in pivoting sports and physical education classes in school. The children's activity levels, episodes of giving way, compliance with the use of the brace, and knee function are monitored monthly via a structured web-based questionnaire. The algorithm is currently being evaluated in a prospective cohort study.

The rehabilitation program is divided into 4 phases and consists of exercises

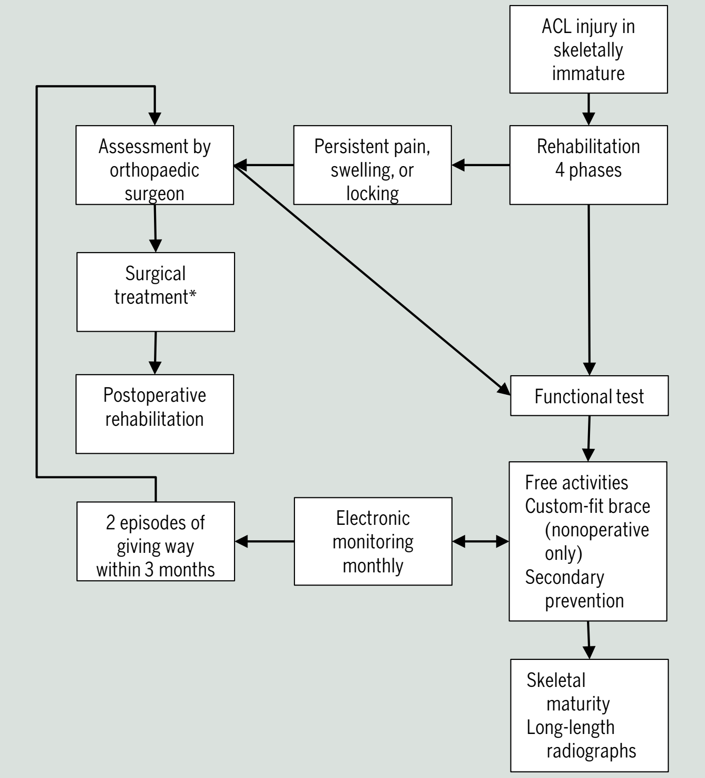

FIGURE 4. Proposed treatment algorithm for anterior cruciate ligament injury in skeletally immature individuals. *Indications for surgical treatment: repairable meniscus injury; inability to continue desired activities; repeated giving-way episodes.

targeted toward regaining range of motion, neuromuscular control, and muscle strength (**FIGURE 5**). Children consult their physical therapist once a week throughout phases 1 and 2 and once a month in phase 3. Rehabilitation to be performed at home is limited to a maximum of 3 exercises, all of which are reviewed and progressed at each physical therapy session. Children are progressed to the next rehabilitation phase when specific functional milestones are reached during each phase.

Phase 1

In the acute phase, the primary goals are to regain active and passive knee extension, resolve intra-articular swelling, and reactivate the quadriceps muscle. Dynamic open-chain unloaded extension exercises, stationary cycling, prone knee extension hangs, and partial weight bearing with a normal gait cycle are performed to achieve the rehabilitation milestones of straight leg raises without extension lag, successful weight-bearing single-leg terminal extension, and unrestricted normal gait patterns.

Phase 2

In the second phase, the primary goal is to normalize the activities of daily living. Neuromuscular exercises focusing on neuromuscular control of terminal knee extension in single-leg stance, step-up, and squatting exercises that avoid dynamic valgus,[46] and low-load, closed-chain quadriceps and hamstring exercises are included in the rehabilitation (**FIGURE 6**). The milestones in phase 2 are normal stair walking and participation in daily activities without experiencing instability or intra-articular swelling.

Phase 3

In the third phase, the primary goals are to be able to run without gait deviations and subsequent intra-articular swelling and to develop the ability to perform single-leg hops, including stable single-leg landings, with adequate neuromuscular control. Double-leg and single-leg hops are initially performed with focus on safe landings and optimal trunk, hip, and knee alignment. Hop exercises are progressed to multihop plyometric movements with stops and cuts. Neuromuscular training balance equipment, such as BOSU balls (BOSU, Canton, OH), is frequently incorporated in the exercises (**FIGURE 7**). Additionally, function-specific quadriceps and hamstring strength exercises are performed as home exercises without external loads. When the milestones of running 15 minutes without subsequent intra-articular swelling and performing single-leg hops with adequate landings are achieved, a functional examination is performed. The functional examination consists of an isokinetic muscle strength test with 5 repetitions at 60°/s[26,30] and 4 single-leg hop tests.[84] Isokinetic muscle strength testing and single-leg hop tests have been documented to be reliable in children and adolescents,[77,104] although validity and reliability have not been investigated in children with ACL injuries. Additionally, the newly developed modified IKDC Subjective Knee Form (Pedi-IKDC) has demonstrated acceptable psychometric performance for the assessment of outcomes in children and adolescents with various knee disorders[62] and may be an appropriate outcome measurement for this population.

Children are allowed to return to their

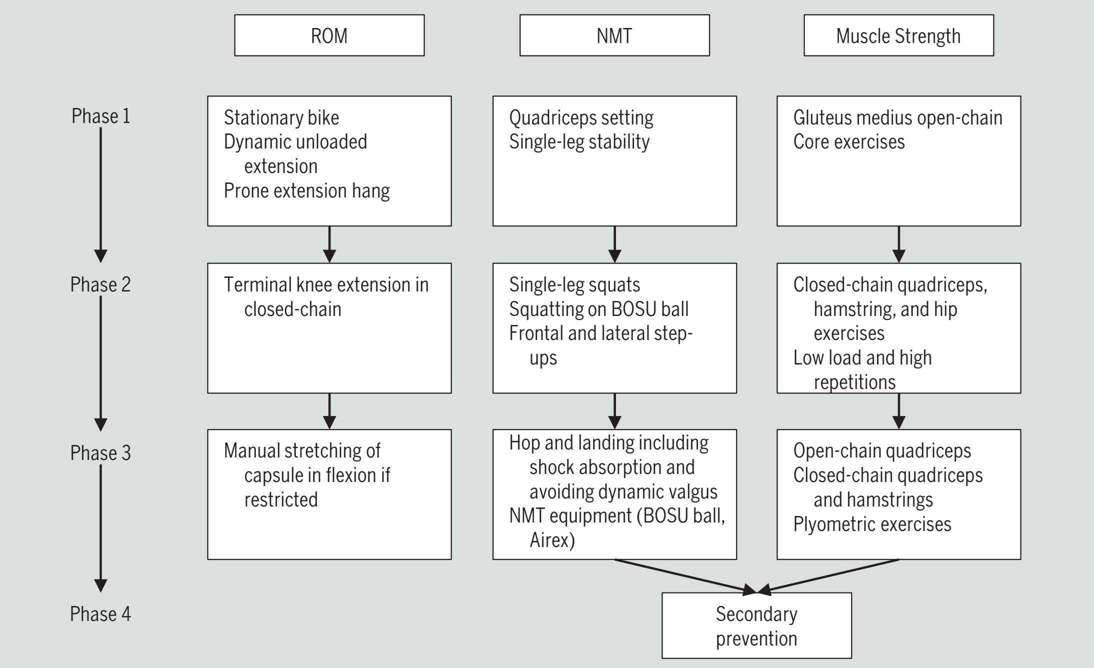

FIGURE 5. Proposed guide for the rehabilitation of anterior cruciate ligament injury in skeletally immature individuals. Progression through the 4-phase program is determined by functional progression milestones. Abbreviations: NMT, neuromuscular training; ROM, range of motion.

preferred activities wearing a custom-fit, functional knee brace, when they can perform all 4 single-leg hop tests and their strength score on the isokinetic test is at least 90% of the value of the uninjured side.

Phase 4

The fourth phase includes a selection of neuromuscular exercises focusing on maintaining functional stability as a secondary prevention measure. Children and their parents are advised to perform the secondary prevention exercises at least twice a week. They are also given the opportunity of consulting their physical therapist once a month for assessment and updates, and they are scheduled for evaluation by the orthopaedic surgeon once a year until skeletal maturity.

The inability to be active in preferred activities or repetitive episodes of giving way point toward performing an ACL reconstruction before skeletal maturity. Additionally, children who have a secondary repairable meniscus injury will usually undergo a meniscus repair with concomitant ACL reconstruction, as this is assumed to improve the prognosis of the meniscus repair.[44] At our treatment center, the transphyseal technique that uses a hamstring graft is preferred. It is also imperative to give the child and parents thorough information about the risks and options involved, including the option of continuing sports that involve fewer pivoting motions until skeletal maturity is reached, when a reconstruction involving less risk can be performed. ACL reconstructions in skeletally immature patients are performed with

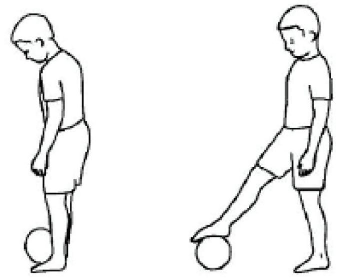

FIGURE 6. Exercise to enhance knee stability when standing on the injured/operated limb and to promote hamstring activation with the injured/operated limb on the ball.

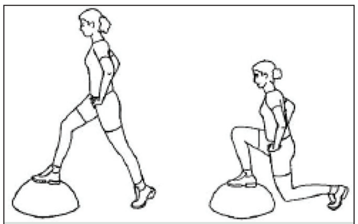

FIGURE 7. Exercise to enhance dynamic knee stability and quadriceps and hamstring muscle strength in phases 2 and 3.

centrally placed vertical drill holes, and fixation material is placed proximal to the femoral epiphysis and distal to the tibial epiphysis. The postoperative rehabilitation program is based on similar phases found in the nonoperative rehabilitation program, although individually adjusted time-based precautions are included in phases 1 and 2 to ensure the incorporation of the ACL graft and healing of meniscus sutures. The main differences between postoperative rehabilitation in skeletally immature patients as compared to adult patients are (1) a slower progression toward jumping and running to reduce the impact loading of the physis, (2) less use of external loads, (3) primarily home-based functional exercises, and (4) a later return to pivoting sports (after 9 to 12 months).

FUTURE DIRECTIONS IN RESEARCH

There is a need for properly sized prospective studies to investigate and report the content and outcomes of treatment after ACL injury and ACL reconstruction in skeletally immature individuals.[48] Validated, reliable, and sensitive outcome measures must be developed to assess dynamic knee stability over time.

Children should be included in studies early after injury, according to predefined inclusion and exclusion criteria and verification of skeletal maturity. Outcome measurements should consist of self-report questionnaires, functional tests, and imaging. Throughout the study, patients should be assessed at regular time intervals. At the final follow-up, full-length radiographs should be taken to assess leg length discrepancies and axis deviations. The follow-up time in such a study should last at least until skeletal maturity is reached. A rehabilitation program based on functional milestones should be included and compliance with rehabilitation should be monitored. Surgical treatment should be initiated before skeletal maturity according to preset functional criteria after an adequate postinjury rehabilitation. One surgical procedure should be utilized and the technique should be thoroughly described.

Additionally, epidemiological studies to identify ACL injury risk factors in children should be performed to facilitate the development of effective strategies to prevent ACL injuries in children. Several well-designed studies have documented important benefits of injury prevention programs for adolescent athletes,[2,32,86] although programs that effectively prevent ACL injuries in children younger than 12 years still need to be developed.[28]

SUMMARY

ACL injuries in skeletally immature individuals are seemingly occurring more frequently as children and adolescents participate in physical activities to a greater extent. Treatment of these injuries is still challenging because of the vulnerability of the epiphyseal growth plates and the lack of knowledge about the functional outcomes of established treatment algorithms. Based on the existing evidence and considering the risks involved with surgical treatment, we propose that all children undergo a well-designed, nonoperative rehabilitation program after injury. The rehabilitation program should include specific exercises to target neuromuscular control and muscle strength through functional training. Children with ACL injuries should be monitored for recurrent giving-way episodes and activity levels. ACL reconstruction using a hamstring graft and a transphyseal technique should be considered if the child is not able to uphold the desired activity level, has a repairable meniscus injury, or experiences recurrent giving-way episodes despite adequate rehabilitation. ◉

ACKNOWLEDGEMENTS: *We acknowledge Hjelp24 NIMI for our research collaboration, and Magnus Pettersen for providing illustrations to the manuscript.*

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Paper II

The Current Evidence for Treatment of ACL Injuries in Children Is Low

A Systematic Review

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Background: There is no consensus on the management of anterior cruciate ligament (ACL) injuries in skeletally immature children, and the methodological quality of published studies is questionable. The transphyseal reconstructions, physeal-sparing reconstructions, and nonoperative treatment algorithms that are advocated have little support in the literature. The purpose of this study was to systematically review the methodological quality of the literature on the management of ACL injuries in skeletally immature children.

Methods: We performed a literature search with use of PubMed to identify prospective or retrospective studies whose primary aim was to assess the outcome after operative or nonoperative treatment of ACL injuries in skeletally immature children. To be included in the analysis, a study had to have a mean duration of follow-up of at least two years and a minimum of ten children in the study had to be verified to be skeletally immature. The methodological quality of the included studies was evaluated with use of the Coleman Methodology Score.

Results: No randomized controlled trials, two prospective cohort studies, and twenty-nine retrospective studies met the inclusion criteria. The Coleman Methodology Score averaged 44.7 ± 9.2 out of 100 (range, 28 to 62). The methodological deficiencies were most evident with regard to the number of included children, the study design, and the description of rehabilitation protocols, outcome criteria, and outcome assessments.

Conclusions: Caution is necessary when interpreting the results of studies on the treatment of ACL injuries in skeletally immature children because of widespread methodological deficiencies. There is a need for appropriately sized prospective studies and detailed descriptions of rehabilitation programs.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

The increased focus on the health benefits of regular physical activities highlights the importance of youth participation in sports[1]. However, there is a concern that participation in sports exposes children to musculoskeletal injuries that may negatively influence their long-term health[2,3]. During the past two decades, there have been an increasing number of studies on anterior cruciate ligament (ACL) injuries in skeletally immature children[4]. The main dilemma is whether surgical treatment can provide an adequate functional outcome without harming the physis or whether nonoperative treatment should instead be advocated until skeletal maturity is reached. Nonoperative management has been associated with an increased risk of secondary injuries and future disability[5-7]. Two recent publications, a systematic review[8] and a meta-analysis[9], have concluded that surgical treatment is safe and provides a good functional outcome. Although concerns have been raised regarding the quality of studies on this topic, the methodological quality of these studies has not been assessed[4,8,9].

In the present study, we review the literature on the treatment of ACL injuries in skeletally immature children with use of the Coleman Methodology Score, which has recently

Disclosure: None of the authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of any aspect of this work. None of the authors, or their institution(s), have had any financial relationship, in the thirty-six months prior to submission of this work, with any entity in the biomedical arena that could be perceived to influence or have the potential to influence what is written in this work. Also, no author has had any other relationships, or has engaged in any other activities, that could be perceived to influence or have the potential to influence what is written in this work. The complete **Disclosures of Potential Conflicts of Interest** submitted by authors are always provided with the online version of the article.

been used to evaluate the methodological quality of studies on a variety of other orthopaedic treatments[10-17].

Materials and Methods

To be eligible for inclusion, published studies had to be randomized controlled trials, prospective studies, or retrospective studies on operative or nonoperative treatment of an intrasubstance ACL injury in skeletally immature children. In addition, the study population had to have a minimum of ten children who were verified to be skeletally immature, and the mean duration of follow-up had to be at least two years. Studies had to be in English, German, or a Scandinavian language.

Search Strategy and Study Selection

Two systematic searches were performed with use of PubMed, and studies published between 1966 and May 2011 were included. The search strategies are shown in the Appendix. The first search (search #13 in the Appendix) aimed to identify studies on surgical treatment of ACL injury in skeletally immature children, and the second search (search #14 in the Appendix) aimed to identify studies on nonoperative and postoperative rehabilitation after ACL injury in this population. The abstracts of the identified studies were reviewed independently by two of the authors to assess eligibility. If an abstract did not provide sufficient information, the full text of the article was reviewed. Additionally, the reference lists of included studies were reviewed to identify additional studies that had not been found through the initial searches. Inclusion of the studies was determined by consensus between the two reviewers. The full text of the included articles was retrieved and assessed for methodological quality. Each included study was categorized, on the basis of the primary treatment described, as involving (1) transphyseal reconstruction, (2) physeal-sparing reconstruction, or (3) nonoperative treatment.

Study Quality Assessment

The Coleman Methodology Score[12] was used to assess the methodological quality of the included studies. This instrument consists of two parts with seven and eleven criteria, respectively, and the total score can range from 0 to 100. Part A has a maximum possible score of 60, and part B has a maximum score of 40 (see Appendix). A high score indicates a study with few confounding factors or other biases. The criteria for the Coleman Methodology Score were developed on the basis of the CONSORT (Consolidated Standards of Reporting Trials) statement[12,18].

In the present study, some of the scoring criteria in part A were modified: (1) the study size (question 1) was altered from the number of tendons to the number of patients; (2) the mean duration of follow-up (question 2) was altered to the minimum duration of follow-up, and the corresponding time criteria were changed from more than twenty-four months to more than five years, from between twelve and twenty-four months to between two and five years, and from less than twelve months to less than two years; (3) the type of study (question 4) was modified to include case series, which were assigned a score of 0 (the same score as retrospective cohort studies); and (4) the description of rehabilitation (question 7) was modified to omit compliance with rehabilitation from the scoring criteria. No modifications were made to the criteria in part B. The studies were scored independently by the reviewers, and any scoring discrepancies were discussed until consensus was achieved.

Source of Funding

This study was funded by the authors' institutions (the Norwegian School of Sport Sciences and Oslo University Hospital).

Results

A flow diagram of the study selection process is shown in Figure 1, which is based on the PRISMA (Preferred

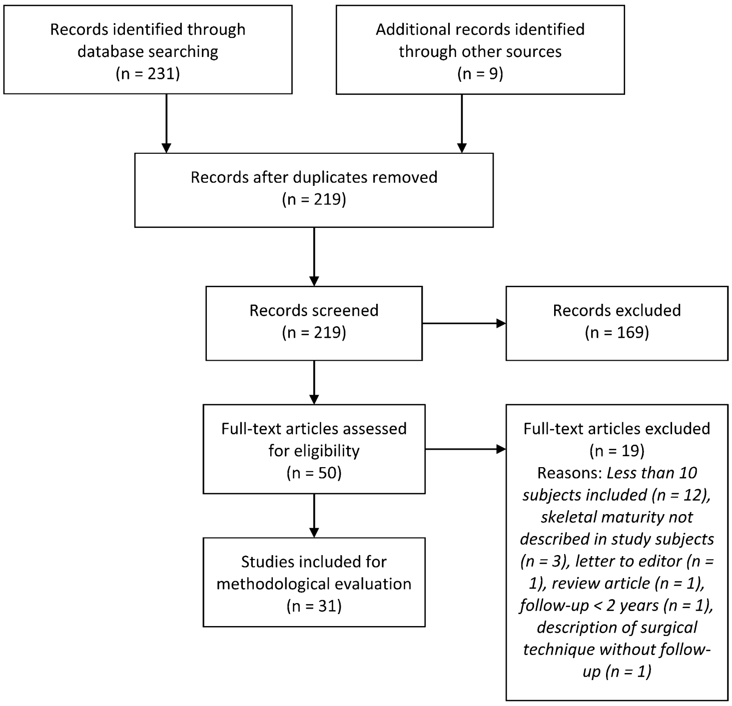

Fig. 1
Flow diagram showing the identification of potentially applicable studies and evaluation of their eligibility.

TABLE I Overview of the Included Studies, Sorted According to the Total Coleman Methodology Score

					Coleman Methodology Score		
Study	No. of Patients	Treatment Algorithm*	Mean Age at Inclusion (Range) *(yr)*	Mean Follow-up (Range) *(yr)*	Part A, Maximum = 60	Part B, Maximum = 40	Total, Maximum = 100
Liddle (2008)	17	T	12.1 (9.5-14.0)	3.8 (2.1-8.3)	37.0	25.0	62.0
Kocher (2007)	59	T	14.7 (11.6-16.9)	3.6 (2.0-10.2)	34.0	26.0	60.0
Nikolaou (2011)	94	T	13.7 (11.6-15.9)	3.2 (2.0-5.0)	37.0	23.0	60.0
Kocher (2005)	44	P	10.3 (3.6-14.0)	5.3 (2.0-15.1)	34.0	26.0	60.0
Janarv (1996)	28	P	13.1 (9.9-15.0)	Minimum, 3.0	29.0	28.5	57.5
Cohen (2009)	26	T	13.3 (11-15)	3.8 (2.0-7.0)	26.0	24.5	50.5
Steadman (2006)	13	P	13 (10-16)	5.8 (2.2-9.4)	27.0	23.0	50.0
Moksnes (2008)	26	N	10.3 (5.2-12.7)	3.8 (2.0-9.0)	19.0	30.5	49.5
Fuchs (2002)	10	T	13.2 (9-15)	3.3 (2.2-5.0)	22.0	26.0	48.0
Shelbourne (2004)	16	T	14.8 (13.1-15.8)	3.4 (std. dev., 1.1)	25.0	23.0	48.0
Bonnard (2011)	57	P	12.2 (6.8-14.5)	5.5 (2.0-14.0)	29.0	19.0	48.0
Woods (2004)	13	N	13.8 (11.0-16.0)	5.8 (1.8-24.5)	23.0	25.0	48.0
Courvoisier (2011)	38	T	14.0 (11.0-15.0)	3.0 (2.0-4.0)	26.0	21.5	47.5
Lipscomb (1986)	24	P	13.5 (10-15)	2.9 (2.0-5.0)	26.0	21.5	47.5
Aronowitz (2000)	21	T	13.4 (11-15)	2.1 (1.0-5.0)	29.0	17.5	46.5
Seon (2005)	11	T	14.7 (13.1-15.5)	6.5 (3.8-10.9)	22.0	24.5	46.5
Marx (2009)	55	T	13.4 (8.4-16.6)	3.2 (1.0-7.5)	27.0	18.0	45.0
Kopf (2010)	14	T	14.4 (11-16)	7.0 (1.9-11.1)	15.0	27.5	42.5
Anderson (2004)	12	P	13.3 (std. dev., 1.3)	4.1 (2.0-8.1)	22.0	19.5	41.5
Mizuta (1995)	18	N	12.8 (10-15)	4.3 (0.8-8.3)	17.0	24.5	41.5
Aichroth (2002)	45	T	13 (11-15)	4.1 (1.0-8.0)	30.0	11.0	41.0
McIntosh (2006)	16	T	13.6 (11.2-14.9)	3.4 (2.0-9.3)	15.0	24.5	39.5
Edwards (2001)	20	T	13.7 (11.8-15.6)	2.8 (1.4-7.4)	19.0	19.5	38.5
Gaulrapp (2006)	53	T	13.9 (9-16)	6.5 (3.0-11.0)	19.0	17.5	36.5
Streich (2010)	31	T	11 (9-12)	5.8 (3.4-7.1)	21.0	15.0	36.0
Henry (2009)	56	T	12.4 (5.0-16.8)	2.3 (1.0-6.8)	17.0	18.5	35.5
Gebhard (2006)	40	P	11.9 (7-14)	2.8 (1.1-17.0)	14.0	20.0	34.0
Micheli (1999)	17	P	11 (2-14)	5.5 (2.1-14.0)	22.0	11.0	33.0
McCarroll (1994)	60	T	13.7 (13-15)	4.2 (2.0-7.0)	17.0	15.0	32.0
Arbes (2007)	20	T	13.9 (9-15)	5.4 (0.5-10.5)	10.0	21.0	31.0
Graf (1992)	12	N	14.5 (11.7-16.3)	Minimum, 2.0	13.0	15.0	28.0

*T = transphyseal reconstruction, P = physeal-sparing reconstruction, and N = nonoperative treatment.

Reporting Items for Systematic Reviews and Meta-Analyses) statement[19]. The systematic search on operative treatment identified 209 potentially eligible abstracts, and twenty-one of the studies[7,20-39] were included. The search on rehabilitation identified twenty-two abstracts, and one of the studies[40] was included. Nine additional studies[5,6,41-47] were identified from manual searches of journals and the reference lists of the included studies and were also included.

Two of the thirty-one included studies were prospective cohort studies[27,30], and the remaining twenty-nine (94%) were retrospective studies; no randomized controlled trials were identified. The total number of participants in the included studies was 966, and the mean number of children per study was 31.2 (range, ten to ninety-four). The nineteen studies on transphyseal reconstruction had a mean of thirty-five children (range, ten to ninety-four), the eight studies on physeal-sparing reconstruction had a mean of twenty-nine children (range, twelve to fifty-seven), and the four studies on nonoperative treatment had a mean of seventeen children (range, twelve to twenty-six). The characteristics of all included studies are presented in the Appendix.

Methodological Quality

The results of the study quality assessments are presented in Table I. None of the studies fulfilled all of the criteria, and the mean Coleman Methodology Score (and standard deviation) was 44.7 ± 9.2. The lowest score was 28[38], and the highest was 62[30]. The mean score was 23.3 ± 7.1 for part A and 21.4 ± 4.9 for part B. The mean scores for the individual sections are shown in Table II. The highest mean scores in part A were for "diagnostic certainty" (4.8 out of 5) and "description of treatment given" (4.3 out of 5), and the lowest score was for "type of study" (0.6 out of 15). The highest score in part B was for "description of

TABLE II Coleman Methodology Score, Mean Section Scores

Section Score (Maximum)	Mean	Range	Standard Deviation
Part A (60)	23.3	10-37	7.1
1. Study size—number of patients (10)	3.5	0-10	
2. Minimum follow-up (5)	1.3	0-2	
3. Number of different treatment procedures included (10)	5.8	0-10	
4. Type of study (15)	0.6	0-10	
5. Diagnostic certainty (5)	4.8	0-5	
6. Description of treatment given (5)	4.3	0-5	
7. Description of preop. and postop. rehabilitation and/or conservative treatment (10)	2.9	0-10	
Part B (40)	21.4	11-30.5	4.9
Outcome criteria (10)	4.7	0-10	
8. Outcome measures clearly defined (2)	1.7	0-2	
9. Timing of outcome assessment clearly stated (2)	0.2	0-2	
10. Use of outcome criteria that has reported good reliability (3)	2.0	0-3	
11. Use of outcome with good sensitivity (3)	0.9	0-3	
Procedure for assessing outcomes (15)	3.9	0-15	
12. Subjects recruited (5)	0.5	0-5	
13. Investigator independent of surgeon/therapist (4)	0.3	0-4	
14. Written assessment (3)	2.4	0-3	
15. Completion of assessment by subjects themselves with minimal investigator assistance (3)	0.7	0-3	
Description of subject selection process (15)	12.8	8-15	
16. Selection criteria reported and unbiased (5)	4.8	0-5	
17. Recruitment rate reported (≥80% = 5; <80% = 3) (5)	4.5	3-5	
18. Eligible subjects not included in the study satisfactorily accounted for (5)	3.4	0-5	
Total score (100)	44.7	28-62	9.2

subject selection process" (12.8 out of 15). Table III compares the Coleman scores of the three different treatment algorithms.

The study by Liddle et al.[30] had the highest Coleman score. That study involved prospective follow-up of seventeen children who had undergone identical ACL reconstructions with a transphyseal technique and hamstring tendon grafts. The study also reported specifically on the postoperative rehabilitation program and secondary injuries, and it used adequate outcome measurements. The two studies by Kocher et al.[7,21] and the recent study by Nikolaou et al.[5] had the next-highest scores. The studies by Kocher were performed with identical designs and are good examples of how retrospective studies can have a sound methodological design. The 2005 study involving physeal-sparing reconstruction and the 2007 study involving transphyseal reconstruction had clear inclusion criteria, relatively large homogenous populations (forty-four and fifty-nine children, respectively), and a treatment algorithm based on physiological maturity and knee function. The

TABLE III Coleman Methodology Score According to Treatment Algorithm*

Section score (Maximum)	Transphyseal (N = 19)	Physeal Sparing (N = 8)	Rehabilitation (N = 4)
Part A (60)	23.6 (10-37)	25.4 (14-34)	18.0 (13-23)
Part B (40)	21.0 (11-27.5)	21.1 (11-28.5)	23.8 (15-30.5)
Outcome criteria (10)	4.8 (0-7)	4.2 (0-8.5)	5.5 (0-10)
Procedure for assessing outcomes (15)	3.4 (0-11)	4.5 (0-12)	4.5 (0-15)
Description of subject selection process (15)	12.7 (8-15)	12.4 (8-15)	13.8 (10-15)
Total score (100)	44.6 (31-62)	46.4 (33-60)	41.8 (28-49.5)

*Values are given as the mean, with the range in parentheses.

study by Nikolaou et al.[5] involved ninety-four skeletally immature children who underwent transphyseal reconstruction with good results as assessed with use of functional questionnaires and return to sports. In these four highest-rated studies, 4.2% (nine) of the 214 grafts sustained a rerupture, and growth disturbance was reported in 0.5% (one) of the patients. Furthermore, 47% (101) of the patients had 104 concomitant meniscal injuries, 67% (seventy) of which were treated with surgical repair. The meniscal repair failed during the follow-up period in 14% (ten) of those patients. However, only 10% (three) of the thirty-one included studies[32,38,43] included validated outcome measures, such as magnetic resonance imaging (MRI) or arthroscopy, for evaluating secondary meniscal tears or cartilage injuries.

Treatment Algorithms and Rehabilitation

Eleven of the nineteen studies on transphyseal reconstruction used hamstrings tendons, two used bone-patellar tendon-bone autograft, four used diverse techniques, one used bone-patellar tendon-bone allograft, and one used Achilles tendon allograft. The eight studies on physeal-sparing reconstruction involved ten different surgical methods. Three of the four studies on nonoperative treatment included a description of an unambiguous algorithm involving primary nonoperative treatment, with optional delayed surgical treatment, in all subjects. None of the studies on nonoperative treatment provided well-described rehabilitation protocols. Rehabilitation guidelines were adequately described in only 3% (one[37]) of the thirty-one included studies. Rehabilitation was inadequately described in 58% (eighteen) of the studies and not described in 39% (twelve). Two studies (6%) included functional preoperative outcome measurements[27,30], whereas the remaining twenty-nine studies (94%) did not include any data on baseline or pretreatment knee function.

Discussion

This systematic review illustrates that studies on the treatment of skeletally immature children with ACL injury have major deficiencies with regard to methodological quality. Thirty-one studies with a total of 966 children were included, but none were randomized controlled trials, two had a prospective study design, and the remaining twenty-nine had a retrospective design. The included studies had a mean Coleman Methodology Score (and standard deviation) of 44.7 ± 9.2 out of a maximum possible score of 100, which suggest that the knowledge base for the management of ACL injuries in skeletally immature children is weak. The present review showed that the published studies have major weaknesses in methodological quality, particularly with regard to study size, study design, and the description of rehabilitation protocols (in part A of the Coleman score) and with regard to the assessment of knee function with adequate measurement tools (in part B of the Coleman score).

The Coleman score evaluates the quality of studies with regard to study design (part A) and the assessment of outcomes, recruitment, and compliance (part B). The included studies had a mean score 23.3 ± 7.1 out of 60 on part A and 21.4 ± 4.9 out of 40 on part B, suggesting that the main deficiencies regarding methodological quality in the literature on the management of ACL injuries in the skeletally immature population involved study design (part A).

Coleman et al.[12] reported a mean Coleman score of 37.3 ± 15.9 for studies on the outcome of surgical treatment of patellar tendinopathy, and Watsend et al.[15] reported a mean score of 52.1 ± 14.0 for studies on posterior cruciate ligament tears. Note that the "operation-specific" nature of Coleman scores for different procedures means that this score should not be used to compare the methodological quality of studies of different medical conditions, and that was not a goal of the present study. To our knowledge, the highest Coleman scores reported are from studies on different techniques of microfracture cartilage repair[11] and collagen meniscus implantation[10], with mean scores of 58.2 ± 3.6 and 67.1 ± 18.6, respectively. In 2005, Jakobsen et al.[14] evaluated the quality of studies on cartilage repair and found a mean Coleman score of 43.5 ± 12.5, with scores of 35.7 ± 9.3 for part A and 7.8 ± 4.7 for part B. Øiestad et al.[16] reported a mean modified Coleman score of 52.2 ± 13 out of 90 for studies involving long-term follow-up of adults with ACL injuries; the mean score was 31.1 ± 9.6 out of 50 for part A and 21.1 ± 6.9 out of 40 for part B. Comparison of the mean Coleman score for the studies in the present review with the scores in the previous studies shows the methodological quality of the studies on treatment of ACL injuries in skeletally immature children to be among the lowest reported. The main difference between the present systematic review and the other reviews is in part A, suggesting that greater attention in future research should be focused on designing adequately sized prospective studies.

Methodological deficiencies in the included studies were found in five criteria in particular: "study size," "type of study," "description of rehabilitation protocols," "outcome criteria," and "procedure for assessing outcomes." The main limitation involving study size and study type was the lack of randomized controlled trials and prospective studies. Thus, there is a need to perform high-quality prospective observational studies on this patient population that describe treatment algorithms, interventions, and outcomes in detail. Manchikanti et al.[48] and Hoppe et al.[49] emphasized that the results of observational studies are particularly valuable for investigating questions regarding etiology, prognosis, and estimates of potential risks. Furthermore, prospective long-term observational studies are suitable for detecting rare or late adverse effects of interventions, and they are more likely to provide an indication of what is accomplished in daily health care practice[50,51]. Thereafter, randomized controlled trials should be performed to compare the effects of different interventions. We recognize that there are practical and ethical limitations because of the low number of pediatric ACL injuries, but well-planned multicenter studies with uniform inclusion criteria and outcome measures should be performed.

The rehabilitation programs, including exercises and progression milestones, were also not well described in the majority of the included studies. Postoperative restrictions involving weight-bearing and knee motion were provided in some studies, but rehabilitation protocols describing exercise selection, dose, progression, and criteria for return to sports on the basis of functional performance were not.

The primary purpose of the published studies was to describe and evaluate surgical techniques. The majority of the studies had adequate descriptions of the surgical techniques, as reflected by the mean score of 4.3 out of 5 for the Coleman criterion "description of treatment given." Although the focus was on the surgical technique, the Coleman score highlights the importance of describing rehabilitation programs because of the known impact of rehabilitation on the functional outcome after orthopaedic surgical treatments. In future studies, there should be an increased focus on describing and assessing compliance with the rehabilitation programs to enhance the strength and clinical relevance of the results.

The major deficiencies involving outcome criteria were the absence of predefined and homogeneous timing of follow-up assessments and the lack of validated outcome measures with good sensitivity. All of the studies except the two with a prospective design had large variations in the time between inclusion or surgical treatment and the follow-up assessment, which significantly reduces the generalizability of the reported results. Additionally, 90% (twenty-eight) of the thirty-one included studies did not document adequate outcome measures for assessing secondary meniscal tears or cartilage injuries at the time of follow-up. Because arthroscopy or MRI was not included in the follow-up examinations, only secondary injuries that were treated during the follow-up period were documented in those studies. Thus, the number of secondary injuries may be underestimated in the published studies on surgical as well as nonoperative treatment and should be interpreted with caution.

Outcome measures with good sensitivity are also needed for young children with ACL injuries; although there is a need for reliable and validated self-reported questionnaires, none of the questionnaires that are frequently used have been validated in this population. There have been conflicting reports on how the International Knee Documentation Committee (IKDC) subjective knee evaluation form (2000 version) is understood by children[52-55]. Good reliability, validity, and responsiveness have recently been reported for the newly developed Pedi-IKDC[56]. Most of the studies in the present review used functional questionnaires, but few studies included performance-based outcome measures. Furthermore, the majority of studies included radiographs as an outcome measure, although only sixteen (52%) received points for having sufficient radiographic evaluations including standing longitudinal radiographs (question 11), which are a requirement for examining lower limb alignment and growth disturbances[57]. MRI has been suggested to be a good radiation-free method to determine skeletal maturity in the future[58], although further validation of this measure is needed[59].

Single-leg hop tests are reliable outcome measures for healthy adults and adults who have undergone ACL reconstruction[60,61]. Single-leg hop tests are recommended in combination with isokinetic strength measurements for functional evaluation of knee stability and ability to return to sports[62,63]. Additionally, isokinetic strength measurements have been documented to be reproducible and reliable in children six to fifteen years of age[64,65], and they are the preferred outcome measure for evaluation of quadriceps and hamstring muscle strength[66]. Three (10%)[27,37,40] of the thirty-one included studies used performance-based functional outcome measures to evaluate knee function at the time of final follow-up.

In the outcome assessment portion of the Coleman score, only three (10%)[27,40,41] of the thirty-one studies received points for reporting consecutive recruitment of patients (question 12); in the other twenty-eight studies, medical records or surgeon files had been searched to identify skeletally immature children with ACL injuries. Additionally, only two (6%) of the studies[27,40] received points for using investigators who were independent of the surgeon or therapist (question 13). Furthermore, only seven (23%) of the studies[7,21,29,39-41,43] included a clear statement that completion of the written assessments were performed by the patients themselves with minimal investigator assistance (question 15). Ultimately, reporting following the guidelines in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement is essential to enable other researchers and clinicians to compare results[51].

We recognize that the present review has limitations. The electronic search was performed with use of only one database; however, because of the small number of published studies and the few research centers publishing on the topic, we are confident that all relevant studies have been included.

An important caution should be noted: although the methodological quality of the published studies was low, that does not mean that the quality of the treatments given in the studies was equally low. The purpose of this paper was not to assess the effect of the treatments applied. Because of the low methodological quality, clinicians and researchers should practice caution when deciding on the treatment recommendations to be given to skeletally immature children who have sustained an ACL injury. There are no studies with solid scientific evidence that can justify advising one treatment algorithm over others. The child and parents should be individually assessed and informed on the basis of a clinical examination, imaging, performance-based functional testing, and an initial rehabilitation program before conclusive advice on treatment of an ACL injury in a skeletally immature patient is provided.

In conclusion, this systematic review demonstrated that the methodological quality of the current literature on treatment of skeletally immature children with ACL injuries was generally low, as measured with use of the Coleman Methodology Score. The four studies with the highest scores reported good functional results with a low rate of growth disturbance. More attention should be paid to methodological quality when designing, performing, and reporting studies on treatment of skeletally immature children with ACL injuries. Particular attention should be given to the design of prospective studies, the inclusion of homogenous populations, detailed reporting of rehabilitation protocols, and the use of adequate outcome measures.

Appendix

eA Tables summarizing the Coleman Methodology Score, the included studies, and the number of studies identified with use of each of the search terms are available with the online version of this article as a data supplement at jbjs.org. ■

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TABLE E-1 Search Terms and Number of Resulting PubMed Search Results*

Search	Search Terms	No. of Studies
#1	"Anterior cruciate ligament"[MeSH]	7768
#2	"Child"[MeSH]	1,371,559
#3	"Adolescent"[MeSH]	1,392,328
#4	"Adult"[MeSH]	4,770,233
#5	"Reconstructive surgical procedures"[MeSH]	44,650
#6	"Surgery"[Subheading]	1,425,756
#7	("Rehabilitation"[MeSH] OR "rehabilitation"[Subheading])	233,413
#8	"Exercise therapy"[MeSH]	22,764
#9	"Prevention and control"[Subheading]	861,445
#10	(#2) OR #3	2,113,011
#11	(#5) OR #6	1,436,491
#12	(#7) OR #8	233,413
#13	((((#1) AND #10) AND #11) NOT #4) NOT #9	209
#14	((((#1) AND #10) AND #12) NOT #4) NOT #9	22

*The search was performed on May 24, 2011.

Table E-2 Coleman Methodology Score[12] Including Scoring Guidelines as Modified in the Present Study

Section	Number or Factor	Score	Details	Comments
Part A: only one score is to be given for each section				
1. Study size: number of patients			Included patients	
	>60	10		
	41-60	7		
	20-40	4		
	<20 or not stated	0		
2. Minimum follow-up in years			All studies included had an average follow-up of >2 years, but if the minimum was <2 years the score given is 0	
	>5	5		
	2-5	2		
	<2	0		
3. Number of different treatment procedures included in each reported outcome. More than one method may be assessed but separate outcomes should be reported			All treatments given	
	One procedure	10		
	More than one method, but ≥90% of subjects undergoing the one procedure	7		
	Not stated, unclear, or <90% of subjects undergoing the one procedure	0		
4. Type of study				
	Randomized controlled trial	15		
	Prospective cohort study	10		

	Retrospective cohort study or case series	0		
5. Diagnostic certainty			Arthroscopy or magnetic resonance imaging	
	In all	5		
	In ≥80%	3		
	In <80%	0		
6. Description of treatment given				
	Adequate (technique stated and necessary details of that type of procedure given)	5	Detailed description of graft type, drill hole direction, and placement of fixation	
	Fair (technique only stated without elaboration)	3	Technique only stated without elaboration	
	Inadequate, not stated, or unclear	0		
7. Description of preoperative and postoperative rehabilitation, and/or conservative treatment				The criterion of compliance with rehabilitation was excluded because we wanted to discriminate between studies that did report some information on rehabilitation protocols and those that did not provide any information
	Well described	10	Weight-bearing, brace/no brace, type of exercises, rehabilitation milestones, and return to sports criteria	
	Not adequately described	5	Only including weight-bearing, brace/no brace, and suggested	

			return to sports time	
	Protocol not reported	0	No information on rehabilitation	
Part A total score		60		
Part B: scores may be given for each option in each of the three sections if applicable				
Outcome criteria				If outcome criteria are vague and do not specify subjects' functional capacity, score is automatically 0 for this section
	8. Outcome measures clearly defined	2	Methods section	
	9. Timing of outcome assessment clearly stated	2	Timing of follow-up predefined and 95% of participants within a standard deviation of 5 months	
	10. Use of outcome criteria that have reported good reliability	3	Related to definition of outcome	There are no validated functional questionnaires for children with ACL injuries.
	11. Use of outcome with good sensitivity	3	Standing long radiographs to assess skeletal growth (1.5) AND isokinetic strength measurements or single-leg hop tests (1.5)	Return to sports rate, clinical tests (Lachman and pivot shift), and KT1000 were not regarded as essential functional outcomes

Procedure for assessing outcomes				
	12. Subjects recruited	5	Results not taken from surgeons' files	
	13. Investigator independent of surgeon/therapist	4	Independent of surgeon/therapist	
	14. Written assessment	3	Use of questionnaires for evaluation of knee function; IKDC, Lysholm, Cincinnati, Tegner, KOOS, or others*	
	15. Completion of assessment by subjects themselves with minimal investigator assistance	3	It should be clearly reported that the subjects completed the questionnaires	
Description of subject selection process				
	16. Selection criteria reported and unbiased	5	Inclusion criteria clearly reported	
	17. Recruitment rate reported		For radiographic and/or functional assessment on follow-up	
	≥80%	5		
	<80%	3		
	18. Eligible subjects not included in the study satisfactorily accounted for, or 100% recruitment	5	Drop-out analyses of the patients not going through follow-up and report on reinjuries	
Part B total score		40		

*IKDC = International Knee Documentation Committee, and KOOS = Knee Injury and Osteoarthritis Outcome Score.

Table E-3 Overview of the Transphyseal Reconstruction Studies Included in the Systematic Review*

Study	No. of Patients	Surgical Method	Concomitant Injuries	Postoperative Complications and Reinjuries	Rehabilitation	Outcome Measures
Aichroth et al. (2002)	45	4-strand HT with metaphyseal fixation	8 lateral and 9 medial meniscus injuries (38%). 10 menisci sutured. 6 osteochondral lesions	3 reruptures (7%)	“Slower.” Brace to resist extension in children with hyperextension of >5°	Lachman, PS, IKDC (reconstructed only), Lysholm
Arbes et al. (2007)	20	BPTB (n = 4), delayed BPTB (n = 3), primary repair (n = 3), nonop. (n = 10)	Not provided	Not provided	Not described	KOOS, IKDC, KT1000 (reconstructed only). Results of nonop. limited
Aronowitz et al. (2000)	21	Achilles tendon allograft	8 menisci repaired and 4 partially resected (57%)	3 secondary surgeries: one partial meniscus resection and two hardware removals	Cylinder cast for 1 week, physical therapy with ROM exercises, and quadriceps and hamstring strength from week 4. RTS when quadriceps strength 90% of contralateral	Lysholm, KT1000, Lachman, long-leg standing radiographs
Cohen et al. (2009)	26	4-strand HT with metaphyseal fixation	9 medial, 5 lateral, and 3 medial and lateral meniscus injuries (65%)	3 reruptures (12%). 5 patients (19%) had >3 mm difference on KT1000 at follow-up	Not described	Lachman, PS, IKDC, Lysholm, RTS, KT1000, radiographs for leg-length discrepancies
Courvoisier et al. (2011)	38	4-strand HT with femoral EndoButton and tibial interference screw	2 medial, 6 lateral, and 2 medial and lateral meniscus injuries at surgery (26%)	5 reruptures (13%). 1 cyclops lesion and 3 hematomas evacuated	Long leg splint. Crutches for 10 days. Not otherwise described	IKDC, KT1000, long-leg standing radiographs
Edwards et	20	HT with vertically	4 medial and 13	4 reruptures	Immediate weight-	Lachman, PS,

al. (2001)		drilled tunnels (n = 16), BPTB (n = 4)	lateral meniscus injuries (85%). 4 menisci sutured	(20%)	bearing, passive motion, and closed chain exercise. Not otherwise described	Lysholm, single-leg hop tests, isokinetic strength, radiographic confirmation of closed physis
Fuchs et al. (2002)	10	BPTB allograft with bone plugs and screws placed in the metaphysis	3 medial, 4 lateral, and 2 medial and lateral meniscus injuries (90%). 4 menisci sutured	Not provided	Not described	RTS, Lysholm, IKDC, radiographic confirmation of closed physis
Gaulrapp et al. (2006)	53	Primary repair (n = 24), semitendinosus augmentation (n = 15), BPTB (n = 14)	Concomitant injuries and additional procedures not reported	3 secondary reconstructions (6%). 5 meniscus revisions	Not described	Lysholm, Tegner, IKDC, KT-1000, radiographs
Henry et al. (2009)	56	Group 1: quadriceps tendon graft (n = 24) and iliotibial band “over the top” (n = 5). Group 2: BPTB (n = 27)	Group 1: 3 medial and 9 lateral meniscus injuries (41%); 5 menisci sutured. Group 2: 11 medial and 8 lateral meniscus injuries (70%); 3 menisci sutured	Group 1: 1 valgus deformity (iliotibial band group). Group 2: 1 rerupture and 1 failed meniscus repair	Group 1: removable brace in extension 30 days and full weight-bearing. Group 2: contention 2 weeks and full weight-bearing	IKDC, KT1000, RTS, clinical exam
Kocher et al. (2007)	59	4-strand HT with metaphyseal fixation	21 lateral, 6 medial, and 4 medial and lateral meniscus injuries (53%). 17 menisci sutured	3 arthrofibrosis. 2 reruptures (3%). 2 of 17 meniscus repairs failed (12%). 1 superficial infection	2 weeks of touch-down weight-bearing, immediate passive mobilization from 0° to 90°. A hinged brace was used for the first two weeks (4-6 weeks if a meniscus repair was	IKDC, Lysholm, RTS, radiographs for angular deformity and leg-length discrepancies

					performed). Further rehabilitation followed traditional rehabilitation guidelines for adults after ACL reconstruction. Patients should also use a custom functional knee brace during cutting and pivoting activities for the first two years after return to sports	
Kopf et al. (2010)	14	HT, not otherwise specified	2 medial and 1 lateral menisci sutured (21%). 1 lateral partially resected	Not provided	Knee brace 0°-90° 6 weeks after surgery. Not otherwise described	Change in tunnel size (MRI), KOS-ADLS, Lysholm, IKDC, KT1000
Liddle et al. (2008)	17	4-strand HT with metaphyseal fixation	3 medial, 6 lateral, and 1 medial and lateral meniscus injuries (59%). 2 menisci sutured	1 rerupture (6%). 1 superficial infection. 1 patient had 5° valgus deformity on operated side	Standard, “slowly”	Lysholm, Tegner, IKDC, KT1000, clinical exam, radiographic confirmation of closed physes
Marx et al. (2009)	55	4-strand HT with a femoral extracortical button and a tibial suture washer or staple	33 meniscus injuries (60%)	5 reruptures (9%)	Not described	IKDC2000, Lysholm, Cincinnati, Tegner, KT1000, clinical evaluation
McCarroll et al. (1994)	60	BPTB, although 2 patients were initially treated with a physeal-sparing procedure and later revised with BPTB	27 meniscus injuries in 40 patients (68%), and not reported in the 20 patients who underwent acute surgical reconstruction	3 reruptures (5%), 1 meniscus tear, 2 arthrofibrosis	Not described	Clinical exam, KT1000, RTS, growth after surgery

McIntosh et al. (2006)	16	4-strand HT with metaphyseal fixation (n = 13), 2-strand HT with metaphyseal fixation (n = 3)	4 medial, 2 lateral, and 2 medial and lateral meniscus injuries (50%). 7 menisci sutured	2 reruptures (13%). 3 failed meniscus sutures. One patient had 1.5-cm overgrowth on the operated side	Early range of motion, running at 3 months, and cutting/pivoting sports at 6 months if functionally stable (not specified)	IKDC, Lysholm, Tegner, Lachman, PS, radiographic confirmation of closed physes
Nikolaou et al. (2011)	94	4-strand HT with femoral and tibial RigidFix pins	36 meniscal tears in 33 patients (35%). 28 menisci sutured and 5 partially resected	4 reruptures (4%). 4 of 28 meniscus repairs failed (14%)	Hinged brace 0°-90° 4 weeks, no weight-bearing first 3 weeks. Not otherwise described	IKDC, Lysholm, Tegner, KT1000, standard radiographs to evaluate growth if clinical left-right discrepancy of 5° or 1 cm was observed
Seon et al. (2005)	11	HT with metaphyseal fixation	6 medial and 6 lateral meniscus injuries. 1 chondral defect on the medial femoral condyle and 1 medial collateral ligament injury	Not provided	Not described	Lysholm, ROM, RTS, limb length, radiographic confirmation of closed physes
Shelbourne et al. (2004)	16	BPTB with metaphyseal fixation	6 medial and 9 lateral meniscus injuries. 3 menisci sutured	1 rerupture (6%). 2 contralateral ruptures (13%). 1 failed meniscus suture	Reference to previously published rehab. program provided	KT1000, IKDC, RTS, Lachman, isokinetic strength, radiographic confirmation of closed physes, full body growth
Streich et al. (2010)	31	Surgical group: 4-strand HT with	12 medial and 4 lateral meniscus	No secondary surgical	Touch-down weight-bearing after 6 weeks	KT1000, IKDC, Lysholm, Tegner,

		metaphyseal fixation. Nonop. group: 4-strand HT with metaphyseal fixation after median 21 months of nonop. treatment on account of secondary injuries	injuries (52%). 7 menisci sutured. 4 osteochondral defects fixated	procedures reported	with brace, indoor cycling after 8 weeks, jogging after 16 weeks, and pivoting sports after 12 months	clinical limb length measurement

*HT = hamstring tendon graft, PS = pivot-shift test, IKDC = International Knee Documentation Committee, BPTB = bone-patellar tendon-bone graft, KOOS = Knee Injury and Osteoarthritis Outcome Score, ROM = range of motion, RTS = return to sports, MRI = magnetic resonance imaging, and KOS-ADLS = Knee Outcome Survey Activities of Daily Living Score.

Table E-4 Overview of the Physeal-Sparing Reconstruction Studies Included in the Systematic Review*

Study	No. of Patients	Surgical Method	Concomitant Injuries	Postoperative Complications and Reinjuries	Rehabilitation	Outcome Measures
Anderson et al. (2004)	12	4-strand HT with all epiphyseal tunnels	8 (75%) concurrent meniscus repairs	Not described	Hinged brace	Full body length growth, IKDC, KT1000
Bonnard et al. (2011)	57	Clocheville technique. Patellar tendon with intra-articular sutures in a groove in tibial epiphysis and interference screw in metaphyseal femoral tunnel	16 meniscus injuries (28%): 2 medial and 6 lateral menisci sutured, 2 medial partially resected, 5 lateral and 1 medial untreated	3 reruptures (5%)	Long-leg cast in 10° flexion for 45 days. Not otherwise described	IKDC2000, Tegner, Rolimeter, single-leg hop. Standing anterior and lateral radiographs
Gebhard et al. (2006)	40	Quadriceps tendon (n = 12); fasciae latae (n = 12); 4, 3, or 2-strand HT (n = 16)	12 menisci repaired (30%)	3 reruptures of quadriceps tendon graft (25%), 4 meniscus sutures failed (33%), 2 mobilizations due to arthrofibrosis	Not described	Lysholm, IKDC, KT1000, radiographs
Janarv et al. (1996)	28	HT with distal insertion preserved, partial medial arthrotomy and tunnel through lateral femoral epiphysis (n = 12); BPTB with same procedure (n = 4); nonoperative (n = 12)	At least 3 meniscus injuries mentioned in the paper, but lack of consistent reporting make an estimate difficult	Not described	Surgically treated knees were immobilized for 6 weeks in 30° of flexion followed by 4 weeks with motion restricted to 30°-90°. Not otherwise described	Lysholm, Tegner, KT1000, isokinetic muscle strength
Kocher et al. (2005)	44	Iliotibial band graft. Combined intra-	4 medial and 23 lateral meniscus	2 reruptures (5%), 4 meniscus	2 weeks of touch-down weight-bearing,	IKDC, Lysholm, RTS,

		articular and extra-articular	injuries (61%). 23 menisci sutured	sutures failed (17%)	immediate passive 0°-90° mobilization. A hinged braced was used for the first two weeks (4-6 weeks if a meniscus repair was performed). Further rehabilitation followed traditional rehabilitation guidelines for adults after ACL reconstruction. Patients should also use a custom functional knee brace during cutting and pivoting activities for the first two years after RTS	radiographic leg length discrepancies
Lipscomb et al. (1986)	24	Intra-articular reconstruction supplemented with extra-articular Ellison or Losee reconstruction	12 medial and 7 lateral meniscectomies, 2 medial and 2 lateral menisci repaired (96%)	Not described	Immobilized 6 weeks in 15° flexion. Full weight-bearing from week 7. Isokinetic strength training from month 4. Swimming from month 5. Bicycling when 95° of flexion. Running from month 7. Full activity from month 9	KT1000, isokinetic strength, clinical evaluation, and radiographs
Micheli et al. (1999)	17	Extra-articular reconstruction using iliotibial band	6 meniscus injuries (35%): 2 medial menisci sutured, 1 lateral meniscus repaired, 1 medial and 2 lateral partial meniscectomies, 1 posterolateral corner repair	Not described	Not described	Lysholm, KT1000, physical examination
Steadman	13	“Healing response”	6 medial meniscus	3 reruptures	Brace and crutches for 6	Lysholm,

et al. (2006)		reinserting the ruptured proximal end of the ACL	injuries (46%), 1 patellar chondral defect	(23%) within 30-55 months	weeks. Stationary cycling for week 7. Progressive strengthening until week 24. Brace during athletic activities the first year	Tegner, Lachman, PS, KT1000, RTS

*HT = hamstring tendon graft, IKDC = International Knee Documentation Committee, BPTB = bone-patellar tendon-bone graft, RTS = return to sports, and PS = pivot-shift test.

Table E-5 Overview of the Nonoperative Treatment Studies Included in the Systematic Review*

Study	No. of Patients	Concomitant Injuries	Post-Treatment Complications and Reinjuries	Rehabilitation	Outcome Measures
Graf et al. (1992)	12	At time of diagnosis, 4 medial and 4 lateral meniscus injuries in 6 patients (50%). 4 medial menisci sutured and 4 physeal-sparing reconstructions at arthroscopy	Nonop. group (n = 8): 7 new meniscus injuries (88%) and delayed reconstructions. Surgical group: 2 reruptures (50%)	Brace during sports. RTS when strength 90% of uninjured side	Arthroscopy, RTS
Mizuta et al. (1995)	18	At time of diagnosis, 8 medial and 7 lateral meniscus injuries in 13 patients (72%)	6 patients (33%) had ACL reconstruction during the follow-up period; 4 medial and 1 lateral meniscus injuries. Nonop. patients (n = 12) sustained 1 additional meniscus injury during follow-up (8%)	Brace during sports. Surgical group: immediate strength, and RTS when strength 90% of uninjured side	Lysholm, RTS, isokinetic strength, clinical exam, radiographs
Moksnes et al. (2008)	26	Not described	Nonop. group (n = 21): 2 medial meniscus injuries during follow-up period (10%). Delayed surgery group: 4-strand HT (n = 4), BPTB (n = 1). 1 medial and 3 lateral meniscus injuries in 3 patients (60%). 2 menisci sutured. Both sutures failed	Not described	KOS-ADLS, VAS, IKDC, Lysholm, single-leg hop tests, isokinetic strength, KT1000, RTS, Lachman, PS
Woods and O'Connor (2004)	13	Not described	At time of surgery, 1 medial, 2 lateral, and 1 medial and lateral meniscus injuries (31%)	Brace "at all times." No pivoting sports or physical education in school	Arthroscopic evaluation, clinical exam, radiographs

*RTS = return to sports, HT = hamstring tendon graft, BPTB = bone-patellar tendon-bone graft, KOS-ADLS = Knee Outcome Survey Activities of Daily Living Score, VAS = visual analog scale, IKDC = International Knee Documentation Committee, and PS = pivot-shift test.

Paper III

Functional outcomes following a non-operative treatment algorithm for anterior cruciate ligament injuries in skeletally immature children 12 years and younger. A prospective cohort with 2 years follow-up.

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Keywords: ACL, Children, Adolescents, Rehabilitation, Activity level
Word count: 3830

ABSTRACT

Background The methodological quality of studies on treatment of ACL injuries in skeletally immature children after ACL injury is low, and no prospective studies have evaluated the functional outcomes following a non-operative treatment algorithm.

Purpose To report changes in knee function and activity level in skeletally immature children following a non-operative treatment algorithm for a minimum of 2 years after ACL injury

Study design Prospective cohort

Methods Forty-six skeletally immature children aged 12 years and younger were evaluated at baseline and subsequent yearly follow-ups using patient-reported outcome measurements, isokinetic muscle strength measurements, single legged hop tests, and clinical examinations over a minimum period of 2 years. Participation in physical activities was monitored using a monthly online activity survey, and the main leisure time sport activity was registered at the yearly follow-ups.

Results Thirty-six (78%) of the children did not undergo an anterior cruciate ligament reconstruction during the follow-up. Statistically significant changes with questionable clinical relevance were discovered with the patient-reported outcome measurements or hop tests. Leg symmetry indexes were consistently above 90% for muscle strength and single legged hop tests throughout the study, and the isokinetic muscle strength improved significantly in the injured limb. Ninety-one percent maintained participation in pivoting sports and/or physical education in school, although 38% of the ACL deficient children changed their main activity from a Level 1 to a Level 2 activity.

Conclusion A non-operative treatment algorithm may be appropriate for ACL injured skeletally immature children, although a reduced participation in Level 1 activities may be necessary for some children.

INTRODUCTION

An increased incidence of knee injuries in children has been reported over the last decade.[1-4] However, low methodological quality of published studies on treatment of ACL injuries in skeletally immature children have been reported in a recent systematic review from our group.[5] No randomized controlled trials and only two prospective studies were identified.[6, 7] Traditionally, skeletally immature children are recommended one of three treatment algorithms after ACL injury; a transphyseal surgical ACL reconstruction algorithm with the standard surgical procedure used for adults,[8] a physeal sparing surgical ACL reconstruction with alternative placement of the graft tunnels to minimize the risk of physeal damage,[9] or a non-operative treatment algorithm with active rehabilitation in which an ACL reconstruction may be advised if persistent knee instability, unacceptable lowered activity level, or secondary injuries occur.[10] There is, however, no consensus with regard to treatment decision criteria in skeletally immature children after ACL injury. Functional performance tests, patient-reported outcome measurements, and muscle strength measurements are standard and valid outcomes for adults with ACL injury.[11-13] Thus, these outcomes are often utilized to determine whether the result of a treatment algorithm has been successful or not in adults with ACL injury.[11, 14-16] In contrast, previous studies on ACL injuries in skeletally immature children have traditionally evaluated knee function with measures such as passive laxity measurements, radiological assessments of possible growth disturbances, and short term return to sports rates. No studies have included functional performance tests to evaluate changes in knee function over time in this population.[5] Additionally, return to pre-injury sport activities is often used as a success criterion following an ACL injury.[17, 18] Other reasons unrelated to knee function may, however, be significant confounders influencing the rate of return to pre-injury activities.[19] Some individuals continue with their pre-injury activities without a well-functioning knee, while others choose to lower their activity level even though their knee is functioning adequately.[20, 21] Thus, a more comprehensive assessment of knee function, including performance based tests, registration of changes in activity level, and clinical measures should also be used in studies on ACL injuries in children.[16, 18] The purposes of this prospective cohort study were twofold; (1) to report changes in knee function over time measured with performance based functional outcomes and patient-reported outcome measurements in ACL injured skeletally immature children following a non-operative treatment algorithm, and (2) to report changes in activity level in skeletally immature children following the treatment algorithm for a minimum of 2 years after ACL injury.

MATERIAL AND METHODS

Forty-six consecutive ACL injured skeletally immature children (47 knees), 12 years and younger, were recruited prospectively from the Department of Orthopedic Surgery, Oslo University Hospital from March 2006 to October 2010. All children followed a non-operative treatment algorithm previously published by our group.[10] The algorithm advocates non-operative management until skeletal maturity is reached for children with open growth plates. No specific activity limitations were advocated, and all children were supplied with a custom-fit knee brace which they were encouraged to wear when participating in pivoting sports and physical education classes in school. An ACL reconstruction was considered if the structured rehabilitation program did not lead to successful restoration of functional stability of the knee, if the child reported multiple giving way episodes, unacceptable reduced activity level, or a symptomatic meniscal injury. A flow-diagram of the study is provided in Figure 1. The inclusion criterion was a traumatic complete intrasubstance ACL injury sustained at the age of 12 years and younger. Individuals with either tibial or femoral ACL avulsion fractures were excluded. The diagnosis was confirmed through conventional diagnostic magnetic resonance imaging (MRI),[22, 23] a positive Lachman test,[24] and an instrumented sagittal side-to-side knee laxity measurement difference of more than 3 mm (Manual maximum test, KT 1000, Med-Metric, San Diego, California, USA).[25] Skeletal immaturity was confirmed from the diagnostic MRIs.

The non-operative treatment algorithm involved a structured supervised rehabilitation through three rehabilitation phases.[10] Progression to the next rehabilitation phase was allowed when specific functional milestones were reached. The children were permitted to return to their preferred activities when they passed a functional test battery at the end of rehabilitation phase three. A secondary prevention program (phase four) consisting of neuromuscular and functional muscle strengthening exercises was encouraged when the children were released from physiotherapy. An identically structured supervised rehabilitation with three phases was administered after ACL reconstruction.

Outcome measurements

The children underwent a functional test battery as soon as they had completed phases one and two of the rehabilitation program,[10] and were able to perform a single legged hop without pain (baseline tests). The same test battery was performed at subsequent follow-ups 1 year and 2 years after baseline. Children who underwent an ACL reconstruction performed identical tests pre-operatively, and at 1 year and 2 years after the ACL reconstruction (Figure 1). The tests were conducted and supervised by the same senior sport physiotherapist (HM), supplemented by specialists in sports physiotherapy from our sports medicine clinic.

Prior to the functional tests the children, together with their parents, completed three patient-reported outcome measurements (the Knee injury and Osteoarthritis Outcome Score (KOOS),[26] the International Knee Documentation Committee Subjective Knee Form (IKDC 2000),[27] and the Knee Outcome Survey Activities of Daily Living (KOS-ADLS).[28] They also completed a visual analogue rating scale (VAS) of knee function from 0 (very poor knee function) to 100 (normal knee function). The children were asked to define their pre-injury main leisure time sport activity, which was classified according to Hefti et al,[29] modified to European sport activities.[18, 30] At subsequent follow-ups, they defined their present main leisure time sport activity. Additionally, a monthly online activity survey (Questback AS, Oslo, Norway) was e-mailed to the families during the course of the study to monitor changes in participation, starting at baseline and ending at 2 years.

All performance based functional tests were preceded by a standardized 10-minute warm up on a stationary bicycle. Thereafter, an isokinetic muscle strength test with five repetitions at a test velocity of 60 degrees per second was performed using a Biodex 6000 dynamometer (Biodex Medical Systems inc., Shirley, New York, USA). Four trial repetitions were performed prior to the five repetitions of maximal effort. The uninjured leg was tested first.

Four single legged hop tests (the single hop test (SH), the triple crossover test (TCH), the triple hop test (TH), and the six meter timed hop test (6m-timed)) previously described by Noyes et al[31] were included. All tests were performed without a knee brace.

The rights of the subjects were protected by the Declaration of Helsinki.

Statistical Analysis

Predictive Analytics SoftWare (PASW) Statistics (version 18.0.2 (April 2, 2010); SPSS Inc., Chicago, IL, USA) was used for all statistical analyses. Analysis of variance (ANOVA) (Within-Subjects model) with repeated measures and Bonferroni post-hoc tests were used to test changes over time with a significance level of .05. If the assumption of sphericity was violated, the Greenhouse-Geiger correction was used to evaluate statistical significance. Moreover, if the assumption for the ANOVA with repeated measures was violated (data not normally distributed or ordinal), statistical differences were calculated using the Friedman test. A statistical significant result from the Friedman test was followed by a post-hoc analysis using Wilcoxon Signed-Rank Test. A Bonferroni correction, based on the number of repeated measurements, was applied using a significance level of p=.017 for three measurements, and p=.013 for four measurements. To adjust for increased height and weight between follow-ups, the peak torque values for isokinetic strength measurements were normalized to the child's body weight (Nm/kg x100). Leg Symmetry Indexes (LSI) were calculated with methods reported in previous studies.[30] Due to the small number of children who underwent ACL reconstruction we did not perform statistical analyses of differences from the pre-operative test to the post-operative tests. The test results of one subject were imputed from post-operative test 1 year after surgery to the 2 year post-operative. The changes in scores from the pre-operative test to the 2 year post-operative test were calculated as; Score from the 2 year post-operative test, minus the score from pre-operative tests.

RESULTS

Forty-six skeletally immature children with intrasubstance ACL injury, 16 (35%) girls and 30 (65%) boys, were included. The mean follow-up time from injury was 3.2 ± 1.1 years (mean ± standard deviation). Baseline characteristics of the children are shown in Table 1.

Table 1. Characteristics of the ACL injured children, n=46

	Mean (SD)	Minimum - maximum
Age at time of injury, years	11.0 (1.5)	7.0 - 12.9
Age at baseline test, years	11.8 (1.3)	9.0 - 14.5
Time from injury to baseline test, months	11.7 (11.5)	1.1 - 48.2

The majority of injuries had occurred during alpine skiing and soccer (Table 2).

Table 2. Activities at time of injury, n=46 (47 knees)

	n (%)
Alpine skiing	23 (48.9)
Soccer	10 (21.3)
Trampoline	3 (6.4)
Playground	3 (6.4)
Bicycle	2 (4.3)
Handball	2 (4.3)
Cross-country skiing	1(2.1)
Ski-jumping	1 (2.1)
Skateboard	1 (2.1)
Motocross	1 (2.1)

The diagnostic MRIs showed 28 (60%) knees with normal menisci, six (13%) knees with medial meniscal injury, 12 (25%) knees with lateral meniscal injury, and one (2%) knee with medial and lateral meniscal injury. All children had open tibial and femoral physes. Throughout the follow-up 36 children (37 knees) (78%) remained ACL deficient (Figure 1). Four surgical procedures due to new symptomatic meniscal injuries were performed in these knees; three medial meniscal repairs, and one medial meniscal debridement. Ten children (22%), eight girls and two boys, underwent an ACL reconstruction due to persistent instability (n=7), a symptomatic meniscal injury (n=2), or unacceptable reduced activity level (n=1). The 10 ACL reconstructions were performed using a transphyseal technique and a quadrupled hamstring tendon autograft, although one graft had to be converted to the iliotibial band because of harvesting failure during surgery. The mean age at the time of ACL reconstruction was 13.5 ± 0.8 years, with a mean time from injury of 22.4 ± 11.7 months. Concomitant surgical procedures were; one medial meniscal repair, one lateral meniscal repair, one medial meniscectomy, and one lateral meniscectomy. Additionally, one child suffered an intraoperative injury to the tibial nerve during bicortical tibial drilling. Surgical procedures subsequent to the ACL reconstruction were performed in three knees; one medial meniscal repair after a new trauma, one re-suture of a lateral meniscal repair, and one debridement of a partial graft rupture.

A total of 970 monthly online activity surveys were e-mailed to the families during the follow-up period, and 836 (86%) were returned. During the non-operative treatment period 91% (n=760) reported monthly participation in pivoting sports and/or physical education classes in school. Eighty-five percent (n=39) of all children reported a Level 1 activity as their main pre-injury activity, and 15% (n=7) reported a Level 2 activity. The number of ACL deficient children who reported a Level 1 activity as their main activity was significantly reduced ($p<.01$) from pre-injury to baseline (17/46, 37%), 1 year (22/42, 52%), and 2 years (17/34, 50%). Among the 10 children who underwent ACL reconstruction 9 (90%) reported a Level 1 activity as their pre-injury activity. There was reduction in reporting a Level 1 main activity from pre-injury to the 2 years post-operative follow-up; Level 1, n=4 (40%); Level 2, n=1 (10%); and Level 3, n=5 (50%).

The KOOS subscale *Activities of daily living* changed statistically significant in ACL deficient children with a mean improvement of 1.0 point from baseline to 1 year, while the subscale significantly declined 3.1 points from 1 year to 2 years (Figure 2). The isokinetic muscle strength for knee extension and knee flexion improved significantly throughout the study ($p<.01$). The LSI of the single hop test improved by a mean 5.9 points ($p=.04$) from baseline to 1 year, while the 6 meter timed hop test declined by a mean 2.7 points ($p=.01$) from 1 year to 2 years (Table 3).

Table 3. Outcomes from baseline to 2 years for non-operated children, n=34[a,b]

	n	Baseline	1 year	2 years	p-value
Height, cm	34	153.6 (12.5)	160.1 (13.1)[c]	165.5 (12.7)[c,d]	<.01[e]
Weight, kg	34	47.3 (13.8)	53.7 (15.7)[c]	59.4 (17.1)[c,d]	<.01
Body mass index	34	19.7 (3.7)	20.6 (4.0)[c]	21.4 (4.8)[c,d]	<.01[e]
Single hop test, LSI (%)	29	90.8 (15.6)	96.7 (14.6)[c]	95.1 (13.1)	.04[e]
Triple crossover test, LSI (%)	28	93.4 (10.1)	96.5 (12.8)	93.4 (11.7)	.63[e]
Triple hop test, LSI (%)	28	92.9 (10.4)	95.6 (11.0)	95.6 (8.7)	.57[e]
Six meter timed hop test (%)	28	94.2 (9.6)	97.8 (9.4)	95.1 (9.5)[d]	.01[e]
Quadriceps muscle strength, (nm/kg)x100	30	195.5 (44.9)	205.4 (43.0)	224.0 (57.1)[c,d]	<.01
Hamstring muscle strength, (nm/kg)x100	30	103.8 (24.3)	113.8 (28.5)	125.0 (32.5)[c,d]	<.01
Quadriceps muscle strength, LSI (%)	30	90.0 (13.1)	94.0 (10.3)	94.5 (11.8)	.21
Hamstring muscle strength, LSI (%)	30	94.8 (20.3)	94.1 (13.4)	92.7 (11.5)	.81
KOS-ADLS	29	89.0 (10.6)	91.0 (9.9)	88.4 (14.5)	.89[e]
Visual analogue scale	28	77.5 (16.4)	84.9 (16.7)	85.3 (18.0)	.11[e]
IKDC2000	28	82.7 (10.5)	87.2 (10.1)	82.9 (17.6)	.71[e]
KOOS pain	28	90.4 (9.5)	92.0 (8.7)	89.6 (13.1)	.60[e]
KOOS symptom	28	85.1 (15.0)	87.0 (11.5)	86.3 (10.9)	.73
KOOS activities of daily living	28	97.9 (4.8)	98.9 (2.5)[c]	95.8 (9.8)[d]	.02[e]
KOOS sport and recreation	28	83.9 (19.5)	85.7 (19.7)	79.1 (23.7)	.16[e]
KOOS quality of life	28	66.9 (21.3)	75.0 (18.5)	70.3 (22.8)	.15

[a] Tests are analysis of variance with repeated measures unless otherwise specified
[b] Values are given as mean (standard deviation)
[c] Significantly different from Baseline
[d] Significantly different from 1 year
[e] Friedman test as data not normally distributed

All children who underwent an ACL reconstruction grew taller (mean 6.6 ± 4.9 cm, minimum 3 cm and maximum 19 cm) from the pre-operative test to the post-operative test at 2 years. Results from the children who underwent ACL reconstruction are presented in Table 4.

Table 4. Pre-operative test to 2 years post-operative in ACL reconstructed children, n=10 (mean (SD))

	Pre-operative	Post-operative 2 years	Change
Single hop test, LSI (%)	98.2 (4.0)	95.1 (12.2)	-3.1 (11.8)
Triple crossover test, LSI (%)	89.3 (8.7)	94.3 (9.1)	5.0 (12.1)
Triple hop test, LSI (%)	92.2 (6.2)	95.8 (4.3)	3.6 (8.8)
Six meter timed hop test, LSI (%)	92.9 (7.0)	95.4 (10.4)	2.5 (13.1)
Quadriceps muscle strength, (nm/kg)x100	209.1 (55.5)	223.5 (36.4)	14.4 (57.1)
Hamstring muscle strength, (nm/kg)x100	109.6 (24.6)	109.0 (19.0)	-0.6 (19.2)
Quadriceps muscle strength, LSI (%)	91.9 (10.8)	93.1 (12.1)	1.2 (15.1)
Hamstring muscle strength, LSI (%)	91.0 (9.3)	88.0 (14.6)	-3.0 (12.0)
KOS-ADLS	81.6 (14.0)	93.7 (6.9)	12.1 (12.5)
Visual analogue scale	62.7 (18.2)	84.0 (15.9)	21.3 (22.7)
IKDC2000	65.1 (13.4)	85.1 (9.4)	20.0 (13.6)
KOOS pain	85.1 (13.3)	89.5 (8.2)	4.4 (14.3)
KOOS symptom	75.7 (27.9)	85.0 (11.6)	9.3 (20.1)
KOOS activities of daily living	96.9 (4.2)	98.1 (3.0)	1.2 (4.3)
KOOS sport and recreation	68.5 (22.2)	85.5 (13.2)	17.0 (27.0)
KOOS quality of life	41.4 (16.9)	71.4 (18.7)	30.0 (32.3)

Pre-operatively, five children had a grade 2 pivot shift and five had a grade 3 pivot shift test. At 2 years post-operatively a grade zero and grade one pivot shift was seen in four and six children, respectively.

DISCUSSION

This is the first prospective cohort study to investigate changes in functional performance following a non-operative treatment algorithm of ACL injuries in skeletally immature children 12 years and younger. The main findings were that a majority (n=36, 78%) of the included children remained ACL deficient with adequate knee function, and that the number of new meniscal injuries was low (n=6, 13%) throughout the follow-up. Ninety-one percent of the ACL deficient children reported consistent participation in pivoting sports and/or physical education classes in school. Still, 13 (38%) of the children who were ACL deficient at the 2 years follow-up did report abandoning pivoting sports (Level 1 activity) as their *main* leisure time sport activity. Knee function measured with patient-reported outcome measurements and single legged hop tests remained unchanged with regard to changes of clinical relevance, while the knee extension and flexion muscle strength significantly improved over the course of the study. The prospective design and the high compliance to follow-up assessments strengthen the findings of this study. No patients were lost to follow up. Additionally, the number of participants was relatively high, and the included population with exclusively skeletally immature children was homogeneous. In total, this study therefore provides new knowledge on the growing challenge of ACL injuries in young children.

The children grew, as expected, significantly taller over the course of the study. The mean growth from baseline to the latest follow-up was 11.3 ± 5.0 cm (minimum 2 cm, and maximum 24 cm). The fact that all included children increased in height during the course of the study, confirmed the determination of skeletal immaturity at inclusion from the diagnostic MRIs. There was a high adherence rate to the online activity survey, and 91% of the ACL injured children reported to be regularly participating in pivoting sports and/or physical education in school. However, from the reports of *main* leisure time sport activity we found a significantly reduced rate of Level 1 activities at all follow-ups. The present study was not designed to answer questions on *why* the children reduced their participation in Level 1 sports. Fear of re-injury and other psychological factors have been shown to influence the rate of participation in pivoting sports after injury and reconstruction in adult ACL injured individuals.[19, 21] Future studies should, thus, include reasons for why children seem to change their leisure time activity patterns after ACL injury.

The reliability and validity of the included patient-reported outcome measurements has not been documented for a population of knee injured children. The KOOS-Child[32] and the Pedi-IKDC,[33] have recently been published, though not in time to be utilized in this prospective cohort. In the present study the KOOS subscale *Activities of daily living* showed statistically significant improvement from baseline to 1 year, and a decline from 1 year to 2 years. Yet, with a mean change of 1.0 point and a very narrow standard deviation, the score seemed to have a ceiling effect for these children. A minimal detectable change of 7-8 points has been reported for the KOOS subscale *Activities of daily living* for the adult ACL injured population,[34] which indicates that the observed changes were probably not of clinical relevance. Furthermore, as indicated by the KOOS subscale *Activities of daily living* (95.8 ± 9.8 at 2 years), and the KOS-ADLS score (88.4 ± 14.5 at 2 years), the ACL deficient children did not seem to have problems with daily activities when following the non-operative treatment algorithm. Such high scores with very minor changes may also indicate that the questionnaires were not meaningful or relevant for this population,[32, 35] which with the implementation of the new KOOS-Child may be avoided in future studies. The mean IKDC2000 score did not change (p=.71) from baseline to 1 year (mean change 4.7 ± 12.4 points), or to 2 years (mean change 1.9 ± 18.8 points). In adults, Anderson et al[36] have reported that 11.5 points is a clinical relevant change. In a previous retrospective study by our group we reported a median IKDC2000 score of 85 (95% CI 71-95) for a comparable group of 20 non-operated skeletally immature children with a median follow up of 2.9 years (2.0 to 5.2 years).[37] The mean IKDC2000 score for ACL deficient children in the present study was 82.9 ± 17.6 at 2 years. Compared to normative data for young adults,[36] this result indicates that the ACL injured children's knee function to some degree is affected by their injury, which also was in accordance with the children's reported decrease in Level 1 activities as their main leisure time sport activity. However, Iversen et al[35] have reported that children found the IKDC 2000 difficult to comprehend and to answer. The new pedi-IKDC have been demonstrated to have acceptable psychometric performance as an outcome measure in children and adolescents with various disorders of the knee, and should be included in future studies to enhance the validity of the patient-reported outcomes.[33]

Kocher et al[9] reported an IKDC 2000 score of 96.7 ± 6.0 points in 42 children in Tanner stages 1 and 2, with average 5.3 years follow up after undergoing a physeal sparing ACL reconstruction. Cohen et al[38] reported an IKDC 2000 score of 91.5 ± 5.7 in 26 slightly older children (11 to 15 years old) with mean 45 ± 18.3 months follow up after transphyseal ACL reconstruction. In the present study, children who underwent an ACL reconstruction after experiencing an unacceptable decline in knee function showed an improvement of mean 20.0 points in the IKDC2000 score from pre-operative to post-operative 2 years. This improvement was probably clinically relevant. Additionally, they showed improvements for the KOOS subscales *Symptoms, Sport and Recreation,* and *Quality of Life* (mean 9.3, 17.0, and 30.0 points, respectively) from pre-operative to 2 years post-operative which was likely clinically important. Assumed minimal detectable change for these subscales in adults are 5-8.5 points, 5.8-12 points, and 7-7.2 points, respectively.[34]

Quadriceps muscle weakness has been associated with ACL injury, and has in many studies been shown to be difficult to recover if an adequately designed rehabilitation program is not performed after the injury.[39] Isokinetic quadriceps muscle strength LSI values of less than 90% has been described as abnormal,[40] and believed to be related to impaired knee function and increased risk of re-injury in adults.[41] The important knee stabilizing contribution of the hamstring muscles have recently been highlighted by Zebis et al,[42] indicating that restoration of knee flexion strength should be emphasized after ACL injury. Isokinetic muscle strength measurements using the peak torque value, with test velocities between 30 and 180 degrees per second, have been documented to be reliable in healthy children,[43, 44] although the reliability and validity has not been investigated in a pediatric ACL injured population. In the present study we found a statistical significant improvement in peak torque values normalized to body weight from baseline and 1 year to 2 years in the ACL deficient children ($p<.01$). Our study did not enable an evaluation on whether the observed increased muscle strength was beyond what is normal due to growth and maturation.[44-46] However, the muscle strength in the non-injured leg also increased significantly from baseline and 1 year to 2 years ($p<.01$), which may suggest that the improvements in strength are related to maturation. Importantly, we found the mean LSI for both knee extension and knee flexion to be above 90% on all follow-ups for the non-operated children. Knee function measured with single legged hop tests was found to be symmetrical with LSI values above 90% for all time points. Still, the results should be regarded with some caution as the reliability and validity of these tests only have been documented for ACL-injured adults.[47] The rehabilitation program implemented in the study was based on the principle that training for immature children should be safe, effective, and enjoyable.[10, 48] Muscle strength gains in children are believed to be facilitated mainly through neural adaptive mechanisms and not hypertrophy.[48] Thus, the rehabilitation was directed towards challenging neuromuscular knee stabilizing strategies and plyometric exercises. The intention was to facilitate increased motor unit activation and changes in motor unit coordination, recruitment, and firing. Observed improvements in muscle strength, and the symmetrical results of single legged hop tests, indicate that the rehabilitation was adequate to facilitate adequate neuromuscular strategies in children following our treatment algorithm.

The rotational knee laxity was assessed clinically using the pivot shift test, and did not change for the non-operatively treated children over the course of the study (p=.83). As expected, among the children who underwent surgical treatment, significantly fewer were classified with a positive pivot shift test after ACL reconstruction. A negative pivot shift test has been associated with a successful outcome after ACL reconstruction in adults,[49] though a relationship between a positive test and functional instability in skeletally immature children with ACL injury has not been established.

The non-operative treatment algorithm implemented in this study has been developed based on the conception that the results of surgical treatments are variable, and the risk of growth disturbances from in skeletally immature children is significant. Additionally, a previous study from our group showed encouraging results after non-operative treatment in a comparable population.[37] There are, however, several other concerns with performing ACL reconstructions in skeletally immature children. Bollen et al[50] have highlighted the uncertain development of the graft when a soft-tissue graft is implanted in the maturing knee, and Park et al[51] have suggested that the youngest patients are likely to have a graft with a smaller diameter than mature patients. Hence, there may be a risk that a small graft in an immature knee may have lower strength when the child matures. Furthermore, Kim et al[52] demonstrated that the angles between the ACL and tibia are changing in all three planes during growth. These changes, and the narrow anatomy in the skeletally immature knee, increases the technical difficulty with regard to obtaining an anatomical placement of the graft in the youngest patients.[52] The technical challenges and the uncertain development of the graft further accentuate the importance of a thorough assessment before a skeletally immature child is recommended an ACL reconstruction.

There are some limitations to this study. The variation in time from injury to inclusion in the study was considerable. This is mainly because a number of the children were not correctly diagnosed despite seeking medical attention after the index injury and subsequent giving way episodes. Further, the included children were living in all parts of our country, and we have not been able to register compliance with the rehabilitation, which is ultimately important for the functional outcome.

CONCLUSION

Seventy-eight percent of the children continued non-operative treatment throughout the 2 years follow-up. The performance-based functional tests showed symmetrical knee function, and the number of surgical procedures for new meniscal injuries was low (n=6, 13%). Ninety-one percent maintained participation in pivoting sports and/or physical education in school throughout the follow-up period, although a significant number of individuals changed their main activity from a Level 1 to a Level 2 activity. The results suggest that ACL deficient skeletally immature children continued to be physically active, but changed their type of sport participation. A non-operative treatment algorithm may be an adequate treatment option with regard to maintaining participation in physical activity with adequate knee function for skeletally immature children following ACL injury.

What are the new findings?

- This is the first study to prospectively investigate the functional outcomes of a non-operative treatment algorithm in skeletally immature children after ACL injury
- ACL injured skeletally immature children remain physically active following a non-operative treatment algorithm
- A majority of ACL injured skeletally immature children report continuing a Level 1 activity as their main leisure time sport activity following a non-operative treatment algorithm

How might it impact on clinical practice in the near future?

- Consultants and clinicians should more confidently be able to recommend a non-operative treatment algorithm to skeletally immature children with an ACL injury and their families.

Acknowledgements

The authors thank Kristin Bølstad, Marianne Bakke Johnsen, Marte Lund, and Carina Wold for their contribution with the data collection. Additionally, The Norwegian Sports Medicine Clinic (NIMI) is acknowledged for the contribution of infrastructure.

FIGURE LEGENDS

Figure 1. Flow diagram of the included subjects

Figure 2. The five KOOS subscales for non-operated children at Baseline, 1 year, and 2 years post-injury, n=34. Abbreviations: ADL, Activities of daily living; Sport/Rec, Sport and recreation; QoL, Knee related quality of life.

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Figure 1. Flow diagram of the included subjects

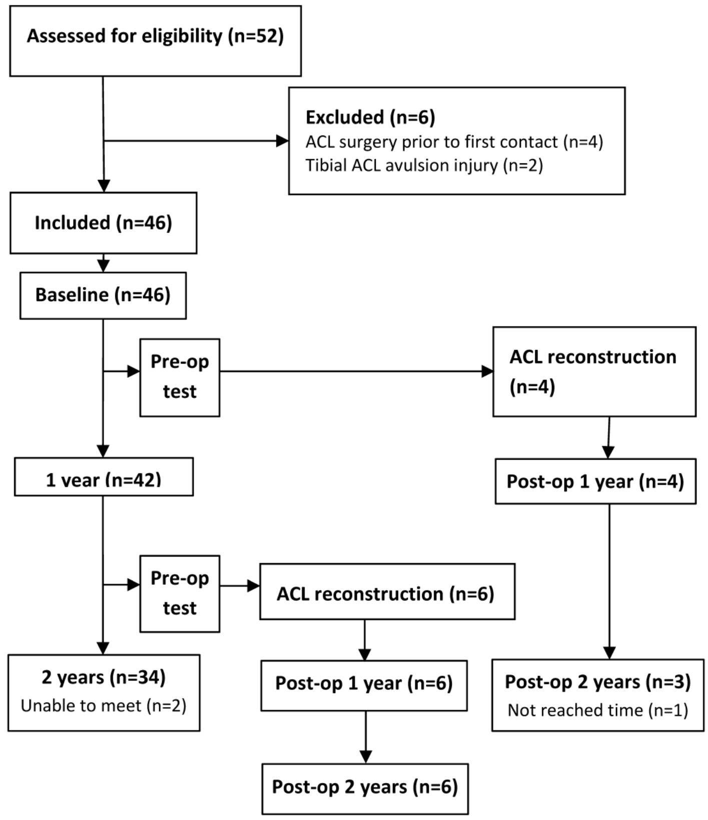
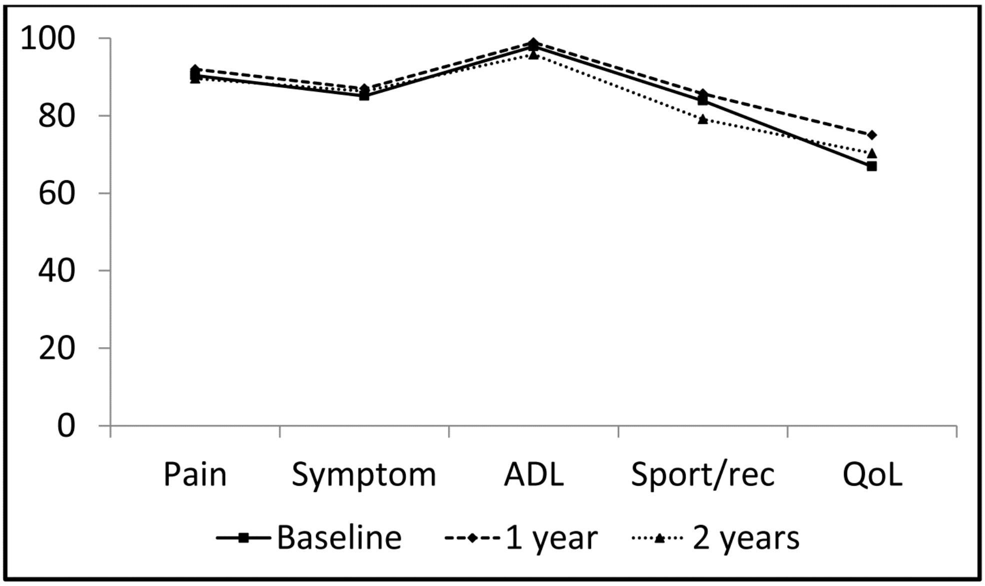


Figure 2. The five KOOS subscales for non-operated children at Baseline, 1 year, and 2 years post-injury, n=34. Abbreviations: ADL, Activities of daily living; Sport/Rec, Sport and recreation; QoL, Knee related quality of life.



Paper IV

Low incidence of new meniscus and cartilage injuries after non-operative treatment of anterior cruciate ligament tears in skeletally immature children: A prospective MRI study.

ABSTRACT

Background: The increased risk of long-term osteoarthritis following concomitant injuries to the menisci or cartilage after an anterior cruciate ligament injury (ACL) in adults is well established. ACL reconstruction is often recommended to skeletally immature children to reduce the risk of secondary injuries. However, the prevalence and incidence of secondary injuries following non-operative treatment of ACL injuries in skeletally immature children is unknown.

Purpose: To prospectively investigate the incidence of new injuries to the menisci and joint cartilage in non-operatively treated skeletally immature children with a known ACL injury using bilateral 3.0T magnetic resonance images (MRI) over the course of one to two years.

Methods: Prospective cohort study. Forty non-operatively treated skeletally immature children (41 knees) with ACL injury were followed up with bilateral 3.0T MRI at two occasions (MRI1 and MRI2). The intraarticular structures were analyzed by two independent MRI radiologists, and described according to previously published guidelines. Monitoring of participation in physical activities was accomplished through a monthly online activity survey. Descriptive statistics and frequencies were extracted from the scoring schemes and compared using Fisher's Exact test.

Results: Fourteen girls (35%) and 26 boys (65%) with an age of 11.0 ± 1.4 years (mean ± standard deviation) at time of injury were included. At MRI1 30 children (31 knees) were still non-operated, while 10 children had undergone an ACL reconstruction. Time from injury to the 3.0T MRI in the 31 non-operated knees was 1.9 ± 1.3 years for MRI1 and 3.8 ± 1.3 years for MRI2. Eighty-eight percent of the nonsurgical treated patients confirmed monthly participation in pivoting sports and/or PE classes in school during the follow-up period. The prevalence of meniscus injuries was 32.3% at MRI1 and MRI2, while the incidence of new meniscus (n=1) and new cartilage injuries (n=1) was 3.2% during the 1.7 ± 0.1 years follow-up.

Conclusion: The incidence of new meniscus injuries (n=1, 3.2%) and cartilage injuries (n=1, 3.2%) was low in 31 non-operated ACL injured skeletally immature knees following non-operative treatment with a total follow-up time from injury of 3.8 ± 1.3 years.

Key terms: anterior cruciate ligament, skeletally immature, meniscus, cartilage, magnetic resonance imaging

What is known about the subject: There is growing documentation suggesting that the incidence of ACL injuries in skeletally immature children is increasing. Conventional wisdom in the orthopedic community is that ACL reconstructions are needed to prevent secondary injuries to menisci and cartilage. However, to our knowledge no prospective studies have evaluated the incidence of new injuries to the intraarticular structures following non-operative treatment in this population.

What this study adds to existing knowledge: This is the first study to prospectively evaluate secondary injuries following non-operative treatment after ACL injuries in skeletally immature children. The low incidence of secondary injuries in the study population may have value with regard to decision making in the clinical setting, because not all children with ACL injury are candidates for ACL reconstruction. Thus, the risks involved with surgical treatment can be balanced against the risks of secondary injuries based on a documented incidence in our population.

Low incidence of new meniscus and cartilage injuries after non-operative treatment of anterior cruciate ligament tears in skeletally immature children: A prospective MRI study.

Previous studies have suggested that persons who have suffered an anterior cruciate ligament (ACL) injury have an increased likelihood for development of long-term knee osteoarthritis (OA).[31, 44, 58] A concurrent or secondary injury to the menisci and/or joint cartilage has been shown to significantly increase the risk of OA further.[10, 15, 21] Consequently, the potential concerns of an ACL injury are particularly serious for individuals sustaining such an injury at a very young age. Although recent evidence suggests that the risk of sustaining an ACL injury during childhood or adolescence is increasing,[45] the true incidence of ACL injuries in the skeletally immature population is unknown.[4, 49] Additionally, the incidence of new secondary meniscus and cartilage injuries in skeletally immature children with ACL injury is also unknown due to the lack of prospective studies.[28] The literature is limited to retrospective studies and case series in which the presence of injuries to the menisci in children who have undergone an ACL reconstruction has been described.[12, 19] Our recent review[42] reports the prevalence of concurrent meniscus injuries to range from 26% to 90% in studies on surgical treatment of ACL injuries in skeletally immature patients. [6, 13] Lawrence et al (2011)[29] reported a significant increase in nonrepairable medial meniscus tears and lateral compartment chondral injuries at the time of surgery in children undergoing ACL reconstruction more than 12 weeks after injury. Samora et al (2011)[47] showed that the majority of meniscus injuries in skeletally immature children with an ACL injury are located in the posterior horn of the lateral meniscus; usually in the vascular zone where the healing potential is good. Additionally, Kraus et al (2012)[28] and Vanderhave et al (2011)[56] have shown that the possibility of repair, and survival of repairs, is substantial in younger patients. Furthermore, cartilaginous tissues in children and adolescents are believed to have a better ability to recuperate normal structure and function after traumatic injury compared to matured cartilage in adults.[18, 51] Hence, it is of utmost importance that reliable and accurate diagnostic modalities are used to monitor the intraarticular structures in individuals who sustain an ACL injury at a young age. Magnetic resonance imaging (MRI) is recommended as the preferred imaging modality in diagnosing ACL injuries and concomitant injuries in skeletally immature children and adolescents.[16]

Conventional wisdom in the pediatric ACL community is that early surgery is needed to avoid meniscal and cartilage injuries. However, to our knowledge no studies have prospectively investigated, and followed over time, the integrity of the menisci and joint cartilage following ACL injury in skeletally immature children. The aim of the present investigation was to prospectively investigate the incidence of new injuries to the menisci and joint cartilage in non-operatively treated skeletally immature children with a known ACL injury using bilateral 3.0T MR images over the course of one to two years.

MATERIAL AND METHODS

The present study investigated the integrity of the ACL, the menisci, and the joint cartilage in 40 consecutively recruited skeletally immature children, 12 years and younger, with a traumatic ACL injury. Bilateral 3.0T MRI was performed at two occasions (MRI1 and MRI2), with an interval between investigations of minimum one and maximum two years. All subjects were recruited from an ongoing prospective cohort study in which the functional and clinical outcomes of ACL injuries in skeletally immature children are investigated. The prospective cohort study was initiated in 2006, and the inclusion criteria were a traumatic complete intrasubstance ACL tear sustained at age 12 and younger.[30] Tibial and femoral ACL avulsion fractures were not included in the study. The diagnosis was confirmed through conventional diagnostic MRI, a positive Lachman test, and an instrumented measured sagittal side-to-side difference of 3 mm or more using maximum manual force (KT-1000, Med-Metric, San Diego, California, USA).[8] The present study results are based on MRI1 and MRI2 from one specific 3.0T machine. The diagnostic MRI scans, on the contrary, were performed in numerous locations prior to referral to our center, with various protocols and lower magnet field strength than in the present study. Thus, the diagnostic MRIs have solely been used for initial diagnosis of the ACL injury.

Recruitment and treatment algorithm

To detect meniscal and cartilage injuries the 40 first enrolled children from the cohort study underwent a 3.0T MRI scan of both knees in 2009/10 (MRI1), and a subsequent MRI scan in 2011/12 (MRI2). All the children had undergone the treatment algorithm of Moksnes et al,[41] which advocates non-operative management.[41] In short; the aim of the treatment algorithm is to provide individually tailored rehabilitation that enables the child to return to activity without ACL reconstruction. As part of the algorithm the children were provided with a custom-made and individually adjusted knee brace, which they were instructed to wear during physical education in school and all other recreational sports activities.

To monitor the activity level of the children, an online activity survey regarding participation in specific activities was e-mailed to the families once a month during the course of the study, starting at MRI1 and ending at MRI2. No specific activity limitations were advocated. ACL reconstruction was considered if a child reported two giving way episodes with subsequent knee effusion and/or pain within any given period of three months, or if they sustained a secondary symptomatic meniscus injury.[41]

Magnetic Resonance Imaging

The overall sensitivity and specificity of MRI for the detection of ACL tears in children is reported to be 95% and 88%, respectively.[30] The sensitivity for acute ACL tears have been reported to be 94% for an abnormal angle with the Blumensaat's line; 79% for increased signal intensity in the substance of the ligament; and 21% for discontinuity in the ligament[30]. With regard to meniscus injuries in adolescents, MRI has been shown to demonstrate injuries with a sensitivity and specificity of 92% and 87% for the medial meniscus, and 93% and 95% for the lateral meniscus.[33] However, in children under 12 years of age the sensitivity and specificity for diagnosing meniscus injuries is reported to be significantly lower; with 62% and 78%, respectively.[23]

At MRI1 and MRI2 all examinations were administered by the same MRI-physicist, using a standardized protocol in one single MRI unit (GE Medical, Signa HDxt 3.0T, United Kingdom) with a transmit/receive eight-channel phased-array knee coil. All patients had sagittal, coronal, and axial proton-density (PD)-weighted fat-suppressed (FS) images.[39, 50] The sagittal PD-weighted images had slice thickness of 3 mm, while the coronal and axial had 2 mm.

Additionally, oblique T2-weighted sagittal images with slice thickness of 2 mm were acquired.

Oblique sagittal images along the plane of the ACL have been suggested to better detect subtle, incomplete tears.[16] Imaging matrix for all images was 384x288.

Two experienced MRI radiologists, with 15 and 13 years of musculoskeletal MRI experience, respectively, analyzed the MR images independently using a Centricity DICOM Viewer

(Version 2.2). While both radiologists were informed about the study inclusion criteria, they were, however, blinded with regard to secondary injuries and treatments performed prior to MRI1 and MRI2. Following the classification of injuries by both radiologists, a consensus meeting was held to reach agreement in cases where discrepancies between the individual readings were present. Each case with initial disagreement was re-investigated by both radiologists together until consensus based on the classification criteria was reached.

MRI analysis and classification

The ACL was classified according to criteria as described by van Dyck et al. (2012)[54] as normal, total rupture, or partial rupture: An ACL that could be followed as a continuous band of low signal intensity from the femoral to the tibial attachment with the ACL fibers parallel to Blumensaat's line was considered a normal ACL. Replacement of the ACL by an edematous mass with non-visualization of its fibers and a wavy contour of the ligament were considered signs of a total ACL rupture. Hyper intense signal within the ACL substance, distortion of fibers without obvious discontinuity, attenuation and/or abnormal orientation of the ACL with respect to Blumensaat's line were all considered MR signs of a partial ACL tear. Although all the 41 knees had a positive Lachman and pivot shift test as well as a KT1000 laxity measurement of more than 3 mm compared to the normal side, we chose to label the latter signals as partial ruptures, though such signals may also be interpreted as signs of scar tissue formation following a total ACL rupture.[23]

The vascularization and maturation of the menisci have been suggested to increase the difficulty in correctly diagnosing pathological conditions in children.[46, 59] However, Sanchez et al (2009)[48] and Major et al (2003)[33] have described that the accuracy of MRI as a diagnostic tool for meniscus injuries in children and adolescents is acceptable. In the present study menisci were classified as being normal, or having a horizontal rupture, a longitudinal rupture, a radial rupture, or a high signal without rupture.[23, 36, 52] A meniscus was considered torn if there was an abnormal signal which broke through the articular surface of the meniscus in two or more images,[7, 9] with particular attention to differentiation between normal vascular structures known to be present in children (high-signal without rupture) and grade 3 ruptures.[52]

Articular cartilage was described as normal or injured based on the International Cartilage Repair Society classification of cartilage injuries.[3] A grade 0 was indicated by a normal signal intensity and surface contour. Grade 1 corresponds to an abnormal signal in the superficial cartilage with intact thickness, while grade 2 was noted if the cartilage showed structural changes in $< 50\%$ of the thickness. A grade 3 injury was stated when structural changes were ≥ 50 % of cartilage thickness, whereas a full-thickness abnormality to the subchondral bone was classified as grade 4. Bone Marrow Lesions (BMLs) were defined as areas of high-signal intensity located adjacent to the articular cartilage and present on 2 or more images.[11]

The study was approved by the Regional Ethical Committee, and all subjects and their parents signed a written informed consent prior to inclusion. The rights of the subjects are protected by the Declaration of Helsinki.

Statistical analysis

Descriptive statistics with average age and time from injury to MRI1 and MRI2, and frequency counts, was extracted from the scoring schemes and analyzed using the Predictive Analytics SoftWare (PASW) Statistics (version 18.0.2 (April 2, 2010); SPSS Inc., Chicago, IL, USA). The frequency of observed menisci with high signal without rupture between the ACL injured and the non-injured side was compared using the Fisher's Exact test.

RESULTS

Forty skeletally immature children with a total intrasubstance ACL injury (41 knees) were assessed at MRI1 and MRI2. There were 14 (35%) girls and 26 (65%) boys, with an average age at injury of 11.0 ±1.4 years (mean ± standard deviation). The majority of injuries had occurred during alpine skiing or soccer (Table 1). Prior to MRI1, 10 patients had their ACL reconstructed according to the criteria in the study. Thus, at MRI1 30 children (31 knees) were non-operated, between which one medial meniscus repair and one partial medial meniscus menisectomy had been performed before MRI1.

The response rate for the monthly survey regarding participation in activities was 88.3% (636 out of 720 surveys were returned), with 88.0% confirming monthly participation in pivoting sports and/or PE classes in school between MRI1 and MRI2. Reports from the diagnostic MRIs on all 41 knees showed 22 (53.7%) knees with normal menisci, 5 (12.2%) with medial meniscus injuries, 13 (31.7%) with lateral meniscus injuries, and 1 (2.4%) knee with medial and lateral meniscus injury. Furthermore, diagnostic reports from the 31 knees which were non-operated at MRI1 showed 20 (64.5%) knees with normal menisci, 4 (12.9%) with medial meniscus injury, and 7 (22.6%) with lateral meniscus injury.

At MRI1, 90.3% (n=28) of the 31 non-operated knees had open physis, and 67.7% (n=21) were still open at MRI2 (Table 2). The prevalence of meniscus injuries was 32.3% at both MRI1 and MRI2, and the incidence of new meniscus injuries was 3.2% (n=1, lateral horizontal rupture) (Table 3). An overview of meniscus injuries and cartilage injuries with sub classification into type of injury at MRI1 and MRI2 is shown in Table 3. There was no significant difference in the frequency of menisci classified with high signal without rupture between the ACL injured knee and the non-injured knee at MRI1 (p=0.65), or MRI2 (p=0.46). The prevalence of knees with cartilage injuries was 9.7% at both MRI1 and MRI2, with one new injury to the medial tibial condyle (MTC) during the study (Table 3). Four BMLs were identified at MRI1 (patella, n=2; medial femoral condyle (MFC), n=1; lateral femoral condyle (LFC), n=1), whereas 3 BMLs were evident at MRI2 (MFC, n=1; LFC, n=1; MTC, n=1). Three (10.0%) children had undergone ACL reconstruction between MRI1 and MRI2; all due to recurrent instability. One partial medial menisectomy had been performed in these 3 children.

Prior to MRI1, 10 (24.4%) children had undergone ACL reconstruction using a transphyseal surgical technique and quadrupled hamstring tendon as graft. The age at time of surgery was 13.1 ± 1.0 years, and time from injury to surgery was 1.6 ± 0.9 years. Five (50%) of these children had concomitant surgical procedures which included repair of 2 medial and 2 lateral menisci, and 2 partial lateral menisectomies. At MRI1 there were 2 knees with medial (20%), 3 knees with lateral (30%), and 1 knee with medial and lateral (10%) meniscus injuries. One new medial meniscus injury was found at MRI2. Three cartilage injuries (1 at the MFC and 2 at the LFC) were observed at MRI1. The injury at the MFC had resolved at MRI2.

DISCUSSION

This is the first study to prospectively investigate the incidence of new secondary meniscus and cartilage injuries in ACL injured skeletally immature children through a continuous period of non-operative treatment. We found the incidence of new meniscus and cartilage injuries in 30 non-operated ACL injured skeletally immature children to be low in our follow-up period (n=1, 3.2%). Additionally, only 1 new cartilage injury was detected from the MR images during the course of the study. The vast majority of children (88.0%) reported a high rate of participation in strenuous activities during the follow-up period, indicating that they were well functioning without apparent restraining symptoms despite the fact that 32.3% had MRI detected meniscus injuries.

The low incidence of new injuries in this population of ACL injured skeletally immature children contrasts the common beliefs of orthopedic surgeons and previous retrospective studies.[29, 35] Lawrence et al (2011)[29] retrospectively reviewed the surgical records from 70 skeletally immature children, from which they found a significant increase of non-repairable medial meniscus injuries and lateral cartilage injuries if ACL reconstruction was performed more than 12 weeks after injury. Additionally, Millet et al (2002)[38] found an association between time from injury to surgery with an increase in medial meniscus injuries. The strength of the present study is the prospective design and the use of a reliable measurement (3.0T MRI). Technological advances has led to MRI systems with higher signal intensity, and preliminary clinical studies suggest that 3.0T MRI provides convincing visualization of the hyaline cartilage and menisci with good diagnostic values.[14, 37, 55, 57] Although we do not have arthroscopic confirmation of the injuries, data from previous studies have indicated a high correlation between MRI findings and arthroscopy using the current classification of meniscus injuries.[7, 9] However, the magnetic susceptibility artifacts may be larger at 3.0T, and the suggested increased values of enhanced magnetic fields are still not solidly confirmed.[16]

The prevalence of knees with meniscus injuries in total was 32.3% at MRI1 and at MRI2. Among the 30 non-operated children, who on average had been ACL deficient for 3.8 ± 1.3 years at the time of MRI2, only 1 new injury occurred during the follow-up period. Interestingly, we also found a prevalence of 10.3% for meniscus injuries in the uninjured knee within our population. Four of the largest retrospective series published have reported prevalences of meniscus injuries ranging from 35% to 69% at the time of ACL reconstruction.[17, 26, 43, 47] All the patients in these previous studies underwent ACL reconstruction within 12 months after the acute injury. Thus, the prevalence of meniscus injuries in the present investigation is in the lower ranges of what has been previously reported in the literature. The low prevalence and incidence of secondary meniscus and cartilage injuries support a non-operative treatment algorithm with regard to secondary injuries in skeletally immature children with ACL injury.[41] Several authors have highlighted the risks involved in surgical ACL reconstruction of the skeletally immature patient compared to reconstructions in a skeletally mature patient. The most commonly discussed adverse event is skeletal growth disturbance which may contain overgrowth, angular deformation, and growth arrest. The prevalence of such adverse events has been shown to be low using transphyseal technique and soft tissue grafts.[5, 12, 19, 25, 40] However, there are several other significant unresolved uncertainties such as the development of the graft,[2, 22] the long-term outcome,[42] prolonged inability to participate in sports and social relationships,[53] and compliance to post-operative rehabilitation protocols.[41] These confounding factors should also be thoroughly considered when deciding which treatment option a skeletally immature child should be advised. The results from the present study increases the level of confidence with which we can advise children and parents with regard to secondary injuries following a non-operative treatment algorithm after ACL injury.

Samora et al[47] found that lateral meniscus tears was more common than medial meniscus tears in skeletally immature children with ACL injury. We were not able to reproduce this finding, as the distribution of lateral and medial meniscus injuries was equal (Table 3). An explanation for the discrepancy may lay in the fact that Samora et al[47] evaluated children at the time of ACL reconstruction, which was performed as early as within 3 months of the ACL injury. The time from injury to follow-up was substantially longer in our prospective investigation, and several authors have described that the pediatric meniscus is highly vascularized and inherit a high potential for healing.[1, 27, 56] The diagnostic MRIs from our population also showed a high proportion of lateral meniscus injuries (lateral injuries, n=7; medial injuries, n=4 in the 31 knees). Thus, there may be an overestimation of lateral meniscus injuries when surgical procedures are performed early after injury because these injuries may resolve naturally over time. In the present study, the majority of the total number of meniscus injuries in the ACL injured knees were longitudinal ruptures (8/12 (67%) at MRI1, and 7/12 (58%) at MRI2). Additionally, the prevalence of a high signal without tear in the ACL injured knees at MRI1 was 29.0% in the medial menisci, and 6.5% in the lateral menisci. The corresponding prevalence's at MRI2 were 25.8% and 3.2% respectively. In the non-injured knees the equivalent prevalence's for menisci with high signal without rupture at MRI1 were 13.8% (medial) and 3.4% (lateral), and at MRI2; 27.2% and 3.4%, respectively. There was no significant difference between injured and non-injured knee with regard to the frequency of observed high signal without rupture (MRI1, p=0.65; MRI2, p=0.46), indicating that the high signals found in this investigation were maturing healthy menisci and not signs of a degenerative process or rupture.

The prevalence of cartilage injuries in ACL injured children have been investigated to a lesser extent than meniscus injuries.[32, 34] Jones et al (2003)[18] have demonstrated that the thickness of uninjured cartilage increases during adolescence in non-injured individuals, and that highly active healthy children develop thicker cartilage compared to more sedentary children. This knowledge supports the assumption that the joint cartilage in children is adaptable to load[32] and our suggestion that it has a potential for healing following injury. We found that one new cartilage injury (MTC) was observed at MRI2, while one cartilage injury (LFC) from MRI1 was not observed at MRI2. These results are in contrast with previous retrospective studies,[20, 29] in which an increase in lateral cartilage injuries with delayed surgical treatment after ACL injury has been reported. The majority of registered cartilage abnormalities were localized on the medial condyles which are comparable to reports in adolescent and adult ACL injured patients.[15] Minor changes in the grading of the observed cartilage injuries was observed (Table 3), although considering the relatively low accuracy in MRI based grading[50] of cartilage injuries these changes are to be considered tentative and should be interpreted with caution. According to von Engelhart et al (2007)[57] 3.0T MRI provides convincing visualization of the hyaline cartilage with good diagnostic values. However, they also point out that the positive predictive values seem to be low for all grades of lesions. There were no increases in the number of observed BMLs from MRI1 to MRI2, which is in accordance with the relatively low incidence of meniscus and cartilage injuries as BMLs may be an indication of recurrent knee instability and repetitive subluxations.

All children included in this study were diagnosed with a total rupture of the ACL through clinical examination, conventional MRIs, and laxity measurements (KT1000) prior to inclusion into the study. Our radiologists' consensus on six (19.4%) of the children was a partial rupture according to the classification criteria (Hyper intense signal within the ACL substance, distortion of fibers without obvious discontinuity, attenuation and/or abnormal orientation of the ACL with respect to Blumensaat's line). The development of scar tissue may keep some of the remnants of the torn ACL attached in the intercondylar notch, or to the posterior cruciate ligament, although the stabilizing function of this tissue is believed to be limited.[24] Kocher et al (2002)[24] have shown that partial ruptures are more common in children and adolescents compared to adults. The present study is encouraging because the meniscus and cartilage injuries were few in the follow-up period. However, 13 of the 40 knees had to go through an ACL reconstruction due to instability and meniscal symptoms. The clinical challenge will still be to identify these patients prior to their meniscal tear. This study has some limitations. Due to the time from injury to MRI1 it is possible that some of the observed meniscus and cartilage injures may have occurred between the index injury and MRI1. Additionally, although this is the first prospective study investigating the integrity of intraarticular structures following ACL injuries in skeletally immature children, the total follow up time of 3.8 ± 1.3 years may be too short to firmly conclude that non-operative treatment is associated with a low incidence of secondary injuries in the long term. Nonetheless, it might be sufficient time for individuals who would prefer to delay surgery until skeletal maturity.

CONCLUSION

This is the first study to prospectively evaluate secondary injuries following non-operative treatment after ACL injuries in skeletally immature children. The incidence of secondary injuries was low (meniscus, n=1 (3.2%), and cartilage, n=1 (3.2%)), and the vast majority of children continued being physically active in sports and their school community. These results may have value with regard to decision making in the clinical setting, because not all children with ACL injury are candidates for ACL reconstruction. Thus, the risks involved with surgical treatment can be balanced against the risks of secondary injuries based on a documented incidence in our population.

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Table 1 Activities at the time of ACL injury, n=41

Activity	n	%
Alpine skiing	20	48.4
Soccer	10	24.4
Team handball	2	4.9
Playground	2	4.9
Bicycle	2	4.9
Trampoline	2	4.9
Cross-country skiing	1	2.4
Motocross	1	2.4
Ski-jumping	1	2.4

Table 2 Descriptive statistics total population and non-operated children

	Total population (n=40)		Non-operated (n=30)	
Sex, male/female	26/14 (65%/35%)		21/9 (70%/30%)	
Side, left/right	24/17 (59%/41%)		19/12 (61%/39%)	
	Total population (n=41 knees)		**Non-operated (n=31 knees)**	
	Mean (±SD)	**min – max**	**Mean (±SD)**	**min – max**
Age at time of injury (years)	11.0 (±1.4)	8.2 – 12.9	10.9 (±1.3)	8.2 – 12.9
Age at time of MRI 1 (years)	13.2 (±1.7)	9.6 – 16.2	12.8 (±1.7)	9.6 – 16.1
Age at time of MRI 2 (years)	14.9 (±1.7)	11.0 – 17.8	14.5 (±1.7)	11.0 – 17.7
Time from injury to MRI 1 (years)	2.2 (±1.4)	0.2 – 5.2	1.9 (±1.3)	0.2 – 4.1
Time from MRI 1 to MRI 2 (years)	1.7 (±0.1)	1.4 – 2.0	1.7 (±0.1)	1.4 – 2.0
	MRI 1, n (%)	**MRI 2, n (%)**	**MRI 1, n (%)**	**MRI 2, n (%)**
Open growth plate femur, yes	36 (88)	29 (71)	28 (90)	21 (68)
Open growth plate tibia, yes	34 (83)	25 (61)	28 (90)	20 (65)

Table 3 Prevalence of pathologic findings in injured and non-injured knee at MRI1 and MRI2 for non-operated children (n=30)

	ACL injured knee, n=31		**Non-injured knee, n=29**	
	MRI 1, n (%)	**MRI 2, n (%)**	**MRI 1, n (%)**	**MRI 2, n (%)**
ACL				
Normal	0	0	29 (100)	29 (100)
Total rupture	25 (80.6)	22 (71.0)	0	0
Partial rupture	6 (19.4)	6 (19.4)	0	0
ACL graft	0	3 (9.7)	0	0
Medial meniscus, injuries	**6 (19.4)**	**6 (19.4)**	**3 (10.3)**	**3 (10.3)**
Normal	16 (51.6)	17 (54.8)	22 (75.9)	21 (72.4)
Horizontal	2 (6.5)	2 (6.5)	2 (6.9)	2 (6.9)
Longitudinal	4 (12.9)	4 (12.9)	1 (3.4)	1 (3.4)
Radial	0	0	0	0
High signal without rupture	9 (29.0)	8 (25.8)	4 (13.8)	5 (17.2)
Lateral meniscus, injuries	**6 (19.4)**	**6 (19.4)**	**0**	**0**
Normal	23 (74.2)	24 (77.4)	28 (96.6)	28 (96.6)
Horizontal	1 (3.2)	2 (6.5) **(1 new injury)**	0	0
Longitudinal	4 (12.9)	3 (9.7)	0	0
Radial	1 (3.2)	1 (3.2)	0	0
High signal without rupture	2 (6.5)	1 (3.2)	1 (3.4)	1 (3.4)
Knees with meniscus injury	**10 (32.3)**	**10 (32.3)**	**3 (10.3)**	**3 (10.3)**
Normal	21 (61.0)	21 (61.0)	26 (89.7)	26 (89.7)
Medial	4 (12.9)	4 (12.9)	3 (10.3)	3 (10.3)
Lateral	4 (12.9)	4 (12.9)	0	0
Medial and lateral	2 (6.5)	2 (6.5)	0	0
Knees with cartilage injury	**3 (9.7)**	**3 (9.7)**	**1 (3.4)**	**1 (3.4)**
MFC	3 (2 grade II, and 1 grade IV)	3 (2 grade III, and 1 grade IV)	1 (grade III)	1 (grade II)
LFC	1 (grade IV)	0	0	1 (grade I)
MTC	1 (grade II)	2 (2 grade II) **(1 new injury)**	0	0
LTC	0	0	0	0
Patella	0	0	0	0
Trochlea	0	0	0	0
Bone Marrow Lesions	4 (12.9)	3 (9.7)	1 (3.4)	1 (3.4)

Appendix I

Approval South East Regional Committee for medical and health research ethics

REGIONAL KOMITE FOR MEDISINSK FORSKNINGSETIKK

Øst-Norge (REK I)

Fysioterapeut Håvard Moksnes
NIMI Ullevål
Sognsveien 75 D
0805 Oslo

Deres ref.: Vår ref.: 684-06288 1.2006.78 Dato: 20. november 2006

Barn med fremre korsbåndsskade. En prospektiv kohortstudie av barn under 13 år

Regional komité for medisinsk forskningsetikk, Øst-Norge, vurderte prosjektet på sitt møte 09.11.06.

Komiteen har ingen innvendinger mot at studien blir gjennomført, men ber om at det utarbeides eget informasjonsskriv for barn over 12 år.

Komiteen ber om å få informasjonsskrivet til barn til orientering.

Med vennlig hilsen

Knut Engedal
professor dr.med.
leder

Ida Nyquist
sekretær

Kopi: Forskningsdirektør Andreas Moan, Ullevål Univeristetssykehus

Postboks 1130, Blindern, 0318 Oslo. Tlf.: 22 84 46 67. Fax: 22 84 46 61

Appendix II

Approval the Norwegian Data Protection Authority

From: Thorstensen Heidi [Heidi.Thorstensen@ulleval.no]
Sent: 29. oktober 2006 13:45
To: Linn Gjersing; mayarna risberg
Cc: Thorstensen Heidi
Subject: Formalisering av personvernet for studien Barn med fremre korsbåndsskade. En prospektiv kohorte studie av barn ≤ 13 år

?
[Ta vare på denne eposten]

Kjære forsker

Viser til melding om behandling av personopplysninger / helseopplysninger. Det følgende er et formelt svar på meldingen. Forutsetningene nedenfor må være oppfylt før rekruttering av pasienter til studien kan starte.

Mandat for tilrådning
Med hjemmel i Personopplysningsforskriftens § 7-12 og Helseregisterlovens § 36 har Datatilsynet ved oppnevning av Heidi Thorstensen som personvernombud ved UUS, fritatt sykehuset fra meldeplikten til Datatilsynet. Behandling og utlevering av person-/helseopplysninger til forskning meldes derfor til sykehusets personvernombud. Konsesjonsplikten gjelder fremdeles, men personvernombudet tar stilling til om melding er dekkende eller om det må søkes om konsesjon hos Datatilsynet, se for øvrig www.datatilsynet.no for oversikt over oppnevnte personvernombud.

Tilrådning med forutsetninger
Personvernombudet har vurdert den planlagte databehandlingen av personopplysninger/helseopplysninger og vurderer denne til å tilfredsstille forutsetningene for melding gitt i personopplysningsforskriften § 7-27 og er derfor unntatt konsesjon, Personvernombudet har ingen innvendninger og tilrår at studien gjennomføres med den planlagte behandlingen av person- / helseopplysninger under forutsetning av følgende:

1. Behandling av personopplysninger/helseopplysninger i studien skjer i samsvar med og innenfor det formål som er oppgitt i meldingen (se vedlagte meldeskjema)
2. Vedlagte samtykke benyttes.
3. Studien remeldes på eget skjema (se www.uus.no/personvern) hvert tredje år, første gang i 2009
4. Melding pr. epost om avsluttet studie sendes personvernombudet senest desember 2030

Øvrige forutsetninger:
a) Positiv uttalelse er innhentet fra Regional Komité for medisinsk forskningsetikk ("REK")
b) Studien er godkjent av avdelingsledelse og forskningsutvalget ved sykehuset og registrert hos FUS v/Evi Faleide

Endringer
Dersom det underveis i studien blir aktuelt å gjøre endringer i behandlingen av de avidentifiserte dataene, eller endringer i samtykket, skal dette forhåndsmeldes til personvernombudet.

Lykke til med studien!

mvh
Heidi
IKKE SENSITIVT INNHOLD

Heidi Thorstensen
IKT-sikkerhetssjef/personvernombud, Konsern IT
Ullevål universitetssykehus HF
Mobil: 48016349
Personvern i medisinsk forskning: www.uus.no/personvern

Fra: Linn Gjersing [mailto:Linn.Gjersing@nimi.no]
Sendt: 26. oktober 2006 09:43
Til: Thorstensen Heidi
Emne: Enda ett nytt prosjekt fra NAR....

Hei, her oppe på NAR slutter vi aldri å produsere nye studier. Dette er en ny barnestudie vi ønsker å melde inn. Håper vi har greid å sette likt avslutningår over alt :)

Ett spørsmål, det er samtykkeskjema du er mest interessert i, ikke sant? De andre spørreskjemaene som personopplysningsskjema, IKDC, KOS etc, vil du at jeg skal sende disse også? Jeg har lagt de ved i denne mailen, men tenkte jeg ville spørre slik at jeg vet til neste gang :)

Linn

Appendix III

Patient informed consent

ULLEVÅL universitetssykehus

Ortopedisk Senter
FOU-enheten, NAR

Informasjon til pasienter og foresatte til barn som har en fremre korsbåndskade ervervet før fylte 13 år og som ønsker å vurdere deltagelse i prosjektet:

«Funksjonsvurdering av barn med fremre korsbåndsskade »

Skade av fremre korsbånd i kneet er en av de hyppigste idrettsskadene vi har. Vi har de siste årene sett en økende tendens til at stadig yngre personer skader fremre korsbånd. Vi vet at for voksne pasienter kan skaden gi varierende funksjon og at noen individer kan trene opp kneet til å fungere helt normalt i alle aktiviteter, mens andre må gjennomgå en operasjon som rekonstruerer korsbåndet før de kan gjenoppta ønskede aktiviteter. Det finnes lite forskning på knefunksjonen hos barn med korsbåndsskade, men erfaringen er at barn med korsbåndsskade fungerer betydelig bedre enn vokse med tilsvarende skade. De fleste barn med korsbåndsskade kan fortsette med sine vanlige aktiviteter uten operasjon etter en periode med rehabilitering. Dersom det blir nødvendig med operasjon underveis i prosjektet så vil dette bli utført etter vanlige behandlingsregimer.
I denne studien ønsker vi å gjennomføre funksjonsvurdering av individer som har pådratt seg fremre korsbåndsskade før de fylte 13 år, og å følge de samme pasientene i 20 år fremover.

Barn under 13 år som har skadet korsbåndet skal undersøkes av professor Lars Engebretsen på Ullevål Universitetssykehus. Alle som inkluderes i forskningsprosjektet skal også testes av fysioterapeut Håvard Moksnes ved NIMI på Ullevål stadion. Testingen består av fire hinketester, en styrketest, en måling av kneets slakkhet og utfylling av spørreskjema om knefunksjon. Ved alle testene sammenlignes funksjonen i det skadde kneet med funksjonen i det friske kneet. Hinketester og styrketester gjøres på forskjellige dager og hver test gjennomføres i løpet av ca.1 time inkludert oppvarming. Den første testen gjennomføres senest seks måneder etter skade, og alle pasienter vil deretter bli invitert til ny test etter ett, to, tre, fem, ti og tjue år.

Det er ingen kjent risiko ved å delta i disse testene.

Du har nøyaktig de samme rettighetene og forsikringsvilkårene som du ville hatt dersom du ikke deltok i denne undersøkelsen. Du har rett til å trekke deg fra undersøkelsen når som helst, og du har da rett til å kreve dataene slettet. Dersom feil oppdages har du rett til å få korrigert opplysningene.

Dataene som innhentes om kne funksjonen din vil lagres i manuelle arkiv med personidentifikasjon som låses inn, og du har til enhver tid full innsynsrett i dataene. Dataene avidentifiseres ved elektronisk lagring på PC for statistiske analyser. Elektronisk lagres dataene kun med nummer. Ingen av dataene sammenholdes med elektroniske registre. Lagringen av data vil foregå i henhold til personsopplysningsloven. Etisk komité har vurdert prosjektet og godkjent gjennomføringen.

Prosjektet planlegges avsluttet i 2028, og alle sensitive persondata vil bli slettet innen 2 år etter at studien er ferdig. Dersom nye studier basert på innsamlede opplysninger blir aktuelle, ber vi om tillatelse til å henvende oss til deg for nytt samtykke for slik bruk.

Dersom du har spørsmål underveis kan du ringe professor Lars Engebretsen 22117464 eller fysioterapeut Håvard Moksnes 23265640 eller h.m@hjelp24.no.

Alle utgifter ved reise og eventuell overnatting vil bli dekket.

Med vennlig hilsen

Lars Engebretsen	Håvard Moksnes
Professor	Fysioterapeut/prosjektleder

Samtykkeerklæring

Jeg har lest og blitt forklart informasjonen på medfølgende informasjonsskriv om prosjektet, og sier meg villig i å delta i undersøkelsen.
Jeg har forstått at deltakelsen er frivillig.

Sted ______ Dato ______

Underskrift ____________________

Underskrift av foresatt ____________________
(dersom pasienten er under 18 år)

Appendix IV
Patient informed consent for children aged 12 to 13 years

Informasjon til barn i alderen 12 til 13 år som har pådratt seg en fremre korsbåndskade før fylte 13 år og som vurderer deltagelse i prosjektet:

«Funksjonsvurdering av barn med fremre korsbåndsskade »

Skade av fremre korsbånd i kneet er en av de vanligste idrettsskadene. Vi har de siste årene sett at stadig flere unge personer skader fremre korsbånd. Vi vet at hos voksne gir skaden forskjellig funksjon. Noen kan trene seg opp, mens andre må operere kneet for å fungere normalt i alle aktiviteter. Det finnes lite forskning på barn med korsbåndsskade, men vår erfaring er at barn med korsbåndsskade oftere fungerer som normalt uten operasjon. Dette prosjektet gjennomføres for at vi skal kunne lære mer om korsbåndsskader hos barn.

Etter en opptrening som varer 3 til 6 måneder kan de fleste barn med korsbåndsskade fortsette med sine vanlige aktiviteter uten operasjon. Noen opplever allikevel at kneet ikke fungerer som det skal og må opereres. Dersom det blir nødvendig med operasjon underveis i prosjektet så vil dette bli utført etter vanlige rutiner.

I denne studien undersøker vi hvordan kneet til barn, som har skadet korsbåndet før de fyller 13 år, fungerer under vanlige daglige aktiviteter og i sport. I prosjektet er det planlagt at alle som ønsker det kommer til å bli fulgt opp i mange år framover.

I prosjektet kommer vi til å teste kneet ditt jevnlig. Når du testes skal du gjennomføre fire hinketester, en styrketest, en måling av kneets stabilitet, og fylle ut spørreskjemaer. Den første testen gjør vi før det er gått seks måneder etter skaden, og alle vil deretter bli invitert til ny test etter ett, to, tre, fem, ti og tjue år.

Det er ingen kjente farer ved å delta i disse testene.

Dersom du underveis i prosjektet finner ut at du ikke ønsker å delta videre – så kan du trekke deg uten å oppgi noen spesiell grunn til dette.

Alle data som vi samler inn blir oppbevart på en måte som gjør at det er umulig for andre å kjenne igjen de som er med i prosjektet. Du kan når som helst be om å få se dine resultater eller kreve at de slettes. Prosjektet er gjennomgått av en etisk komité som har godkjent at denne studien er trygg å gjennomføre.

Prosjektet planlegges avsluttet i år 2028.

Dersom du har spørsmål underveis kan du ringe professor Lars Engebretsen 22117464 eller fysioterapeut Håvard Moksnes 23265640 eller havard.moksnes@nimi.no.

Med vennlig hilsen

Lars Engebretsen	Håvard Moksnes
Professor	Fysioterapeut og prosjektleder

Samtykkeerklæring
Jeg har lest og blitt forklart informasjonen på medfølgende informasjonsskriv om prosjektet, og sier meg villig i å delta i undersøkelsen.
Jeg har forstått at deltakelsen er frivillig.

________________ ______
Sted Dato

________________________ ________________________
Underskrift Underskrift av foresatt
(dersom pasienten er under 18 år)

Appendix V

Patient informed consent online activity survey

ULLEVÅL universitetssykehus

Ortopedisk Senter
FOU-enheten, NAR

Månedlig oppfølgingsundersøkelse ved bruk av Questback spørreskjema

I forbindelse med din deltagelse i prosjektet "Funksjonsvurdering av barn med fremre korsbåndsskade", ønsker vi å sende deg en internettbasert spørreundersøkelse. Du vil motta undersøkelsen en gang i måneden i ti år; totalt 120 ganger.

Undersøkelsen blir sendt deg per e-post, og vil ta 2-3 minutter å besvare. Spørsmålene omhandler ditt aktivitetsnivå, kneets funksjon, samt spørsmål om hvorvidt det er fastsatt noen dato for eventuell operasjon av kneet. Undersøkelsen er kryptert, hvilket innebærer at ingen opplysninger vil være tilgjengelig for andre enn deg og oss som mottar dine svar.

For øvrig henvises det til samtykke du allerede har signert for formål og varighet av studien, samt dine rettigheter.

Vi vil gjerne at du på denne følgende linjen skiver inn e-post adresse som du tillater at vi kan benytte;____

Samtykkeerklæring: Jeg er villig til å delta i Questback-spørreskjema undersøkelsen	**Jeg bekrefter å ha gitt tilstrekkelig informasjon om Questback-spørreskjemaundersøkelsen:**
--- (Signert av prosjektdeltaker, dato) --- (Signert av foresatt, dato)	-- (Prosjektleder/prosjektmedarbeider, dato)

Ullevål universitetssykehus HF
0407 OSLO

Telefon: 22 11 74 64
Telefaks: 23 01 52 70
Besøksadresse: Kirkeveien 166
Bankgiro: 1644 06 05897
Foretaksnr.: 983 971 784

HELSE ØST

Appendix VI
Knee injury and Osteoarthritis Outcome Score

Bergen 15 May 2007

Norwegian KOOS, version LK1.0

The KOOS form was translated into Norwegian in the following way.

Translation done at The Norwegian Arthroplasty Register (NAR)

- KOOS was translated from the Swedish version by two researchers in orthopedics. The choice of using the Swedish version was based on the assumption that cultural differences between the two neighbour countries would be minimal due to similarities in language and lifestyle.
- The translation was checked by two bilingual orthopedic surgeons (Swedes with permanent address in Norway).
- The form was tested on knee arthroplasty patients to clarify potential misinterpretations.

Translation done by The Norwegian National Knee Ligament Registry (NKLR)

- A translation from the English version was done by an orthopedic researcher.
- Another translation from the Swedish version was done by a former researcher at the Norwegian School of Sport Sciences who is bilingual in Norwegian and Swedish.
- The translations were compared, and due to only minor differences in the use of synonyms, the NKLR chose a wording as close to the Swedish translation as possible. This is due to the fact that the creators of the KOOS form are Swedish, even though the first form was made in English.

Finally the NAR and the NKLR versions were compared, minor adjustments were done, and the translators agreed upon a common translation. The final validated Norwegian version is named KOOS Norwegian version LK1.0

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KOOS – SPØRRESKJEMA FOR KNEPASIENTER

DATO: _____/_____/_____ FØDELSENR (11 siffer): ___________________

NAVN: ____

Veiledning: Dette spørreskjemaet inneholder spørsmål om hvordan du opplever kneet ditt. Informasjonen vil hjelpe oss til å følge med i hvordan du har det og fungerer i ditt daglige liv. Besvar spørsmålene ved å krysse av for det alternativ du synes passer best for deg (kun ett kryss ved hvert spørsmål). Hvis du er usikker, kryss likevel av for det alternativet som føles mest riktig.

Symptom

Tenk på de **symptomene** du har hatt fra kneet ditt den **siste uken** når du besvarer disse spørsmålene**.**

S1. Har kneet vært hovent?

Aldri	Sjelden	I blant	Ofte	Alltid
☐	☐	☐	☐	☐

S2. Har du følt knirking, hørt klikking eller andre lyder fra kneet?

Aldri	Sjelden	I blant	Ofte	Alltid
☐	☐	☐	☐	☐

S3. Har kneet haket seg opp eller låst seg?

Aldri	Sjelden	I blant	Ofte	Alltid
☐	☐	☐	☐	☐

S4. Har du kunnet rette kneet helt ut?

Alltid	Ofte	Iblant	Sjelden	Aldri
☐	☐	☐	☐	☐

S5. Har du kunnet bøye kneet helt?

Alltid	Ofte	I blant	Sjelden	Aldri
☐	☐	☐	☐	☐

Stivhet

De neste spørsmålene handler om **leddstivhet**. Leddstivhet innebærer vanskeligheter med å komme i gang eller økt motstand når du bøyer eller strekker kneet. Marker graden av leddstivhet du har opplevd i kneet ditt den **siste uken**.

S6. Hvor stivt er kneet ditt når du nettopp har våknet om morgenen?

Ikke noe	Litt	Moderat	Betydelig	Ekstremt
☐	☐	☐	☐	☐

S7. Hvor stivt er kneet ditt **senere på dagen** etter å ha sittet, ligget eller hvilt?

Ikke noe	Litt	Moderat	Betydelig	Ekstremt
☐	☐	☐	☐	☐

Smerte

P1. Hvor ofte har du vondt i kneet?

Aldri	Månedlig	Ukentlig	Daglig	Hele tiden
☐	☐	☐	☐	☐

Hvilken grad av smerte har du hatt i kneet ditt den **siste uken** ved følgende aktiviteter?

P2. Snu/vende på belastet kne

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P3. Rette kneet helt ut

Ingen	Lett	Moderate	Betydelig	Svært stor
☐	☐	☐	☐	☐

P4. Bøye kneet helt

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P5. Gå på flatt underlag

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P6. Gå opp eller ned trapper

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P7. Om natten i sengen (smerter som forstyrrer søvnen)

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P8. Sittende eller liggende

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

P9. Stående

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

Funksjon I hverdagen

De neste spørsmål handler om din fysiske funksjon. **Angi graden av vanskeligheter du har opplevd den siste uken ved følgende aktiviteter på grunn av dine kneproblemer**.

A1. Gå ned trapper

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A2. Gå opp trapper

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

Angi graden av **vanskeligheter** du har opplevd ved hver aktivitet den **siste uken**.

A3. Reise deg fra sittende stilling

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A4. Stå stille

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A5. Bøye deg, f.eks. for å plukke opp en gjenstand fra gulvet

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A6. Gå på flatt underlag

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A7. Gå inn/ut av bil

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A8. Handle/gjøre innkjøp

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A9. Ta på sokker/strømper

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A10. Stå opp fra sengen

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A11. Ta av sokker/strømper

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A12. Ligge i sengen (snu deg, holde kneet i samme stilling i lengre tid)

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A13. Gå inn og ut av badekar/dusj

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A14. Sitte

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A15. Sette deg og reise deg fra toalettet

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

Angi graden av **vanskeligheter** du har opplevd ved hver aktivitet den **siste uken.**

A16. Gjøre tungt husarbeid (måke snø, vaske gulv, støvsuge osv.)

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

A17. Gjøre lett husarbeid (lage mat, tørke støv osv.)

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

Funksjon, sport og fritid

De neste spørsmålene handler om din fysiske funksjon. Angi graden av vanskeligheter du har opplevd **den siste uken** ved følgende aktiviteter på grunn av dine kneproblemer.

SP1. Sitte på huk

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

SP2. Løpe

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

SP3. Hoppe

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

SP4. Snu/vende på belastet kne

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

SP5. Stå på kne

Ingen	Lett	Moderat	Betydelig	Svært stor
☐	☐	☐	☐	☐

Livskvalitet

Q1. Hvor ofte gjør ditt kneproblem seg bemerket?

Aldri	Månedlig	Ukentlig	Daglig	Alltid
☐	☐	☐	☐	☐

Q2. Har du forandret levesett for å unngå å overbelaste kneet?

Ingenting	Noe	Moderat	Betydelig	Fullstendig
☐	☐	☐	☐	☐

Q3. I hvor stor grad kan du stole på kneet ditt?

Fullstendigl	I stor grad	Moderat	Til en viss grad	Ikke i det hele tatt
☐	☐	☐	☐	☐

Q4. Generelt sett, hvor store problemer har du med kneet ditt?

Ingen	Lette	Moderate	Betydelige	Svært store
☐	☐	☐	☐	☐

Takk for at du tok deg tid og besvarte samtlige spørsmål!

Until otherwise is decided it is recommended that future revisions of the Norwegian KOOS form are done by The Norwegian Arthroplasty Register. If someone find that any questions from the questionnaire is difficult to understand or difficult to answer, we will be thankful to receive information on this.

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Appendix VII

International Knee Documentation Committee Subjective Knee Form

2000 IKDC Kne evaluerings skjema

Navn:___________________________________ Dato:_________________Skadedato:_______________

SYMPTOMER:

Grader symptomene på det høyeste aktivitetsnivå som du tror du kan fungere uten betydelige symptomer, selv om du ikke egentlig driver med aktiviteter på dette nivået.

1. Hva er det høyeste aktivitetsnivå du tror du kan drive med uten betydelige knesmerter?

- ❑ Veldig harde aktiviteter som hopping og vendinger som ved basket eller fotball
- ❑ Harde aktiviteter som tungt fysisk arbeid, ski eller tennis
- ❑ Moderate aktiviteter som moderat fysisk arbeid, løping eller jogging
- ❑ Lette aktiviteter som gange, husarbeid eller hagearbeid
- ❑ Umulig å foreta noen av de overnevnte aktiviteter på grunn av knesmerter

2. I løpet av de <u>siste 4 uker</u> (eller siden kneskaden); hvor ofte har du hatt smerter (sett ring rundt)?

Aldri 0 1 2 3 4 5 6 7 8 9 10 Alltid

3. Hvis du har smerter; hvor intense er de (sett ring rundt)?

Ingen smerte 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige smerte

4. I løpet av de <u>siste 4 uker</u> (eller siden kneskaden); hvor <u>stivt</u> eller <u>hovent</u> har kneet ditt vært?

- ❑ Ikke i det hele tatt
- ❑ Litt
- ❑ Moderat
- ❑ Veldig
- ❑ Ekstremt

5. Hva er det høyeste aktivitetsnivå du tror du kan drive med uten betydelig <u>hevelse</u> i kneet?

- ❑ Veldig harde aktiviteter som hopping og vendinger som ved basket eller fotball
- ❑ Harde aktiviteter som tungt fysisk arbeid, ski eller tennis
- ❑ Moderate aktiviteter som moderat fysisk arbeid, løping eller jogging
- ❑ Lette aktiviteter som gange, husarbeid eller hagearbeid
- ❑ Umulig å foreta noen av de overnevnte aktiviteter på grunn av hevelse

6. I løpet av de <u>siste 4 uker</u>, (eller siden kneskaden); har kneet låst seg (sett ring rundt)?

JA **NEI**

7. Hva er det høyeste aktivitetsnivå du tror du kan drive med uten betydelig <u>svikt</u> av kneet?

- ❑ Veldig harde aktiviteter som hopping og vendinger som ved basket eller fotball
- ❑ Harde aktiviteter som tungt fysisk arbeid, ski eller tennis
- ❑ Moderate aktiviteter som moderat fysisk arbeid, løping eller jogging
- ❑ Lette aktiviteter som gange, husarbeid eller hagearbeid
- ❑ Umulig å foreta noen av de overnevnte aktiviteter på grunn av svikt av kneet

IDRETTSAKTIVITETER:

8. Hva er det høyeste aktivitetsnivå du vanligvis kan delta i (nå)?

- ❑ Veldig harde aktiviteter som hopping og vendinger som ved basket eller fotball
- ❑ Harde aktiviteter som tungt fysisk arbeid, ski eller tennis
- ❑ Moderate aktiviteter som moderat fysisk arbeid, løping eller jogging
- ❑ Lette aktiviteter som gange, husarbeid eller hagearbeid
- ❑ Umulig å foreta noen av de overnevnte aktiviteter på grunn av kneet

9. Hvordan påvirker kneet din evne til å (sett kryss):

		Ikke vanskelig i det hele tatt	Litt vanskelig	Moderat vanskelig	Ekstremt vanskelig	Kan ikke i det hele tatt
a	Gå opp trapper					
b	Gå ned trapper					
c	Knele/ gå ned på kne					
d	Gå ned på huk/ gjøre knebøy					
e	Sitte med bøyd kne					
f	Reise deg opp fra stol					
g	Løpe rett frem					
h	Hinke på ditt skadede ben					
i	Starte og stoppe raskt					

FUNKSJON:

Hvordan vil du gradere din knefunksjon på en skala fra 0 til 10 der 10 er normal, utmerket funksjon og 0 er at du ikke kan gjøre noen av dine daglige aktiviteter som også kan inkludere idrett?

10. FUNKSJON FØR KNESKADEN:

Kan ikke gjøre daglige aktiviteter 0 1 2 3 4 5 6 7 8 9 10 Ingen begrensninger i daglige aktiviteter

NÅVÆRENDE KNEFUNKSJON:

Kan ikke gjøre daglige aktiviteter 0 1 2 3 4 5 6 7 8 9 10 Ingen begrensninger i daglige aktiviteter

(Original artikkel: Irrgang et al. Development and Validation of the International Knee Documentation Committee Subjective Knee Form. The American Journal of Sports Medicine 2001. vol. 29 no.5 pp. 600-613)
Oversatt av NAR- Ortopedisk senter, UUS, Oslo; 2005, til og med trinn IV etter retningslinjer utarbeidet av:
Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality-of-life measures: literature review and proposed guidelines. J Clin. Epidemiol 1993. vol. 46 pp. 1417-32.

Appendix VIII
Knee Outcome Survey Activities of Daily Living Scale and Visual Analogue Scale

Vurdering av kneets tilstand (KOS)
Gradering av daglige aktiviteter

***Navn:*__________________________________ *Dato:*________________*Skadedato:*______________**

Instruksjoner:
*Det følgende spørreskjema er laget for å kartlegge symptomene og begrensningene du opplever ved daglige aktiviteter på grunn av din kneskade. Vennligst besvar hvert spørsmål ved å **krysse av for det utsagnet som best beskriver deg i løpet av de 1 til 2 siste dagene.** For hvert spørsmål er det mulig at flere utsagn kan beskrive din funksjon, men vi ønsker at du bare krysser av for det utsagnet som **best** beskriver deg i dine daglige aktiviteter*

Symptomer

1. I hvilken grad påvirker hvert av de følgende symptomer nivået på din daglige aktivitet? (Kryss av for ett svar på hver linje)

	Jeg har aldri symptomet	**Jeg har symptomet, men det påvirker ikke min aktivitet**	**Symptomet påvirker min daglige aktivitet litt**	**Symptomet påvirker min aktivitet moderat**	**Symptomet påvirker min aktivitet svært mye**	**Symptomet hindrer meg fra all daglig aktivitet**
Smerte						
Stivhet						
Hevelse						
Svakhet						
Halting						
Glipp, svikt eller kollaps av kneet						
Score	**5**	**4**	**3**	**2**	**1**	**0**

Vurdering av kneets tilstand (KOS)
Gradering av daglige aktiviteter
Side II

Funksjonelle begrensninger ved daglig aktivitet

2. Hvordan påvirker kneet din evne til å… (kryss av for ett svar på hver linje)

	Ingen problemer med aktiviteten	Aktiviteten er ubetydelig vanskelig	Aktiviteten er litt vanskelig	Aktiviteten er ganske vanskelig	Aktiviteten er veldig vanskelig	Kan ikke gjøre aktiviteten
Gå?						
Gå opp trapper?						
Gå ned trapper?						
Stå?						
Knele (gå ned på kne)?						
Gå ned på huk/ Gjøre knebøy?						
Sitte med bøyd kne?						
Reise deg opp fra stol?						
Score	5	4	3	2	1	0

3. Hvordan vil du gradere din kne funksjon i dine vanlige daglige aktiviteter på en skala fra veldig dårlig (0) til normal (100)?
Merk av en loddrett strek på linjen.

0 ———————————————— 100

Veldig dårlig knefunksjon — Normal knefunksjon

(Originalartikkel: Irrgang et al. "Development of a Patient-Reported Measure of Function of the Knee" *<u>American Journal of Sports Medicine</u> 1998. vol. 80 pp. 1132-1145)*
Oversatt av NAR- Ortopedisk senter, UUS, Oslo; 2005, til og med trinn IV etter retningslinjer utarbeidet av: Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality-of-life measures: literature review and proposed guidelines. J Clin Epidemiol 1993. vol. 46 pp. 1417-32.

Appendix IX
Checklist Magnetic Resonance Imaging

Checklist MRI Children ACL

ID number:

Side injured/uninjured:

Examination date:

ACL	☐ Normal	☐ Partial	☐ Total		
PCL	☐ Normal	☐ Partial	☐ Total		
Medial meniscus	☐ Normal	☐ Horisontal	☐ Longitudinal	☐ Radial	☐ Høysign uten ruptur
Lateral meniscus	☐ Normal	☐ Horisontal	☐ Longitudinal	☐ Radial	☐ Høysign uten ruptur

Cartilage - localisation, size (edge healthy cartilage: sagital x coronal) and grading

Medial femurcondyle	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___
Lateral femurcondyle	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___
Medial tibiacondyle	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___
Lateral tibiacondyle	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___
Patella	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___
Trochlea	☐ Normal	☐ 1	☐ 2	☐ 3	☐ 4	Size: _____	Bonebruise___

Growth plates - open or closed

Femur	☐ Open	☐ Closed
Tibia	☐ Open	☐ Closed

Comments on bonebruise:

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